

Combined steroid and statin treatment could reduce 'accelerated aging' in preterm babies

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Potentially lifesaving steroids commonly given to preterm babies also increase the risk of long-term cardiovascular problems, but a new study in rats has found that if given in conjunction with statins, their positive

effects remain while the potential negative side effects are "weeded out."

University of Cambridge scientists gave newborn rats, which are naturally born prematurely, combined [glucocorticoid](#) steroids and statin therapy. The results, published today in *Hypertension*, show that the combined treatment led to the elimination of negative effects of steroids on the cardiovascular system while retaining their positive effects on the developing respiratory system.

Preterm birth (before 37 weeks) is one of the greatest killers in perinatal medicine today. One in ten babies is born [preterm](#) in high-income countries; this can increase to almost 40% in low- and middle-income countries.

Preterm babies are extremely vulnerable because they miss out on a crucial final developmental stage in which the [hormone cortisol](#) is produced and released exponentially into the unborn baby's blood. Cortisol is vital to the maturation of organs and systems that are needed to keep the baby alive once born.

For example, in the lungs, cortisol ensures that they become more elastic. This allows the lungs to expand so the baby can take its first breath. Without cortisol, the newborn lungs would be too stiff, which leads to respiratory distress syndrome (RDS) and could be fatal.

The established clinical treatment for any pregnancy threatened with [preterm birth](#) is glucocorticoid therapy, given via the mother before the baby is born and/or directly to the baby after birth. These synthetic steroids mimic the natural cortisol by speeding up the development of organs—including the lungs—which means the preterm baby is much more likely to survive.

Lead author Professor Dino Giussani from the Department of Physiology, Development and Neuroscience at the University of Cambridge said, "Glucocorticoids are a clear lifesaver, but the problem with steroids is that they speed up the maturation of all organs. For the baby's lungs this is beneficial, but for the heart and circulation system it can be damaging—it resembles accelerated aging."

A previous clinical study by Professor Paul Leeson's laboratory at Oxford University had found that people who had been exposed to glucocorticoid therapy as unborn babies, via their mothers, showed measures of cardiovascular health typical of people a decade older.

Cambridge researcher Dr. Andrew Kane, involved in the rat study, thought that this accelerated aging might result from steroids causing oxidative stress. Steroids lead to an imbalance of molecules known as [free radicals](#), which result in a reduction in nitric oxide. Nitric oxide is extremely beneficial to the cardiovascular system—it increases blood flow and has anti-oxidant and anti-inflammatory properties.

To test whether a lack of nitric oxide could be the origin of the adverse negative cardiovascular side effects associated with glucocorticoid therapy, the researchers combined the steroid treatment with statins, which are widely used to lower cholesterol and are known to increase [nitric oxide](#).

Researchers gave the synthetic steroid dexamethasone, combined with the [statin](#) pravastatin, to rat pups. There were three other groups—one receiving dexamethasone alone, one receiving pravastatin alone and a control group that received saline. Measures of respiratory and cardiovascular function were then taken when the rats had grown to "childhood."

The Cambridge scientists found that steroids produced adverse effects

on heart and blood vessels, and molecular indices associated with [cardiovascular problems](#). But if statins were given at the same time, the rats were protected from these effects. Crucially, the statins did not affect any of the beneficial effects of steroids on the respiratory system.

"Our discovery suggests that combined glucocorticoid and [statin therapy](#) may be safer than glucocorticoids alone for the treatment of [preterm babies](#)," said Professor Giussani.

"We're not saying to stop using glucocorticoids, as they are clearly a life-saving treatment. We're saying that to improve this therapy—to fine tune it—we could combine it with statins. This gives us the best of both worlds—we can maintain the benefits of steroids on the developing lungs, but 'weed out' their adverse side effects on the developing heart and circulation, thereby making therapy much safer for the treatment of preterm birth."

The team plan to replicate the experiment in sheep, which have a similar physiology to humans, before conducting human clinical trials.

More information: Combined statin and glucocorticoid therapy for the safer treatment of preterm birth., *Hypertension* (2023). [DOI: 10.1161/HYPERTENSIONAHA.122.19647](#)

Provided by University of Cambridge

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