

Some antibiotics prescribed during pregnancy linked with birth defects

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Children of mothers prescribed macrolide antibiotics during early pregnancy are at an increased risk of major birth defects, particularly heart defects, compared with children of mothers prescribed penicillin,

finds a study published by *The BMJ* today.

The researchers say these findings show that macrolides should be used with caution during pregnancy and if feasible alternative antibiotics should be prescribed until further research is available.

Macrolide antibiotics (including erythromycin, clarithromycin, and azithromycin) are—widely used to treat common bacterial infections. They are often used as alternatives for patients with [penicillin](#) allergy.

Previous studies suggest evidence of rare but serious adverse outcomes of macrolide use, especially for unborn babies. The adverse outcomes might be associated with the pro-arrhythmic (heart rhythm problems) potential of macrolides. Policy advice about macrolide use in pregnancy varies.

To address these uncertainties, a team of researchers based at UCL set out to assess the association between [macrolide antibiotics](#) prescribed during pregnancy and major [malformations](#) as well as four [neurodevelopmental disorders](#) ([cerebral palsy](#), epilepsy, ADHD, and [autism spectrum disorder](#)) in [children](#).

Researchers analysed data from 104,605 children born in the UK from 1990 to 2016 with a median follow up of 5.8 years after birth. A further 82,314 children whose mothers were prescribed macrolides or penicillins before pregnancy, and 53,735 children who were siblings of children in the study group acted as negative control cohorts.

Major malformations were recorded in 186 of 8,632 children whose mothers were prescribed macrolides at any point during pregnancy and 1,666 of 95,973 children whose mothers were prescribed penicillins during pregnancy.

After taking account of potentially influential factors, the researchers found macrolide prescribing during the first three months (the first trimester) of pregnancy was associated with an increased risk of any major malformation compared with penicillin (28 v 18 per 1000) and specifically cardiovascular malformations (11 v 7 per 1000).

The increased risks were not observed in children of mothers whose macrolides were prescribed in later pregnancy (during the second to third trimester).

Macrolide prescribing in any trimester was also associated with a slightly increased risk of genital malformations (5 v 3 per 1000). No statistically significant associations were found for other system specific malformations or for any of the four neurodevelopmental disorders.

This is an observational study, so can't establish cause, and the researchers point to some limitations, such as being unable to examine treatment exposure during known critical periods for specific malformations and neurodevelopmental disorders.

However, results were largely unchanged after further analyses, suggesting that the findings withstand scrutiny.

If the associations are shown to be causal, the researchers estimate that an additional 4 children with cardiovascular malformations would occur for every 1000 children exposed to macrolides instead of penicillins in the first trimester.

"These findings show that macrolides should be used with caution during [pregnancy](#) and if feasible alternative [antibiotics](#) should be prescribed until further research is available," they conclude.

More information: Associations between macrolide antibiotics

prescribing during pregnancy and adverse child outcomes in the UK:
population based cohort study, *BMJ* (2020).

www.bmj.com/content/368/bmj.m331

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