

Prenatal exposure to anti-nausea drug in '60s, '70s tied to increased risk of colorectal cancer

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Prenatal exposure to an anti-nausea drug commonly used in the 1960s and 1970s has been shown to increase risk of colorectal cancer in adult



offspring, according to a study by researchers at UTHealth Houston.

The study, led by Caitlin Murphy, Ph.D., MPH, associate professor at UTHealth Houston School of Public Health, was published today in *JNCI Cancer Spectrum*.

Incidence rates of colorectal cancer are increasing among adults born in and after the 1960s, which Murphy said implicates pregnancy-related exposures introduced at that time as <u>risk factors</u>. Dicyclomine—used to treat spasms caused by irritable bowel syndrome—was initially included in Bendectin, a drug prescribed during pregnancy in the 1960s to prevent nausea and vomiting.

"Our findings suggest that events in the earliest periods of life—including the womb—can affect risk of cancer many decades later," said Murphy, who was first author on the study. "As many as 25% of <u>pregnant women</u> received Bendectin through the mid-1970s, and there may be long-lasting consequences for <u>offspring</u> that continue today."

The researchers analyzed data from Child Health and Development Studies, a multi-generational cohort that enrolled more than 14,500 pregnant women (who bore 18,751 offspring) in Oakland, California, between 1959 and 1967. Through <u>medical records</u>, they determined that about 5% of offspring, or 1,014 children, were exposed in utero to Bendectin.

Per 10,000 offspring, incidence rates of colorectal cancer were three times as high in those exposed to Bendectin compared to offspring not exposed.

Murphy believes the higher risk of colorectal cancer in offspring exposed to the drug may be driven by dicyclomine, which was contained



in the three-part formulation of Bendectin used during the 1960s. It is suspected that dicyclomine may directly target the developing gastrointestinal tract of the fetus, she said, adding that some studies suggest infants born to women who received Bendectin during pregnancy are more likely to have gastrointestinal birth defects.

After reports of birth defects and concerns in the wake of the thalidomide tragedy, the manufacturer removed dicyclomine from the drug's formula in 1976. Pregnant women in the late 1950s and early 1960s were prescribed a drug containing thalidomide to relieve morning sickness, which led to a scandal when more than 10,000 offspring were born with a range of severe deformities.

Still, Murphy said experimental studies are needed to clarify these findings and identify mechanisms of risk.

"Dicyclomine is still used in <u>clinical practice</u> to treat <u>irritable bowel</u> <u>syndrome</u>. It is designated as Pregnancy Category B by the U.S. Food and Drug Administration, meaning there are not adequate studies of pregnant women to determine risk to the fetus," she said. "Medications prescribed to pregnant women may contribute to higher rates of cancer among offspring exposed in the womb."

More information: Caitlin C Murphy et al, In utero exposure to antiemetic and risk of adult-onset colorectal cancer, *JNCI Cancer Spectrum* (2023). <u>DOI: 10.1093/jncics/pkad021</u>

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