

**Francella A et al.** The safety of 6-mercaptopurine for childbearing patients with inflammatory bowel disease: a retrospective cohort study. *Gastroenterology* 124, 9-17, 2003

Type of study	Retrospective cohort
Where	New York
When	From the late 1950-1997
Characteristics of the cohort	Newborns whose parents with inflammatory bowel disease (IBD) were exposed and not exposed to studied drug at the time of conception and during pregnancy
Characteristics of the treated diseases	Ulcerative colitis (33%), Crohn's disease (67%)
Exposure definition	All pregnancies occurring after the diagnosis of IBD, except abortions, classified into 4 groups: - group A: pregnancies involving patients (male+female) treated with 6-MP, who stopped the drug before a conception - group B1: pregnancies involving patients (male+female) who were taking 6-MP at the time of conception - group B2: pregnancies involving female patients who continued taking 6-MP throughout the entire pregnancy Treatment with 6-MP: mean dose 70mg (25mg every other day-175mg daily); duration of therapy: 1 month-16 years
Ascertainment of drug exposure	- Patients contacted by telephone survey, questioned as to whether they had ever conceived (female) or had been responsible for a conception (male) after developing IBD. Detailed account of IBD diagnosis, current/past medications obtained - Verification of 6-MP exposure by review of each patient's individual medical records
Size of the studied cohort	485 patients received drug, 462 contacted, 155 had conceived at least 1 pregnancy after developing IBD (79 females, 76 males), 325 eligible pregnancies (171 females, 154 males): Exposed to the studied drug: 84 conceptions (40 women+44 men), 61 deliveries-group A; 61 conceptions (24 women+37 men), 48 deliveries-group B1; 15 conceptions (females), 14 deliveries-group B2 Unexposed reference group: 165 conceptions (92 women+73 men), 131 deliveries-group C
Exposed cohort	Newborns exposed to the studied drug
Control cohort	Pregnancies (male+female) that occurred before treatment with 6-MP (group C)
Malformations definition	Major/minor congenital birth defects: not indicated
Malformations ascertainment/pregnancy outcome	- Not indicated - The follow-up time to evaluate all childhood outcomes was variable, with the minimum of 18 months from birth
Prevalence of malformations among control offspring	4%
Analysis	Outcomes analyzed comparing pregnancies from men and women who had taken or were currently taking the studied drug to controls: - OR and 95% CI were estimated (according to gender of the affected parent, maternal smoke, maternal age at the conception, use of other medications, type of IBD), $X^2$ tests, including Fisher exact tests used for comparison - Clustered binary regression analyses to compare successful pregnancy outcome rates between all exposed and nonexposed conceptions used

Strengths	<ul style="list-style-type: none"> <li>- Exposure data information based on recorded data and patient recall</li> <li>- Information on reproductive end points, infections, neoplasia, other drugs use</li> </ul>
Weaknesses	<ul style="list-style-type: none"> <li>- The follow-up time to evaluate all childhood outcomes was variable</li> <li>- Not indicated if information on maternal drug use was available at the time of paediatrician's examination</li> <li>- No information on compliance, refused to participate, malformations definition/ascertainment</li> </ul>
Main results	<p>There was no statistical difference in conception failures, abortion secondary to a birth defect, major congenital malformations, neoplasia, or increased infections among male or female patients taking 6-MP compared with controls (RR 0.85, 95% CI 0.5-1.6, P=0.59). 6-MP use before or at conception or during pregnancy appears to be safe</p>