1. **Do preoperative narcotics increase the risk of postoperative complications in Crohn’s disease?**

The use of narcotic medications to treat pain has increased dramatically since 1996, leading to a worrisome “opioid epidemic” with nefarious societal side-effects. Crohn’s patients may require narcotics to treat pain, although these drugs have been associated with an increased risk of complications, including sepsis and death in studies using the TREAT registry. However the association does not prove causality, and often opioids are used as an indicator of severe or complicated disease course. The authors of this paper evaluated the association between preoperative narcotics and postoperative complications, using retrospective data from a single institution IBD database. The exposure to narcotics was determined using an electronic prescription system. A total of 1461 abdominal operations in 1331 CD patients were considered eligible for the study and of these, 18% received preoperative narcotics. Patients using narcotics were more likely to have penetrating disease, perianal disease, previous surgeries or be current smokers or ex-smokers. The risk of overall complications, surgical complications, thromboembolism, prolonged ileus, readmission and the length of hospital stay were all increased in narcotic users compared to non-users. On multivariate analysis, urgent surgery, preoperative narcotic use and increased operative bleeding were independently associated with an increased risk of postoperative morbidity. There were more deaths (1.1% vs. 0.2%) in the narcotic user group, but the causes of death could not be attributed to opioid use (sepsis and DIC).

**Comments:** Although this study showed an association between preoperative narcotic use and postoperative complications, including mortality in Crohn’s disease, it did not demonstrate causality. In fact, patients receiving opioids were older, had longer disease duration and were overall sicker both from the Crohn’s disease as well as the anesthesia (ASA score) standpoint. More than 3 times as many patients required perioperative transfusions in the narcotic group. There was also no assessment for a dose effect which would be expected if a causality relationship were true. Yet, these findings should serve as another warning regarding an increased risk of postoperative complications in patients who use narcotics at baseline. It remains to be determined if switching to non-narcotic analgesics in these patients can decrease the risk of overall and postoperative complications.


2. **Consensus statements for the management of IBD in pregnancy.**

IBD during pregnancy poses a challenging circumstance, in which the health of both the mother
and the offspring must be considered when selecting optimal therapy. Adequate management of IBD at conception and during pregnancy is crucial because active disease is the biggest risk factor for adverse pregnancy outcomes including: miscarriage, spontaneous abortion, prematurity and low birth weight. Recently the FDA has abandoned the letter risk classification of drugs during pregnancy because it was believed that it lead to misinterpretation. In this very important paper, an international consortium of IBD specialists and epidemiologists have developed a set of consensus guidelines for the management of IBD during pregnancy and postpartum, based on a detailed, critical review of the literature to date. Consensus was reached on 29 of the 30 recommendations considered. Among these, the most relevant are the following:

a. Preconception counseling and access to specialist care are paramount in optimizing disease management;

b. In general, women on 5-ASA, thiopurine, or anti-tumor necrosis factor (TNF) monotherapy for maintenance should continue therapy throughout pregnancy;

c. Discontinuation of anti-TNF therapy or switching from combination therapy to monotherapy may be considered in very select low-risk patients;

d. Women who have a mild to moderate disease flare while on optimized 5-ASA or thiopurine therapy should be managed with systemic corticosteroid or anti-TNF therapy, and those with a corticosteroid-resistant flare should start anti-TNF therapy;

e. Endoscopy or urgent surgery should not be delayed during pregnancy if indicated;

f. Decision regarding cesarean delivery should be based on obstetric considerations and not the diagnosis of IBD alone, with the exception of women with active perianal Crohn’s disease;

g. With the exception of methotrexate, the use of medications for IBD should not influence the decision to breast-feed and vice versa;

h. Live vaccinations are not recommended within the first 6 months of life in the offspring of women who were on anti-TNF therapy during pregnancy.

Comments: This paper is an invaluable resource for practitioners who aim to optimize their practice and educate their IBD patients about the best management options for IBD during pregnancy. In addition, Table 1 can be used as a handout in the office when addressing important aspects of IBD management in pregnancy including specific information about drug classes, individualized management of thiopurines and biologics, specific recommendations about C-section and breast feeding, etc. Figure 2 offers a practical algorithm for dealing with active disease in pregnancy. As expected, there is limited information about trafficking inhibitors. The central ideas in this paper are: active disease is the principal risk factor for adverse pregnancy outcomes or, what’s good for the mother is good for the baby; don’t stop something that works (unless there is a very good reason, such as is the case with methotrexate); a reassuring message about endoscopy and surgery in pregnancy. The part that was intentionally left out covers the use of radiological investigations in IBD which is reviewed separately in the gynecological literature (Obstet Gynecol. 2016 Feb;127(2).


3. **Will a statin a day keep the cancer away?**

Patients with UC and Crohn’s colitis have an increased risk of cancer. Chronic active inflammation
is believed to be a promoter of neoplasia through activation of cellular growth factors. Preventive strategies have therefore focused on optimal control of inflammation, although some drugs, such as 5-ASA compounds were presumed to have direct chemopreventive properties. Statins (cholesterol-lowering agents) have been inversely associated with the risk of colon cancer. In this study, investigators analyzed data from 11,001 patients with IBD receiving care at hospitals in the Greater Boston metropolitan area over a period of 12 years, of which almost 1,400 (12.5%) received one or more statin prescriptions. CRC cases in this cohort were identified from an administrative database. Patients receiving statins were more likely to be older, male, smokers with more medical comorbidities and more likely to have UC, but less likely to receive immunosuppressive therapy. Over a follow-up period of 9 years, 2% of statin users developed CRC compared with 3% of nonusers (age-adjusted odds ratio, 0.35; 95% confidence interval, 0.24-0.53). On multivariate analysis adjusted for multiple known risk factors for CRC, the negative association of statin use with CRC remained significant. (OR 0.42). Adjusting for the number of previous colonoscopies also did not seem to affect this association. The authors conclude that statin use may be inversely associated with the risk of CRC in IBD.

Comments: There is a biologically plausible explanation for this effect as statins are known to downregulate a number of pro-oncogenic proteins such as Ras and Rho through post-transcriptional modification. In addition, animal models have suggested that statins may induce apoptosis in the gut epithelium. Whether these results support this theory is a different matter. Statin and non-statin users in this cohort were quite heterogeneous with likely different propensity risk for colon cancer. Patients in the statin group were almost 25 years older at IBD “diagnosis” (i.e. first IBD contact) and were less than half as likely to use biologics. This suggests that their disease duration, extent and severity may have been substantially lower compared to non-users. There is no information on disease extent, previous colectomy (partial or total), 5-ASA and aspirin use, all of which are known to affect the risk of CRC. Finally, statin users may have had more effective screening and surveillance colonoscopies before and after their diagnosis of IBD (given the advanced age) compared to non-users in which diagnostic colonoscopies may have been more prevalent. Even if the effect were real, the absolute risk reduction is modest (1%), translating into a NNT of 100. While I agree that further prospective studies are warranted, it is difficult to imagine a scenario in which statins would be prescribed in IBD patients without a concomitant cholesterol-lowering indication.