

# Test Your Knowledge: Ten Questions on Inflammatory Bowel Disease

This quiz is related to the Perspective in the August issue of *PLoS Medicine* (DOI: 10.1371/journal.pmed.0020230).

Gavin Yamey

## Question 1. Roughly how many people in the United States have inflammatory bowel disease?

- About 1 million
- About 5 million
- About 10 million

## Question 2. Which of the following best reflects the evidence on the association between smoking and ulcerative colitis?

- There is good evidence that smokers are at increased risk of developing ulcerative colitis
- There is good evidence that there is no association between smoking and ulcerative colitis
- There is good evidence that smokers are at reduced risk of developing ulcerative colitis

## Question 3. Which of the following best reflects the evidence on the association between appendectomy and ulcerative colitis?

- There is good evidence that appendectomy is associated with a reduced incidence of ulcerative colitis
- There is good evidence that there is no association between appendectomy and ulcerative colitis
- There is good evidence that appendectomy is associated with an increased incidence of ulcerative colitis

## Question 4. Which of the following best reflects our knowledge on the incidence of inflammatory bowel disease in developing countries?

- The incidence is lower in developing countries than in developed countries, and there has been no increase in recent decades
- The incidence is higher in developing countries than in developed countries
- The incidence is lower in developing countries than in developed countries, but there is evidence of an increase in recent decades in developing countries that have undergone industrialization

## Question 5. Roughly what proportion of children with Crohn disease experience growth retardation if treatment cannot completely control the disease activity?

- 1%–5%
- 15%–40%
- 60%–90%

## Question 6. Based on randomized controlled trials, which one of the following treatments is best proven to *rapidly* induce remission in patients with Crohn disease?

- Glucocorticoids
- Azathioprine/6-mercaptopurine
- Low-dose oral cyclosporine

## Question 7. Roughly what percentage of patients that have been successfully induced into remission with glucocorticoids are still in remission 12 months later?

- Less than 5%
- 10%–15%
- 20%–40%

## Question 8. Based on the best evidence from randomized controlled trials, which one of the following treatments is best proven to maintain remission in Crohn disease?

- Corticosteroids
- Azathioprine
- Oral 5-aminosalicylic acid

## Question 9. Which one of the following treatments for active ulcerative colitis would be preferable in male patients who are concerned about fertility?

- 5-aminosalicylic acid
- Sulfasalazine
- Methotrexate

## Question 10. Which one of the following best reflects the evidence on the value of surveillance colonoscopy in patients with extensive ulcerative colitis?

- There is weak evidence, from case-control studies, that cancers tend to be detected at an earlier stage in patients who are undergoing surveillance and that these patients have a better chance for recovery

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Gavin Yamey is a senior editor at *PLoS Medicine*. E-mail: [gyamey@plos.org](mailto:gyamey@plos.org)

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- There is conclusive evidence that surveillance colonoscopy prolongs survival in patients with extensive ulcerative colitis
- There is no clinical evidence that surveillance has any value for patients with extensive ulcerative colitis

### Answer 1. About 1 million

About 1 million people in the US have Crohn disease or ulcerative colitis [1,2].

#### References

1. Crohns and Colitis Foundation of America (2005) About the epidemiology of IBD. New York: Crohns and Colitis Foundation of America. Available: <http://www.cffa.org/about/press/epidemiologyfacts>. Accessed 28 July 2005.
2. Loftus EV Jr (2004) Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 126: 1504–1517.

### Answer 2. There is good evidence that smokers are at reduced risk of developing ulcerative colitis

Since the first report in 1982 of an inverse association between smoking and ulcerative colitis [1], many subsequent studies have shown that the odds ratio for developing ulcerative colitis among current smokers is consistently less than one [2]. A meta-analysis in 1989 found that current smokers are 40% as likely as those who have never smoked to develop ulcerative colitis [3].

#### References

1. Harries AD, Baird A, Rhodes J (1982) Non-smoking: A feature of ulcerative colitis. *BMJ* 284: 706.
2. Loftus EV Jr (2004) Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 126: 1504–1517.
3. Calkins BM (1989) A meta-analysis of the role of smoking in inflammatory bowel disease. *Dig Dis Sci* 34: 1841–1854.

### Answer 3. There is good evidence that appendectomy is associated with a reduced incidence of ulcerative colitis

A meta-analysis of 17 case-control studies involving almost 3,600 cases and over 4,600 controls showed an overall odds ratio of 0.312 (95% confidence interval, 0.261–0.373;  $p < 0.001$ ) in favor of appendectomy [1]. Even in studies that used multivariate analysis to control for other important factors, such as cigarette smoking, the association between appendectomy and a reduced incidence of ulcerative colitis was still significant [2]. It is unclear whether the association is a causal one.

#### References

1. Koutroubakis IE, Vlachonikolis IG, Kouroumalis EA (2002) Role of appendicitis and appendectomy in the pathogenesis of ulcerative colitis: A critical review. *Inflamm Bowel Dis* 8: 277–286.
2. Loftus EV Jr (2004) Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 126: 1504–1517.

### Answer 4. The incidence is lower in developing countries than in developed countries, but there is evidence of an increase in recent decades in developing countries that have undergone industrialization

The incidence of inflammatory bowel disease is lower in developing countries than in developed countries, but there is evidence of an increase in recent decades in developing countries that have undergone industrialization [1,2].

#### References

1. Shanahan F (2002) Crohn's disease. *Lancet* 359: 62–69.
2. Loftus EV Jr (2004) Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 126: 1504–1517.

### Answer 5. 15%–40%

Roughly 15%–40% of children with uncontrolled Crohn disease have growth retardation [1,2].

#### References

1. Griffiths AM, Nguyen P, Smith C, MacMillan JH, Sherman PM (1993) Growth and clinical course of children with Crohn's disease. *Gut* 34: 939–943.
2. Newby E, Sawczenko A, Thomas A, Wilson D (2005) Interventions for growth failure in childhood Crohn's disease. *Cochrane Database Syst Rev* 2005: CD003873.

### Answer 6. Glucocorticoids

The controlled trials of the National Cooperative Crohn's Disease Study [1] and the European Cooperative Crohn's Disease Study [2] established that corticosteroids were effective for the induction of remission in Crohn disease for the duration of the studies (6–17 weeks) [3].

A systematic review of randomized placebo-controlled trials of azathioprine or 6-mercaptopurine (the active metabolite of azathioprine) in adult patients found that the odds ratio of a response to therapy compared with placebo in active Crohn disease was 2.36 (95% confidence interval, 1.57–3.53) [4], but induction of remission takes longer than with corticosteroids [4,5]. The clinical effect is reported to have a prolonged time to onset, with response rates only significantly increasing after 17 weeks of therapy [4,5].

A systematic review found that low-dose oral cyclosporine (5 mg/kg/day) is not effective for treating active Crohn disease [6].

#### References

1. Summers RW, Switz DM, Sessions JT Jr, Beckett JM, Best WR, et al. (1979) National Cooperative Crohn's Disease Study: Results of drug treatment. *Gastroenterology* 77: 847–869.
2. Malchow H, Ewe K, Brandes JW, Goebell H, Elms H, et al. (1984) European Cooperative Crohn's Disease Study (ECCDS): Results of drug treatment. *Gastroenterology* 86: 249–266.
3. Yang YX, Lichtenstein GR (2002) Corticosteroids in Crohn's disease. *Am J Gastroenterol* 97: 803–823.
4. Sandborn W, Sutherland L, Pearson D, May G, Modigliani R, et al. (2005) Azathioprine or 6-mercaptopurine for induction of remission in Crohn's disease. *Cochrane Database Syst Rev* 2005: CD000545.
5. Carter MJ, Lobo AJ (2001) Lack of effect of intravenous azathioprine on time to respond for steroid treated Crohn's disease. *Gut* 48: 295–296.
6. McDonald JWD, Feagan BG, Jewell D, Brynskov J, Stange EF, et al. (2005) Cyclosporine for induction of remission in Crohn's disease. *Cochrane Database Syst Rev* 2005: CD000297.

### Answer 7. 10%–15%

About 10% of patients that have been successfully induced into remission with glucocorticoids are still in remission 12 months later [1].

#### Reference

1. Candy S, Wright J, Gerber M, Adams G, Gerig M, et al. (1995) A controlled double blind study of azathioprine in the management of Crohn's disease. *Gut* 37: 674–678.

### Answer 8. Azathioprine

A systematic review of the effectiveness of azathioprine in maintaining remission of quiescent Crohn disease identified five randomized controlled trials [1]. The drug had a positive effect on maintaining remission (the odds ratio for maintenance of remission was 2.16 [95% confidence interval, 1.35–3.47], with a number needed to treat of seven).

A systematic review of the effectiveness of corticosteroids in maintaining remission of quiescent Crohn disease found that these drugs are not effective for maintaining remission [2].

A third systematic review found no evidence to suggest that oral 5-aminosalicylic acid preparations are superior to

placebo for the maintenance of medically induced remission in patients with Crohn disease [3].

#### References

1. Pearson DC, May GR, Fick G, Sutherland LR (2005) Azathioprine for maintenance of remission in Crohn's disease. *Cochrane Database Syst Rev* 2005: CD000067.
2. Steinhart AH, Ewe K, Griffiths AM, Modigliani R, Thomsen OO (2005) Corticosteroids for maintenance of remission in Crohn's disease. *Cochrane Database Syst Rev* 2005: CD000301.
3. Akobeng AK, Gardener E (2005) Oral 5-aminosalicylic acid for maintenance of medically-induced remission in Crohn's Disease. *Cochrane Database Syst Rev* 2005: CD003715.

#### Answer 9. 5-aminosalicylic acid

There are fewer side effects associated with 5-aminosalicylic acid than with sulfasalazine. In particular, male infertility is associated with sulfasalazine and not with 5-aminosalicylic acid, so 5-aminosalicylic acid may be preferred for patients concerned about fertility [1].

There have been case reports of reduced sperm count with the use of methotrexate [2,3], though this is reported as reversible [2,3].

#### References

1. Sutherland L, MacDonald JK (2005) Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochran Database Syst Rev* 2005: CD000543.
2. Sussman A, Leonard JM (1980) Psoriasis, methotrexate, and oligospermia. *Arch Dermatol* 116: 215–217.
3. Zubay Fife R (1993) Methotrexate use in juvenile rheumatoid arthritis. *Orthop Nurs* 12: 32–36.

#### Answer 10. There is weak evidence, from case-control studies, that cancers tend to be detected at an earlier stage in patients who are undergoing surveillance and that these patients have a better chance for recovery.

A systematic review found that while there is no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive ulcerative colitis, there is evidence that cancers tend to be detected at an earlier stage in patients who are undergoing surveillance, and these patients have a correspondingly better prognosis [1]. The review's authors noted that lead-time bias could contribute substantially to this apparent benefit.

#### References

1. Mpfu C, Watson AJ, Rhodes JM (2005) Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. *Cochran Database Syst Rev* 2005: CD000279.

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