



# THE UNIVERSITY *of* EDINBURGH

## Edinburgh Research Explorer

### Upper Gastrointestinal Involvement in Pediatric Crohn's Disease Reply

**Citation for published version:**

Van Limbergen, J, Wilson, DC, Russell, RK, Drummond, HE & Satsangi, J 2009, 'Upper Gastrointestinal Involvement in Pediatric Crohn's Disease Reply' *Gastroenterology*, vol 136, no. 7, pp. 2409-2410., 10.1053/j.gastro.2009.04.044

**Digital Object Identifier (DOI):**

[10.1053/j.gastro.2009.04.044](https://doi.org/10.1053/j.gastro.2009.04.044)

**Link:**

[Link to publication record in Edinburgh Research Explorer](#)

**Document Version:**

Publisher final version (usually the publisher pdf)

**Published In:**

Gastroenterology

**Publisher Rights Statement:**

© 2009 AGA Institute

**General rights**

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

**Take down policy**

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact [openaccess@ed.ac.uk](mailto:openaccess@ed.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.



2. IBD working group of the European Society for the Pediatric Gastroenterology HaN. Inflammatory bowel disease in children and adolescents: recommendations for diagnosis—the Porto criteria. *J Pediatr Gastroenterol Nutr* 2005;41:1–7.
3. Lennards-Jones JE. Classification of inflammatory bowel disease. *Scan J Gastroenterol* 1989;24(Suppl 170):2–6.
4. North American Society of Pediatric Gastroenterology HaN, Colitis Foundation of America, Bousvarous A, Antonioli DA, Colletti AB, et al. Differentiating ulcerative colitis from Crohn disease in children and young adults: report of a working group of the North American Society of Gastroenterology, Hepatology and Nutrition and the Crohn's and Colitis Foundation of America. *J Pediatr Gastroenterol Nutr* 2007;44:653–674.
5. Grill BB, Lang R, Markowitz R, et al. Delayed gastric emptying in children with Crohn's disease. *J Clin Gastroenterol* 1985;7:216–226.
6. Lenaerts C, Roy CC, Vaillancourt M, et al. High incidence of upper gastrointestinal tract in children with Crohn disease. *Pediatric* 1989;83:777–781.
7. Kugathasan S, Judd RH, Hoffman RG, et al. Epidemiologic and clinical characteristics of children with newly diagnosed inflammatory bowel disease in Wisconsin: a statewide population-based study. *J Pediatr* 2003;143:525–531.
8. Gupta N, Bostrom AG, Kirschner BS, et al. Gender differences in presentation and course of disease in pediatric patients with Crohn disease. *Pediatrics* 2007;120:e1418–e1425.

doi:10.1053/j.gastro.2008.12.077

**Reply.** In his comment on our recent paper describing the phenotype of childhood-onset inflammatory bowel disease (IBD), Dr Matary highlights several important issues pertaining to the investigation and classification of involvement of the upper gastrointestinal (GI) tract in pediatric Crohn's disease (CD).<sup>1,2</sup> To enable a comparison of the pediatric phenotype with adult-onset disease, we used the Montreal classification of IBD rather than a more detailed, anatomic classification of disease extent which we have previously used in the genotype-phenotype analysis of NOD2/CARD15 variants.<sup>3</sup> Our investigation protocol based on the ESPGHAN Porto-criteria, adhered to by the pediatric gastroenterologists at the 3 recruiting centers, states that biopsies are taken routinely from the upper GI tract during the investigation of pediatric IBD.<sup>4</sup> Involvement of any anatomic location was defined as either macroscopic, microscopic, or both. Macroscopically, the minimum criteria for involvement of a disease location were ulceration or the presence of an aphthous lesion. Erythema and/or edema did not suffice to score a site as affected by CD. Microscopically, non-specific inflammation or inflammatory changes that could be otherwise explained (eg, reflux esophagitis or *Helicobacter pylori* gastritis) were not classified as CD. Interobserver variability was addressed by the quality control of phenotypic data by a dedicated database manager (HED) after review of the case notes (including endoscopy, pathology, and radiology reports).

The application of the recent Montreal classification, which has addressed some of the difficulties of previous systems in classifying pediatric IBD (specifically the in-

volvement of the upper GI tract, which precluded classification of lower GI disease in the Vienna classification), makes comparisons with historical datasets troublesome.<sup>5,6</sup> In these older datasets, as for example that described in the study by Lenaerts et al,<sup>7</sup> the upper GI tract was typically not investigated in the absence of clear upper GI-related symptoms, as acknowledged in their manuscript. In the absence of clear upper GI symptoms, esophagogastroduodenoscopy is also rarely performed in the investigation of adult-onset CD.<sup>8</sup> However, involvement of the upper GI tract has been reported to be as high as 75% in prospective adult CD studies where esophagogastroduodenoscopy was routinely performed.<sup>9,10</sup> Furthermore, in the Montreal classification, jejunal disease is scored as upper GI disease (the L1 category is limited to ileal disease), which further compromises comparison with older classification systems, dividing the GI tract into the upper, small bowel, and colon.

Our finding that >60% of children affected by Crohn's disease display involvement of the upper GI tract is, therefore, comparable with contemporary prospective studies in adult onset CD and further highlights the importance of a comprehensive assessment of our pediatric CD patients.

JOHAN VAN LIMBERGEN

DAVID C. WILSON

Department of Pediatric Gastroenterology and Nutrition and

Royal Hospital for Sick Children Edinburgh, United Kingdom

Child Life and Health, University of Edinburgh  
Edinburgh, United Kingdom

RICHARD K. RUSSELL

Department of Pediatric Gastroenterology

Yorkhill Hospital

Glasgow, United Kingdom

HAZEL E. DRUMMOND

JACK SATSANGI

Gastrointestinal Unit

Molecular Medicine Centre

Western General Hospital

University of Edinburgh

Edinburgh, United Kingdom

1. El-Matary W. Upper gastrointestinal involvement in pediatric Crohn's disease. *Gastroenterology*. In press.
2. Van Limbergen J, Russell RK, Drummond HE, et al. Definition of phenotypic characteristics of childhood-onset inflammatory bowel disease. *Gastroenterology* 2008;135:1114–1122.
3. Russell RK, Drummond HE, Nimmo ER, et al. Genotype-phenotype analysis in childhood-onset Crohn's disease: NOD2/CARD15 variants consistently predict phenotypic characteristics of severe disease. *Inflamm Bowel Dis* 2005;11:955–964.
4. IBD Working Group of the European Society for Paediatric Gastroenterology HaN. Inflammatory bowel disease in children and adolescents: recommendations for diagnosis—the Porto criteria. *J Pediatr Gastroenterol Nutr* 2005;41:1–7.
5. Silverberg MS, Satsangi J, Ahmad T, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: Report of a Working Party of the 2005 Montreal

World Congress of Gastroenterology. *Can J Gastroenterol* 2005; 19:5A–36A.

6. Gupta N, Bostrom AG, Kirschner BS, et al. Gender differences in presentation and course of disease in pediatric patients with Crohn disease. *Pediatrics* 2007;120:e1418–e1425.
7. Lenaerts C, Roy CC, Vaillancourt M, et al. High incidence of upper gastrointestinal tract involvement in children with Crohn's disease. *Pediatrics* 1989;83:777–781.
8. Nikolaus S, Schreiber S. Diagnostics of inflammatory bowel disease. *Gastroenterology* 2007;133:1670–1689.
9. Hommes DW, van Deventer SJ. Endoscopy in inflammatory bowel diseases. *Gastroenterology* 2004;126:1561–1573.
10. Witte AMC, Veenendaal RA, van Hogezaand RA, et al. Crohn's Disease of the Upper gastrointestinal tract: the value of endoscopic examination. *Scand J Gastroenterol* 1998;33:100–105.

#### Conflicts of interest

The authors disclose no conflicts.

#### Funding

Johan Van Limbergen was funded by a Research Training Fellowship from Action Medical Research, The Gay-Ramsay-Steel-Maitland or Stafford Trust and the Hazel M. Wood Charitable Trust. Jack Satsangi was the holder of by a Wellcome Trust Programme Grant (072789/Z/03/Z). David C. Wilson is the holder of a Medical Research Council Project Grant (G0800675).

Financial assistance was also provided by Schering-Plough and the GI/Nutrition Research Fund, Child Life and Health, University of Edinburgh.

doi:10.1053/j.gastro.2009.04.044

In the January 2009 issue of *GASTROENTEROLOGY*, the Comment From the Editor described 8 cohorts of patients with acute Hepatitis C in North America in an effort to heighten awareness of this interesting patient population. The following letters highlight additional unique and valuable acute hepatitis C cohorts in North America and further emphasize the important window of opportunity to identify at-risk populations within correctional facilities. Collectively, these cohorts provide important opportunities to better understand the epidemiology, natural history, and effective therapeutic approaches of acute hepatitis C in North America, as well as the early pathogenetic mechanisms.

## Acute Hepatitis C Infection in Correctional Settings

Dear Sir:

We greatly appreciated the recent spotlight on the important epidemiologic, immunologic, and virologic research that is ongoing in US cohorts of acute hepatitis C infection.<sup>1</sup> We would like to take this opportunity to highlight an additional aspect of acute hepatitis C that is evidenced in our work within the Massachusetts correctional system, where we have initiated screening programs for acute hepatitis C virus (HCV) infection during the medical intake examination for recently incarcerated inmates. More than 3200 inmates have been screened with a short questionnaire eliciting information regarding high-risk behaviors. Through the help of medical providers based in the correctional system, we have identified >140 subjects at high risk of infection; surprisingly, 37 cases of acute HCV infection were subsequently diagnosed over a 15-month period (manuscript in prep-

aration). These results demonstrate that, beyond the well-known epidemic of chronic HCV in the correctional system, there is also a high rate of acute HCV infection, mainly among recently incarcerated new drug users.<sup>2</sup>

The Centers for Disease Control and Prevention mandated in 2003 that primary and secondary HCV prevention efforts should be focused on injection drug users and specifically cited prison facilities as an ideal setting for such efforts.<sup>3</sup> However, the feasibility and the acceptability of such interventions were unknown. Since 2006, we have found widespread acceptance of our interventions, including HIV testing and immunizations against hepatitis A and B infection. We are examining the utility of new algorithms of expanded diagnostic criteria for acute HCV infection in new-onset injection drug users, who often have no prior record of serologic testing. We have also shown that treatment of acute HCV infection in the prisons is feasible, safe, and effective. As noted in our pilot project,<sup>4</sup> we have found that the burden of most new HCV infections is occurring in Caucasian subjects, although there is wide representation of Hispanics and blacks within our prison population. Furthermore, study of these interesting trends is being planned.

Despite some exemplary exceptions,<sup>1</sup> the diagnosis and treatment of acute HCV in injection drugs users has been generally low. However, our concentrated efforts within the structured environment of the correctional setting demonstrate that this avenue of intervention has high yield among a largely underserved patient population. Because more than half of US inmates are incarcerated owing to new drug use offenses, there is indeed a “window of opportunity” to make a difference.<sup>5</sup>

**BARBARA MCGOVERN**

Associate Professor  
Tufts University School of Medicine  
Lemuel Shattuck Hospital  
Jamaica Plain, Massachusetts

**ARTHUR KIM**

Clinical Instructor in Medicine  
Harvard Medical School  
Massachusetts General Hospital  
Boston, Massachusetts

**GEORG LAUER**

Harvard Medical School  
Massachusetts General Hospital  
Boston, Massachusetts

1. Cox A, Page K, Bruneau J, et al. Rare birds in North America: acute hepatitis C cohorts. *Gastroenterology* 2009;136:26–39.
2. Baillargeon J, Wu H, Kelley MJ. Hepatitis C seroprevalence among newly incarcerated inmates in the Texas correctional system. *Public Health* 2003;117:43–48.
3. Weinbaum C, Lyerla R, Margolis H. Prevention and control of infections with hepatitis viruses in correctional settings. *MMWR Recomm Rep* 2003;52:1–36.
4. McGovern B, Wurcel A, Kim A, et al. Acute hepatitis C virus infection in incarcerated injection drug users. *Clin Infect Dis* 2006; 42:1663–1670.