a Patient-reported Experience and Outcome Measures in Pediatric Bowel Management'' (1,2). They raise 2 important points which warrant further discussion, including the age range used to develop the survey and the potential for complex psychosocial issues in children with constipation.

The first point was that our survey does not elicit age-specific concerns of patients because it was generated using a group of patients with a wide age range (2.8–23.6 years of age) that may require different treatments. We agree that the treatments included in bowel management and the perception of these treatments may vary based on the age of the child. Furthermore, we agree that a survey to assess the patient's perception of their bowel management regimen would likely benefit from age-specific tailoring of the questions. The goal of this survey, however, was to assess the burden of therapy as perceived by the caregivers to reflect the impact of the patient's bowel management regimen on the entire family unit. To that end, each question was designed, developed, and validated in a cohort with a wide age range to allow the survey to be used independent of specific treatments or patient age.

The second point was that constipation in children can involve complex psychosocial issues which are not being assessed by our survey. We concur with the authors that constipation in children can have both significant psychosocial causes and implications. We also are advocates for a patient-centered approach to treatment with inclusion of the child in the discussion and treatment decision making. However, the purpose of our survey is to assess the impact of the bowel management treatments on the family unit and not to assess the psychosocial status of the child before, during, or after treatments.

We believe that decision making about a patient's bowel management program should take a patient-centered approach incorporating both the patient's age and psychosocial status and allowing the patient to participate as much as they are capable. This approach to care will allow for selection of the most appropriate treatments for each individual patient within the context of their family situation. Our survey can be used to assess the burden of that treatment regimen on the family unit and serial scores can be used to assess the subsequent impact of changes in the patient's treatment regimen.

Peter C. Minneci and Katherine J. Deans
Center for Surgical Outcomes Research, Abigail Wexner Research Institute and Department of Surgery, Nationwide Children's Hospital, Columbus, OH

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A Novel *CFC1* Mutation in a Family With Heterotaxy and Biliary Atresia Splenic Malformation Syndromes

To the Editor: Ten percentage of infants with biliary atresia (BA) present with polysplenia/asplenia associated with situs inversus, digestive tract anomalies or cardiac defects referred as BA splenic malformation (BASM) syndrome (1). Several BASM syndrome candidate genes have been reported, including *CFC1* encoding the Cryptic Family 1 (CFC1) involved in heterotaxy syndrome (OMIM 605376) (2–4). Only few patients with BASM syndrome harbouring a heterozygous *CFC1* mutation have been reported (4–6).

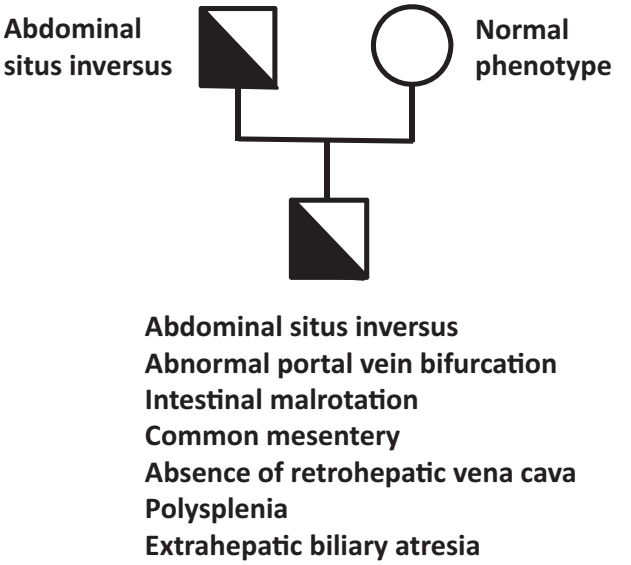

FIGURE 1. Pedigree and mutation analysis of *CFC1* gene in a family. Semifilled symbol indicates heterozygous status for p.(Gly83Val) mutant. DNA sequence analysis was performed in each individual reported here, after obtaining informed consent in accordance with protocols for human studies approved by our medical center.

We report a novel heterozygous *CFC1* mutation in an only child born from nonconsanguineous parents. The child had laterality defects associated with BA (Fig. 1). Sanger sequencing of *CFC1* 6 exons and intron-exon junctions (NCBI: *NM_032545*) identified the c.248G>T; p.(Gly83Val) mutation in exon 4 encoding the highly conserved epidermal growth factor (EGF) motif. This amino acid change was not reported in ClinVAR and not detected in over 200 chromosomes of control individuals. In silico analyses predict either a deleterious effect (Mutation Taster, Polyphen2) or a benign effect (SIFT). The fact that the mutants p.(Arg78Trp) and p.(Arg112Cys), previously reported in patients with BASM and/or heterotaxy syndromes, are also located close to or in the EGF motif and lead to abnormal cellular localization/activity, suggests a disease-causing effect of the p.(Gly83Val) mutant (3). Alternatively, the mutation involves the first nucleotide of *CFC1* exon 4 and could affect splicing, as strongly suggested by splicing prediction programs (NNSPLICE −90.7%, MaxEnt −33.8%, human splicing finder −4.8%). Abnormal splicing should delete the entire EGF motif encoded by exon 4. The sequence change was inherited from a father with an abdominal situs inversus without BA, consistent with an autosomal dominant inheritance and incomplete penetrance leading to variable expressivity (4–6). The search for *CFC1* mutations in patients with BASM syndrome deserves to be continued.

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[*‡]Emmanuel Gonzales, [†‡]Anne Davit-Spraul, and [*‡]Emmanuel Jacquemin

[*]*Pediatric Hepatology and Liver Transplantation Unit, National Reference Centre for Biliary Atresia*

[†]*Biochemistry Unit, Bicêtre Hospital, Assistance Publique – Hôpitaux de Paris, University of Paris Sud/Paris Saclay, Le Kremlin-Bicêtre*

[‡]*Inserm U1174, Hepatinov, University of Paris Sud/Paris Saclay, Orsay, France*

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