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EDITORIAL

R.I.P. for IND B

Luis de la Torre Mondragón, MD
Professor of Pediatric Surgery, National Autonomous University of Mexico

Miguel Reyes-Múgica, MD
Editor in Chief, Pediatric and Developmental Pathology

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For the last 35 years, pediatric specialists in the fields of pathology, surgery, and gastroenterology dealing with intestinal motility disorders in children have been immersed in a controversy surrounding the entity intestinal neuronal dysplasia type B (IND B), described by Dr William Meier-Ruge in 1971. Since its initial portrayal, difficulties have arisen in the accurate diagnosis, treatment, and understanding of this purported nosological entity. Scores of publications defining signs and symptoms of its clinical presentation, establishing histological diagnostic criteria, and recommending therapeutic approaches have appeared, and have created entire schools of specialists and resulted in dedicated clinical centers where the sophisticated testing required for IND B diagnosis is available. Lack of diagnostic reproducibility has dominated the scene, and even meetings among experts devoted to finding a consensus have failed and have resulted in persistent disagreement. Confusion has prevailed. Increasingly, 2 opposing lines of understanding—the believers and the nonbelievers in IND B—have grown apart from each other, despite attempts to bring them together and unify their viewpoints. Diagnostic criteria have been defined, challenged, redefined, modified, and abandoned at different times by individuals in both groups. Furthermore, animal models have been described by some, although their "IND B-like" phenotype has not been confirmed by others. The ultimate negative consequences of this chaos may have led to unsound surgical approaches. Parental anxiety has been fed. Even litigation may have ensued as a sad corollary.

However, and hopefully, this scenario might be forever changed as a consequence of the joint efforts of Drs Meier-Ruge and Bruder, the champions of IND B, and of Dr Kapur, another recognized expert in the field of pediatric intestinal dysmotility whose seminal contributions to these problems continue breaking new ground. These 3 authors have set out to definitely address the challenges in understanding IND B through an exchange of questions and answers focusing on the specific areas causing disagreement and/or irreproducibility, and setting the stage for a change in our interpretation of the clinical significance and therapeutic implications of identifying IND B. In their "Current Practice in Pediatric Pathology" article (see pages 444 to 452 of this issue) [1], Kapur invites answers to questions that have puzzled us for years, and Meier-Ruge and Bruder respond candidly, always seeking to clarify the issue without falling into the temptation of

defending an argument not supported by the facts or based only on the traditionally sustained opinions of their school and its adepts. The authors deserve recognition for their commitment to approaching this issue while keeping in mind the benefit of the patients, who will be the ultimate beneficiaries of this exchange. It goes without saying that it is not easy to modify or abandon long-held positions (tradition is usually more powerful than logic), and we are indebted to Drs Meier-Ruge and Bruder for their candor.

The main conclusions of this exchange do away with the existence of IND B as a nosological entity with a clear clinical significance. Given the fact that *dysplasia* originates etymologically from *dys*, meaning abnormal, and a derivative of the Greek πλασζ, formation, almost any deviation from the normal patterns of development affecting the intestinal nervous system would fit within the concept of IND. This may in part explain why many people grew fond of using such a theoretical concept to be applied to patients with clinical symptoms that suggest intestinal obstruction but show ganglion cells in the nerve plexuses. However, the definition of "normal" in regards to intestinal innervation continues to represent an elusive target, and it may not be a practical goal to pursue given the existence of variations not only depending on age and location of the biopsies, but also related to changes induced by manipulation of tissues and many other circumstances. Probably most pediatric pathologists with experience in development would agree that the younger tissues are, the more cellular they appear, possibly reflecting the natural decrease in cell numbers as tissues mature. The intestinal nerve plexuses are no exception, and most of the IND B features considered diagnostic criteria are "cured" by age.

Therefore, it may not be practical to assess subtle quantitative variations whose evaluation requires extensive and sophisticated methodology not available in most surgical pediatric pathology laboratories.

Be that as it may, it is probably fair to say that in the current state of affairs, only the extremes of these variations, namely positive or negative for ganglion cells, have proven to be clearly identifiable, and we should probably stick to this possibly oversimplified approach while no other reproducible, practical, and treatable findings can be diagnosed. However, it is likely that there are still many variants of Hirschsprung disease and other dysganglionoses whose histological features, genetic basis, and therapeutic approaches are yet to be discovered. Let us then put to rest the issue of IND B and get back to one of our most important principles: *primum non nocere.*

REFERENCE

1. Meier-Ruge W, Bruder E, Kapur RP. Intestinal neuronal dysplasia type B: one giant ganglion is not good enough. Pediatr Dev Pathol 2006;9: 444–452.