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Topical Review

A Refined Approach to Evaluating Global Developmental Delay for the International Medical Community

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ABSTRACT

BACKGROUND: Global developmental delay is usually defined as significant delay in two or more domains of development. Etiologic diagnosis generally proves difficult and the etiology remains undetermined in up to 62% of these children. Those in whom an etiology is established generally undergo an exhaustive and costly diagnostic evaluation, even though this may not change the medical or therapeutic management of the delay. The history and physical examination may provide up to 40% of etiologic diagnoses if adequately conducted. **METHODS:** We performed a critical review of the literature on global developmental delay via PubMed. **RESULTS:** Five major etiologic categories for global developmental delay were identified and traits of the history and physical examination suggestive for their diagnosis were described. Additionally, current diagnostic tools and their benefits and limitations were appraised. **CONCLUSIONS:** We propose an improved approach to enhance clinical diagnosis in both resource-rich and resource-limited settings favoring early intervention and management.

Keywords: global developmental delay, etiologic yield, global health, pediatrics

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Introduction

Developmental disabilities are a growing cause of morbidity in the modern world. This has become a diagnostic and therapeutic challenge especially in the context of cost containment brought about by recent socioeconomic concerns.[1,2] Isolated developmental delays (motor, speech) pose a specific diagnostic challenge, but their management is more contained than that of global developmental delay. Global developmental delay is generally defined as significant delay in two or more domains of development[3] (in which "significant" is defined as two or more standard deviations below the mean reference norms for age) and usually limited to children up to the age of 5. This very definition brings forth many caveats, from the misunderstanding of its implications (as a continuum of "delay" rather than a disability and the variability of the blanket term "global")[4,5] to its characterization as a diagnosis rather than the manifestation of an underlying etiology.

Several studies have sought to define the causes of global developmental delay. Although an etiologic diagnosis often remains a mystery (anywhere from 20% to 62% are undetermined in the literature),[6,7] identified etiologies have been grouped into several main causes (Table 1).[8] The identification of the etiology of global developmental delay is a time- and resource-intensive process that has gained attention in the current economic climate. Disorganized and "shotgun" approaches to diagnosis have been discouraged[9] in favor of structured diagnostic algorithms proposed by scholars and major academic associations in the English-speaking world.[3,10-12] These have largely homogenized the approach from a level of etiologic suspicion as incited by a full history and physical and leading down pathways of neuroimaging, metabolic or genetic testing (Fig 1). Indices of suspicion, alongside the existence of newborn screens (that eliminate many major and/or treatable causes) have

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TABLE 1.
Causes of global developmental delay

Group	Causes
Prenatal intrinsic	Genetic/metabolic disorders
	Central nervous system malformations
Prenatal extrinsic	Teratogens/toxins
	Infectious
Perinatal	Asphyxia
	Prematurity
	Neonatal complications
Postnatal	Infectious
	Psychosocial
	Traumatic
	Toxins

Adapted, with permission, from Wilska et al.[8]

been acknowledged in every step of the proposed flow charts; however, this end point often requires advanced testing.

Several studies recognize the history and physical examination as the most important elements in the diagnostic process in global developmental delay,[13-15] with others identifying checklists and focused approaches that enhance the diagnostic yield of tests for specific etiologies commonly associated to global developmental delay.[16-18] There is growing support for a conservative, observative, and empirical approach to the evaluation focusing more directly on the treatment of the delays themselves rather than the underlying etiologies in light of cost- and time-effectiveness; however, this approach remains under dispute.[19,20] To address this controversy, we reviewed the existing literature via electronic resources (such as the PubMed database) on the topic of global developmental delay to identify its most common etiologies and the current diagnostic approach and management outcomes. We offer a targeted, empirical approach in the context of a likely etiology that may not be readily evident in a first clinical visit. Five major etiologic groups were selected for review on the basis of existing literature to encompass the most common causes of undetermined global developmental delay (Table 2).[6,7,13,14,21-26] Major and commonly preventable causes readily detected by a standardized newborn metabolic screen were not included but should be considered in settings where such screens have not been performed. Critical appraisal of literature for the diagnostic process and therapeutic management for each cause was conducted.

Common etiologies of global developmental delay

Perinatal asphyxia

Asphyxia neonatorum is the result of a constellation of intrauterine and perinatal events that preclude the fetal brain from obtaining adequate blood (and therefore oxygen) flow. The events that characterize the cerebral response and lead to neonatal encephalopathy or hypoxic-ischemic encephalopathy are best described elsewhere.[27-29] Asphyxia neonatorum and hypoxic-ischemic encephalopathy represent up to 55% of the diagnostic yield in the literature for the diagnosed causes of global developmental delay.

The severity of hypoxic-ischemic encephalopathy relates to the presence and severity of significant neurodevelopmental comorbidities.[30,31] Although asphyxia neonatorum and subsequent hypoxic-ischemic encephalopathy do not have a pathognomonic clinical presentation, survivorship is often preceded by an extensive course of care in the neonatal intensive care unit. Improving peripartum care has increased this survivorship, and in spite of the significant benefits of established interventions such as therapeutic cooling,[32-34] hypoxic-ischemic encephalopathy still presents significant risk for developmental disability.[35,36] Therefore, thorough investigation of the perinatal and neonatal history could yield worrisome clues such as nonreassuring intrauterine fetal tracings, low Apgar scores at 5 and 10 minutes, or

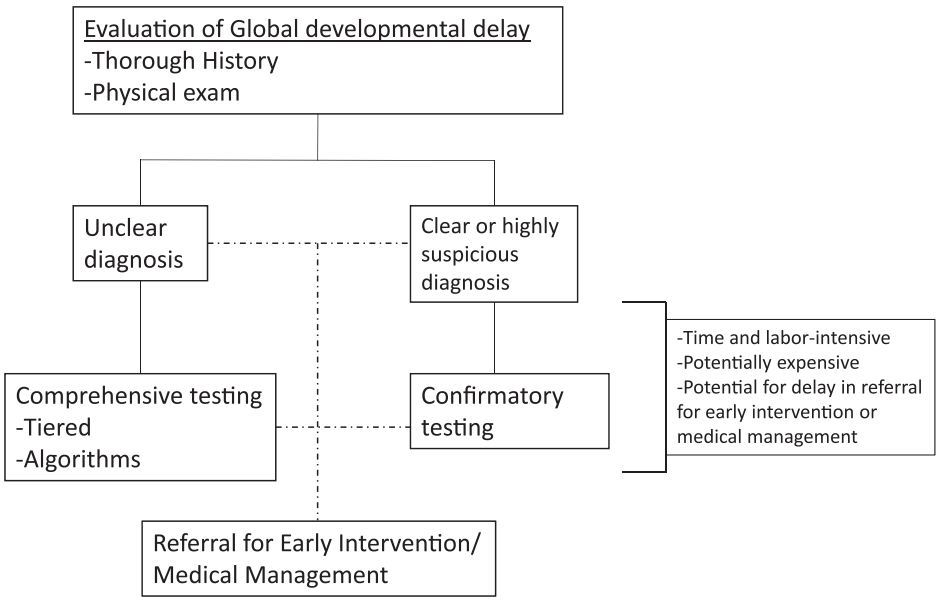

FIGURE 1.
Currently accepted diagnostic algorithm for global developmental delay with concerns.