

REVIEW

IDENTIFICATION AND MANAGEMENT OF CHILD DEVELOPMENT -PRACTICE PARAMETERS

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Key words: developmental delay, causes, identification, management.***Correspondence:** Nada Pop-Jordanova, Macedonian Academy of sciences and arts, Skopje, Republic of North Macedonia. E-mail: npopjordanova@gmail.com**Received:** 28-Nov-2021; **Revised:** 20-Jan-2022; **Accepted:** 25-Feb-2022; **Published:** 23-Jun-2022**Copyright:** © 2022, Nada Pop-Jordanova. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.**Competing Interests:** The author have declared that no competing interests

The main characteristics of children are phenomena of growth and development. Child development could be defined as a complex unfolding of a series of skills and adaptations, with very predictable stages, that occur in multiple dimensions at approximately the same time and in approximately the same order. There are several types of developmental delays in children. These delays can affect child's physical, cognitive, communication, social, emotional, or behavioural skills. Developmental delays are common in childhood, occurring in 10%-15% of preschool children in different forms. Global developmental delays are less common, occurring in 1%-3% of preschool children. The article gives some practice parameters for identification and management of child development based on the newest published articles included in the PubMed database.

ПРЕГЛЕД НА ЛИТЕРАТУРА

ИДЕНТИФИКАЦИЈА И УПРАВУВАЊЕ СО ДЕТСКИОТ РАЗВОЈ- ПРАКТИЧНИ ПАРАМЕТРИ

Нада Поп-Јорданова¹¹ *Македонска академија на науки и уметности, Скопје, Република Северна Македонија***Извадок****Цитирање:** Поп-Јорданова Н. Идентификација и управување со детскиот развој- практични параметри. Арх Ј Здравје 2022;14 (1)

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Клучни зборови: застој во развојот, причини, идентификација, управување.***Кореспонденција:** Нада Поп-Јорданова, Македонска академија на науки и уметност, Скопје, Северна Македонија

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Примено: 28-ное-2021; **Ревидирано:** 20-јан-2022; **Прифатено:** 25-фев-2022; **Објавено:** 23-јун-2022**Печатарски права:** ©2022 Нада Поп-Јорданова. Оваа статија е со отворен пристап дистрибуирана под условите на нелокализирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираат оригиналниот(ите) автор(и) и изворот.**Конкурентски интереси:** Авторот изјавува дека нема конкурентски интереси.

Главна карактеристика на децата е феноменот на раст и развој. Детскиот развој може да се дефинира како комплекс од серија вештини и адаптации, со предвидливи стадиуми, кои се јавуваат во разни димензии на приближно слично време и со приближно ист редослед. Постојат неколку вида застој во развојот кај децата. Може да го зафатат физичкиот, когнитивниот, комуникативниот, социјалниот, емоционалниот развој или поведението. Застојот во развој е чест во детството и се јавува кај 10-15% претшколски деца во разни форми. Глобалниот застој на развојот е поредок и се јавува кај 1-3% од претшколските деца. Овој напис дава некои практични насоки за идентификација и постапки за справување со детскиот развој базирани на најнови публикации соржани во базата ПубМед.

Introduction

Being a long-term paediatrician and psychologist, as well as an educator, I feel an obligation to give some suggestions about issues related to the public health. In this context I think that the developmental delay is not enough evaluated in the curricula of medical studies in our country and this article is devoted to this issue.

The main characteristics of children are phenomena of growth and development, processes that permit to rich maturity and functioning of the whole organism. Child development stages are theoretical milestones, some of which are asserted in nativist theories. As a reminder, nativist theorists are based on the hypothesis from Noam Chomsky and argue that children are born with an **innate ability** to organize laws of language, which enables them to easily learn a native language. They believe that children have language-specific abilities that assist them in mastering a language. Opposite to this, constructivism is based on a **theory of learning** in which the learners (children) construct the language through experiencing things and reflecting on those experiences. Cognitive constructivism was developed by Piaget, a well-known developmental psychologist.

However, development is quite different than growth. Growth only refers to the child getting bigger in size (changes in quantity). When we talk about normal development, we are talking about changes in quality, i.e., developing skills like: gross motor, fine motor, language, cognitive and social skills. Still, children reach developmental milestones at their own pace, and some move faster than others. It is known that two siblings in the same family, even tweens, may reach milestones at different rates.

Developmental delays are common in childhood, occurring in 10%-15% of

preschool children in different forms. Global developmental delays are less common, occurring in 1%-3% of preschool children. In this way, developmental delay is really the problem of the public health^{1,2,3}.

The main obligation of the paediatricians is to assess the development of every child and to alarm even minimal deviation of the norm. Minor, temporary delays are usually no cause for high concern, but an ongoing delay or multiple delays in reaching milestones can be a sign for different problems later in life.

For the purpose of this article a systematic search was conducted using PubMed and retrieving published articles in the last two decades. In addition, a bibliography of 160 articles available at the American Academy of Neurology Web site (<http://www.aan.com/>) were identified and reviewed for preparation of parameters discussed in this article. The following key words were used: developmental delay, children, screening. Important results obtained from this review are presented in this article.

Epidemiology

Globally, approximately 53 million children are supposed to have identifiable developmental problems delay. Since 95% of the population resides in low and middle-income countries, there is an increased risk of developmental delays and disorders. Although the exact prevalence of developmental delay is unknown, according to the World Health Organization (WHO), 10% of the population in each country has a disability of one or another kind. In the United States, roughly 15% of children have been reported to have at least one developmental problem. In England, the prevalence of intellectual delay in children under the age of five and

adults is 2.7% and 2.17%, respectively. The incidence rate for general developmental delay is 1% to 3% in school-age children or younger. Autism prevalence is approximately 2.5%. These numbers change each year, but unfortunately, they are increasing^{4,5}.

The prevalence of delay in development involving respective domains among children is based on data reported in children getting services by USPSTF (United States Preventive Services Taskforce). For the United States, they are as follows: cognitive (1% to 1.5%); learning disability (8%); speech and language (2% to 19%) and any delay (15%)⁶.

According to Drakenstein Child Health Study (DCHS) conducted in Western Cape, South Africa, the risk of low developmental performance in the high-risk environment was higher among

boys. Likewise, several other studies have also reported a slightly increased incidence in males, possibly due to genetic variability on the X-chromosome⁷.

There are several types of developmental delays in children. These delays can affect child's physical, cognitive, communication, social, emotional, or behavioural skills. Often, developmental delays affect more than one area of a child's development. When a child has delays in many or all of these areas, it is called global developmental delay.

Aetiology

Some developmental delays have an identifiable cause. However, for many children, the cause of the delay, or multiple delays, is not clear. Boxes 1 and 2 show common aetiologies for delay, as well as test needed for the evaluation.

Box 1. Common aetiologies of developmental delay:^(2,8)

Prenatal

- Genetic disorders: Down syndrome, fragile X syndrome, chromosomal microdeletion or duplication
- Cerebral dysgenesis: microcephaly, absent corpus callosum, hydrocephalus, neuronal migration disorder
- Vascular: occlusion, haemorrhage
- Drugs: cytotoxic, anti-epileptic
- Toxins: alcohol, smoking
- Early maternal infections: rubella, cytomegalovirus, toxoplasmosis
- Late maternal infection: varicella, malaria, HIV

Perinatal

- Prematurity, intrauterine growth retardation, intraventricular haemorrhage, periventricular leucomalacia
- Perinatal asphyxia: hypoxic-ischaemic encephalopathy
- Metabolic: symptomatic hypoglycaemia, bilirubin-induced neurological dysfunction

Postnatal

- Infections: meningitis, encephalitis
- Metabolic: hypernatraemia, hyponatraemia, hypoglycaemia, dehydration
- Anoxia: suffocation, near-drowning, seizure
- Trauma: head injury, either accidental or non-accidental
- Vascular: stroke

Others

- Social: severe understimulation, maltreatment, malnutrition (deficiency of iron, folate and vitamin D)
- Maternal mental health disorder
- Unknown

Box 1: Common causes for developmental delay

Box 2. Additional tests for children referred to a Child Development Unit:**Genetic evaluation**

- Child appears syndromic
- Clinical findings suggestive of any genetic condition
- Family history of developmental delay/intellectual disability

Creatine phosphokinase test

- Gross motor delay, especially in boys

Screening for inborn errors of metabolism

- Unexplained global developmental delay and a history of regression

TORCH (toxoplasmosis, rubella cytomegalovirus, herpes simplex and HIV) screen

- Macrocephaly/microcephaly

Neuroimaging

- Focal neurological deficits/abnormal neurological findings

Electroencephalography

- History suggestive of seizures/regression

Box 2: Needed evaluations for global developmental delay

Routine screening for inborn errors of metabolism in children with global developmental delay has a yield of about 1% that can increase up to 5%, in particular situations such as relatively homogeneous and isolated populations. When stepwise screening is performed, the yield may increase to about 14%. In our country, unfortunately due to financial deficit and disorganization, screening programs are not regularly performed in all obstetric settings⁸.

Forms of delay

Having in mind all written before, child development could be defined as “a complex unfolding a series of skills and adaptations, with very predictable stages, that occur in multiple dimensions at approximately the same time and in approximately the same order.” To assess whether an infant or a child is developing at a healthy and normal pace, paediatricians and child development experts consider four domains (or aspects) of development:

- Motor skills, including large (or gross) motor skills, such as roll-

ing over, crawling and learning to walk and run, and fine motor skills, such as the ability to pick up and eat small pieces of food or hold a pencil and draw or write.

- Sensory skills, including how a child uses the senses (taste, smell, touch, sound and sight) to learn about the environment.
- Social skills, including how an infant interacts with parents and caregivers, and then with others, including siblings, extended family and strangers.
- Cognitive skills, including how child’s attention, memory, thinking and learning skills develop and grow.

A significant delay is defined as a performance two standard deviations or more below the mean on age-appropriate, standardized norm-referenced testing. The term global developmental delay is usually reserved for younger children (i.e., typically less than 5 years of age), whereas the term mental retardation is usually applied to older children when IQ testing is more valid and reliable.

Cognitive delays may affect child's intellectual functioning, interfering with awareness and causing learning difficulties that often become apparent after a child begins school. Children with cognitive delays may also have difficulty communicating and playing with others.

Shaken baby syndrome, seizure disorders, and chromosomal disorders that affect intellectual development, such as Down syndrome, may increase the risk of a cognitive delay. This type of delay may occur also in children who have experienced a brain injury due to an infection, such as meningitis, which can cause swelling in the brain known as encephalitis. In most cases, however, it is not possible to identify a clear reason for this type of delay.

Motor skills' delay interfere with a child's ability to coordinate large muscle groups, such as those in the arms and legs, and smaller muscles, such as those in the hands. Infants with gross motor delays may have difficulty rolling over or crawling; older children with this type of delay may seem clumsy or have trouble walking up and down stairs. Those with fine motor delays may have difficulty holding onto small objects, such as toys, or doing tasks such as tying shoes or brushing teeth. Some motor delays result from genetic conditions, such as achondroplasia, which causes shortening of the limbs, and conditions that affect the muscles, such as cerebral palsy or muscular dystrophy. They may also be caused by structural problems, such as a discrepancy in limb length.

Social, Emotional, and Behavioural Delays are mainly related with neurobehavioral disorders such as autism spectrum disorder and attention deficit hyperactivity disorder.

Due to differences in brain development, they may process information or react to their environment differently than children of the same age. These delays can have an impact on a child's ability to learn, communicate, and interact with others.

Some **speech delays** are receptive language disorders, in which a child has difficulty understanding words or concepts. Children with this type of speech delay may have trouble identifying colours, body parts, or shapes. Others are expressive language disorders, in which a child has a reduced vocabulary of words and complex sentences for his or her age. A child with this type of speech delay may be slow to babble, talk, and create sentences. Often, a child with a speech delay has a combination of receptive and expressive delays.

Children may have speech delays due to physiological causes, such as brain damage, genetic syndromes, or hearing loss. Other speech delays are caused by environmental factors, such as a lack of stimulation. In many instances, however, the cause of a child's speech delay is unknown.

The **evaluation of the developmental delay** is based on one-on-one diagnostic play sessions and evidence-based measurement tools such as the Bayley Scales of Infant and Toddler Development and the Mullen Scales of Early Learning.

Delay in development is generally determined when a child does not attain developmental milestones as compared to peers from the same population. Statistical terms are often used to classify the degree of delay into mild (functional age (FA) <33% below chronological age (CA), moderate (FA 34% to 66% of CA), and severe (FA <66% of CA). "De-

velopmental delay” is a general descriptor of a broad phenotype that must then be specified by carefully determining one or more elements linked to the area of disrupted development.

Most developmental disabilities occur before a child is born, but some, as mentioned before, can occur after birth due to infection, injury, or other factors. In this context the first step in the evaluation of developmental delay is **metabolic screening as well as cytogenetic studies**.

In the group of innate causes for global developmental delay, in addition to Down syndrome, Rett syndrome is believed to be the most common cause of developmental delay in females. Seizures, autistic-like behavior, ataxia, intermittent hyperventilation, and stereotypic hand movements occur in most patients with Rett syndrome mainly after the age of 18 months together with microcephalia. Rett syndrome is believed to be one of the leading causes of global developmental delay/mental retardation in females and is caused by mutations in the X-linked gene encoding methyl-CpG-binding protein 2 (*MECP2*). About 80% of patients with Rett syndrome have *MECP2* mutations. The prevalence of Rett syndrome in the general population is approximately 1 to 3 individuals per 10,000 live births.

The accumulated data suggest that cytogenetic studies will be abnormal in 3.7% of children with global developmental delay, a yield that is likely to increase in the future as new techniques are employed. In mixed populations (both males and females), a yield of between 0.3% and 5.3% (average yield of 2.6%) has been demonstrated for fragile X testing. The higher range of this yield exists for testing amongst males. There is a

suggestion that clinical preselection for the fragile X syndrome amongst males may improve diagnostic testing beyond routine screening.

Having in mind the mentioned facts, the main recommendation is to conduct a routine metabolic screening for inborn errors of metabolism together with some cytogenetic testing of child with developmental delay even in the absence of dysmorphic features or clinical features suggestive of a specific syndrome. In children with unexplained moderate or severe developmental delay, additional testing using newer molecular techniques (e.g., FISH, microsatellite markers) to assess for subtelomeric chromosomal rearrangements (6.6%) may be considered.

What is the role of lead and thyroid screening in children with global developmental delay?

Lead is the most common environmental neurotoxin. Studies over several decades have shown a relation between marked elevations in serum lead levels, clinical symptoms and cognitive deficits (but not definitively mental retardation). Our team (paediatricians together with public health professionals) evaluated children in the Veles region. Our assessment confirmed a negative correlation between blood lead level and IQ in a sample of school children from Veles region where the lead factory was active (Fig.1)9. Additionally, some other direct negative effects from lead poisoning were proven. The pressure of scientists and public health professionals was so hard ending with the closure of the lead factory in Veles. Still, some consequences from lead toxicity are present.

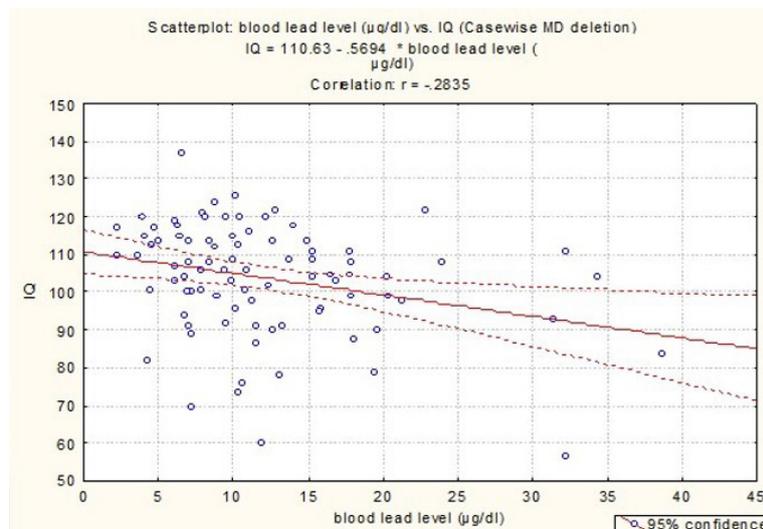


Figure 1: Correlation of blood lead level and IQ

Unrecognized congenital hypothyroidism is a potentially treatable cause of later developmental delay. Delay in diagnosis and treatment beyond the newborn period and early infancy has been clearly linked to later often substantial, neurodevelopmental sequelae. Implementation of newborn screening programs has been extremely successful in eliminating such sequelae.

What is the diagnostic yield of **EEG** in children with global developmental delay?

An EEG can be obtained when a child with global developmental delay has a history or examination features suggesting the presence of epilepsy or a specific epileptic syndrome. Data are insufficient to permit making a recommendation regarding the role of EEG in a child with global developmental delay in whom there is no clinical evidence of epilepsy.

What is the diagnostic yield of **neuroimaging** in children with global developmental delay?

Available data from some studies show that CT contributes to the etiologic diagnosis of global developmental delay in approximately 30% of children, with the yield increas-

ing if physical examination findings are present. MRI is more sensitive than CT, with abnormalities found in 48.6% to 65.5% of children with global delay with the chance of detecting an abnormality increasing if physical abnormalities, particularly cerebral palsy, are present.

In this context, the presence of physical findings (e.g., microcephaly, focal motor findings) increases the yield of making a specific neuroimaging diagnosis, and physicians are advised to consider obtaining a scan in this population. If available, MRI should be obtained in preference to CT scanning when a clinical decision has been made that neuroimaging is indicated.

Are vision and hearing disorders common in children with global developmental delay?

Several studies have shown that children with global developmental delay are at risk to have primary sensory impairments of vision and hearing. Estimates of vision impairment or other visual disorders range from 13% up to 50% whereas significant audiological impairments occur in about 18% of children based on data in one series of patients¹⁰.

However, it is recommended that children with global developmental delay undergo appropriate vision and audiometric assessment at the time of their diagnosis. Vision assessment can include vision screening and a full ophthalmologic examination (visual acuity, extra-oculo-movements, fundoscopic). Audiometric assessment can include behavioral audiometry or brain-stem auditory evoked response testing when feasible.

Treatments for developmental delays vary according to the specific delay. Some treatments include physical therapy for help in motor skill delays, and behavioural and educational therapy for help with ASD and other delays. A new report shows that a severe developmental brain disorder due to fragile X syndrome might be treated with drugs that inhibit a neurotransmitter receptor called mGluR5. The idea, that mGluR5 stimulates excessive protein synthesis in fragile X neurons disrupting their functions, became well validated by experiments in the lab of David et al.¹¹ and some others worldwide, using several animal models of the disease. In the future some other new approach in the treatment of developmental delay might appear.

Issues related to quality of life and social support of families who have children with developmental delay need also further studies. They should include the benefits that medical testing confers by reducing parental concerns related to determining a specific etiology and by providing important information regarding prognosis, genetic counseling, alleviation of parental anxiety, and planning future educational and treatment needs.

Conclusion

There are different forms and causes for developmental delay. The incidence of development delay globally is about 1-10% in the school period. The regular neonatal screening and cytogenetic studies are needed for early and exact diagnosis. The earlier diagnosis gives better prognosis based on specific therapeutic approach. In order to help these children some different therapeutic methods are available. For early diagnosis and prevention massive neonatal screening are needed.

This paper has presented an overview of the common etiological factor as well as of some parameters in diagnostic approach. Further studies in this field are important and needed.

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