Autism Spectrum Disorders: State-of-the-Art (Review)

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© **E.D. Bozhkova,** MD, PhD, Head of the Scientific Department, Acting Head of the Department of General and Clinical Psychology;
O.V. Balandina, Head of the University Center for Psychology and Children Development;
A.A. Konovalov, MD, DSc, Professor, Department of Preventive Medicine, Faculty of Doctors' Advanced Training

Privolzhsky Research Medical University, 10/1 Minin and Pozharsky Square, Nizhny Novgorod, 603005, Russia

Autism spectrum disorders are a group of disorders, the occurrence of which is associated with the impairment of brain development. Typical for them are difficulties in social interaction and communication.

Current epidemiological aspects of autistic disorders, methods of their diagnosis and correction as well as risk factors of the disease development are considered in the review. Numerous investigations confirm that timely identification of autistic disorders and child inclusion in the programs of early intervention may be the basis of effective rehabilitation and will be able to improve the prognosis for their socialization. High prevalence of autism spectrum disorders requires active work on designing screening procedures, creating scientifically grounded and standardized normative routing system for this category of patients, and implementing countrywide the programs rendering aid to children with this pathology and their parents.

Key words: autism spectrum disorders; autism; autism screening; risk factors for autism development; epidemiology of autism.

Introduction

Autism is defined as a disorder arising due to the impairment of brain development and is characterized by prominent and comprehensive deficit of social interaction and communication as well as by restricted interests and repetitive stereotyped actions. The diagnosis of "autism" is confirmed in early childhood on the basis of symptoms manifested during the first three years of life [1–6].

For a long time, early childhood autism was referred in ICD-10 (International Classification of Diseases) and DSM–IV (Diagnostic and Statistical Manual of Mental Disorders) to the group of psychological developmental disorders rather diverse in structure. In 2013, the concept of autism changed. The term "autism spectrum disorders" (ASD) appeared in DSM-V including autism (Kanner's syndrome), Asperger's syndrome, childhood disintegrative disorder, and nonspecific pervasive developmental disorder [7].

At the 67th session of the World Health Assembly (2014), a resolution "Comprehensive and coordinated efforts for the management of autism spectrum disorders" was adopted in which the necessity of detailed study of autism as an important social problem on a global scale was pointed out [8].

According to the Autism Speaks organization (2017), there are over 70 million people with autism, boys being diagnosed ASD almost 5 times more often than girls [9].

Autism spectrum disorder is a neurobiological disease, the symptoms of which persist and change throughout lifetime. Therapeutic methods for younger children are aimed at the correction of neuro-psychic development whereas in adolescents these methods are directed to the maintenance of the order in the living space and achieving self-dependence. As they grow up, the character of help is shifting more towards socialization, active communication, and gaining independence due to getting higher education and searching for a job [10]. The majority of investigations demonstrate that not only patients with ASD but their parents and close environment also need support [11].

All this determines the creation of a scientifically grounded and standards-based system of routing for this category of patients. It has been established that in case of timely rendering of help to patients with ASD, about 70% can study at general educational institutions [12].

The aim of the study is to summarize the current concepts of autism spectrum disorders based on the data of the advanced experience in Russia and abroad.

Epidemiology of autism spectrum disorders

The increase of autism prevalence estimates from 1960 to 1990s from 4 to 40 per 10,000 children [1, 13, 14] has attracted attention of the investigators worldwide. Such a sharp increase is not believed to be related to the actual growth of the disease incidence [15, 16]. So, the Danish scientists showed that high prevalence of ASD in children born in 1980–1991 years is likely to be caused

Corresponding author: Aleksey A. Konovalov, e-mail: konovalov.mobile@gmail.com

by the widening of diagnostic criteria and improvements in diagnostic tools [16].

Epidemiological investigations show that ASD prevalence grows all over the world. Presently, according to the estimates of WHO, about 1 of 160 children suffer from this disease [17].

To determine ASD prevalence is more difficult than the disorders with clear biological markers. Symptoms differ by the degree of severity and may be displayed in children with various intensity of cognitive impairment [18–20]. Interesting findings have been obtained studying the ratio of men and women with ASD. So, in the work of Loomes et al. [21], during screening procedures and active ASD detection this ratio was 3:1. Russel et al. [22] demonstrated that in children with the established diagnosis of ASD the ratio amounted almost to 5:1. It is not unlikely that it is connected with different prominence of the symptoms in men and women. Some investigators believe that girls are more liable to imitation of social actions and therefore masking of autistic symptoms takes place [23].

The number of people suffering from ASD grows rapidly [24]. By 2020, every thirtieth resident of the planet is predicted to suffer from this disorder to various degrees, and in 5 years it will be every second person [25].

Serious barriers on the way of studying ASD epidemiology arise due to the differences in classifications of the registered cases.

Thus, according to the ICD-10, in the Republic of Belarus, “childhood autism” (F84.0) and “atypical autism” (F84.1) were encountered most frequently. 447 children (60.53% of the total number of children with ASD) were followed up by psychiatrists at the beginning of 2015 with the diagnosis of childhood autism. The diagnosis of atypical autism was established in 26.51% of the entire cohort of children with ASD. Childhood disintegrative disorder was noted in 3.39% of cases; hyperactive disorder in combination with mental retardation and stereotyped movements was found in 3.03%; Asperger’s syndrome in 5.09% [26].

Data on autism prevalence in Russia have not been yet sufficiently systematized, the appropriate investigations were started only several years ago.

Currently, the prevalence estimates of various clinical ASD forms are scarcely highlighted in foreign literature. The last investigations of this kind were carried out over 10 years ago. Then, with the appearance of ASD group in DSM-V, it was considered inappropriate to distinguish the disorders within the group [27] since the prognosis of the course and the choice of correction programs are determined not by the form of the disease but rather the intensity and combination of concrete symptoms [28].

Risk factors for the development of autism spectrum disorders

Genetic factors are believed to play the most important role in the ASD development. The risk is found to increase with the relation degree of the child with the family member suffering from this disease. Besides, it unambiguously grows in children if the first child in the family was sick with the disease [29–31].

Hallmayer et al. [1] investigated the twins who had in their pair at least one child with the validated diagnosis of autism spectrum disorders or early childhood autism. Early childhood autism was identified in 58% of cases in both monozygotic twins in the male pair and in 21% of dizygotic twins. In female twins, this kind of autism was diagnosed in 60% for monozygotic pairs and 27% for dizygotic. Autism spectrum disorders were more pronounced. They were found in 77% for monozygotic pairs of male twins and in 31% for dizygotic. Female twins had ASD in 50% of cases in monozygotic pairs and in 36% in dizygotic.

Some researchers [32–34] have established that an increased risk of ASD development is associated with prematurity and low body mass of the newborns. It is interesting to note that the ratio of boys and girls in the group of premature babies with ASD is 2.1:1 that is lower than in the general population (4:1) [32].

Parents’ age is also no less important. It has been shown that each time the average age of mothers and fathers increases by 10 years, the probability of developing autism in children grows by 18 and 21%, respectively [35].

Gardener et al. [36] report in their meta-analysis about perinatal and neonatal factors associated with the risk of autism development. Fetal malpresentation, umbilical cord entanglement, fetal distress syndrome, birth traumas, multiple pregnancy, bleeding during pregnancy, delivery in summer, small gestational age, congenital abnormalities, low Apgar score, feeding problems, aspiration of meconium, anemia in newborns, blood group or Rh incompatibility, hyperbilirubinemia are referred to these factors. Gestational diabetes also increases significantly the risk of ASD development [37].

The results of several studies showed that maternal infection during pregnancy enhances the probability of ASD occurrence in infants. The disease is observed most frequently in children whose mothers needed hospitalization during pregnancy because of the complications caused by this infection [38]. But at the same time, it is necessary to take into consideration the type of the infectious agent as well as the duration and localization of the infectious process. It has been established that viral infections are in no way connected with ASD development. The investigators explain it by various response of the maternal immune system to viral and bacterial infection [39, 40]. And finally, urogenital and skin infections in mothers significantly increase the risk of autism development in a child [41, 42].

Of interest are the works devoted to the study of those children who appeared owing to the novel reproductive technologies [43, 44]. IVF and ICSI enhance, with varying degrees of probability, the risk of ASD development though it is likely that in this case not only

the quality of the reproductive procedure (including the quality of the embryos) but factors that led the parents to infertility also play the role [45].

The interconnection of vaccination and ASD has been discussed till now. Some authors believe vaccination to be the factor increasing the load on the body's immune system and promoting the disease development. Among other causes, presence of mercury-containing preservatives in some vaccines is mentioned [46]. However, numerous studies did not find any proof in favor of a higher risk for ASD in immunized children [47–50]. Moreover, there are investigations demonstrating the protective effect of vaccines. For example, in children vaccinated against parotitis, measles, and rubella, insignificant reduction of the risk for ASD development has been noted [51].

Some investigations report potential effect of toxic environmental substances (pesticides, heavy metals, some building materials, solvents, and other matters) on autism development [52–54]. Their dose-dependent connection in the perinatal and early neonatal periods has been established [55, 56]. Environmental factors may act synergistically or in parallel with the genetic factors in the critical periods of nervous system development [57].

The last works on ASD etiology were devoted to the mechanism of symptom development in this condition [58, 59]. The neurophysiological studies revealed impairments in the function of mirror neurons [60], structure of the cerebellum and neuromediator connections in its area [61], synaptic connections, and also in the differentiation of neurons in various regions of the brain [62]. The understanding of the ASD development mechanisms will make it possible to explain comorbidity of autistic disorders and other diseases (epilepsy, psoriasis, autoimmune diseases) [63, 64].

Organization of help to children with ASD in different countries

Till 1970s, help to children with ASD in the USA was often restricted by placing them in specialized boarding schools and rendering support to their families. Later special programs started to appear in different states: for example, the program "Treatment and Education of Autistic and Related Communication Handicapped Children" in North Carolina. In 70–80s, behavioral intervention methods were worked out oriented at the natural approach to teaching: "Pivotal Response Teaching" and "Incidental Teaching" which have proved their effectiveness [65].

In 1981, the so-called Early Start Denver Model (ESDM), was proposed which represents a comprehensive approach directed to the correction of autism in infants of 12–48 months of age. It takes into consideration natural periods of child development and time of ASD manifestation. It contains target skills for each specific age period and offers a set of correction educational procedures. Teaching may be conducted by specialists and/or parents in groups as well as via individual sessions of therapy [66, 67].

Organization of early intervention systems is different in various US states, but, in any case, a family is usually attached to the coordinator who presents information about the services available in the region of residence. Kids with ASD under 3 years study at home under the guidance of parents or specialists which is called "natural environment teaching" [68]. At the age of three years, a child proceeds to the system of education according to an individual plan [69].

The effectiveness of the Denver model is validated by a number of works. Dawson et al. [70, 71] carried out a randomized investigation with 48 kids aged between 18–30 months. Children in ESDM group showed significant improvement of cognitive and speech capabilities (elevation of IQ by 17 points compared to 7 points in the comparison group), adaptive behavior, and reduction of autistic symptoms. In 7 (30%) kids in the ESDM group, the diagnosis changed from autistic disorder to the unspecified developmental disorder. It happened only in 1 child (5%) in the comparison group. Patients undergone the intensive ESDM rehabilitation program have demonstrated a more marked improvement of social interaction, social communication, and symbolic play with participation of parents [70]. After 1 and 2 years from the beginning of the therapy, EEG was registered during viewing the photographs of female faces and toys in a random order on the monitor screen. Kids from the ESDM group responded better to the social information relative to the children from the group training according to the standard correction programs [71].

In Chinese children receiving 26-week course of ESDM consisting of regular training sessions, functional activity of the brain cortex has changed that made them closer to their peers with typical development. Their parents were noted to reduce the stress level whereas in the comparison group an opposite tendency was observed [72].

Investigations of the scientists from the Netherlands confirm the importance of early screening, diagnosis, and immediate referral of younger children with ASD to join scientifically-grounded correction programs. It has been proved that symptoms of autism revealed by screening in early childhood (under 2 years) allow specialists to make a diagnosis the consistency of which is preserved in 91% of cases over the period of subsequent observation [73].

In Great Britain, the program EarlyBird was developed by the National Autistic Society in 1997 to help parents of preschool children with ASD. Parents work on the alteration of their own speech communication, analyze their kid's behavior, initiate visual contact. More than 27,000 families in 14 countries of the world received help on the program. Its effectiveness was proved in relation to parents and guardians of patients with ASD [74].

The system of rendering help in Israel (ALUT) is

built on the basis of psychological and educational rehabilitation taking into account the needs of a child and its family. A correction service for kids under 3 years in the group includes 14-hour group sessions a week with a speech therapist, pathologist, psychologist as well as training for parents. The intervention programs are coordinated by a multidisciplinary team of specialists and cover speech, communication, learning, and motor skills. Parents together with the team of specialists determine the child's challenges and the main therapeutic goals [75].

In addition to screening and early intervention, great attention in the European countries is paid to the inclusive secondary and higher education [76]. Thus, in 2003, the National Council for Special Education (NCSE), was founded in Ireland providing 12-stage system of education for handicapped children [77]. In Finland, more and more attention is also given to education for individuals with ASD [78].

Thus, the world practice of rendering help to children with ASD is implemented first of all by means of early forms of diagnosing, correction, and socialization.

Organization of help to children with ASD in Russia

One of the main directions of the national policy in the field of children and adolescent health is the reduction of the number of disabled people with mental disorders [79].

According to the data of the Russian Ministry of Health, in 2015 the number of patients with ASD at the age under 18 years was equal to 17,700, in 2016 this value increased to more than 22,000 people. That is, the coefficient of people with ASD in 2016 amounted to 150 per 10,000 population making Russia the fourth country in the world for ASD prevalence [80].

Until recently, there was no statistics on autism among the adult population since the diagnosis usually was changed for schizophrenia or mental retardation after the age of 18. Only in the letter from the Ministry of Health of the Russian Federation dated October 4, 2017 No.17-1/10/1-6371 it was defined that age is not the ground for diagnosis revision.

In 2015, the "Foundation for children in difficult life situation and government executive bodies" launched a pilot project for rendering a comprehensive medico-social and psychological-pedagogical assistance to children with ASD realizing the theses of "The National Strategy for Action in the Interests of Children for 2012–2017". Specialized consulting and diagnostic centers were arranged, training seminars were conducted among the outpatient healthcare professionals, interdepartmental plans on the comprehensive assistance to children with ASD were elaborated in the regions participating in the project (Voronezh, Novosibirsk regions and Krasnoyarsky krai). Summarizing the results of the project, Moscow State University of Psychology and Education issued methodological recommendations and forms of normative documentation [81, 82].

Screening of ASD diseases was carried out using the guidelines for ASD monitoring of different standardization degree. The most common of them was screening test for autism for younger children M-CHAT widely used in the world practice (in Great Britain, USA, and other countries including Spain, South Korea, Turkey, and countries of South-East Asia) [83–85]. The M-CHAT test has sensitivity of 0.87 and specificity 0.99, i.e. a negative result denotes absence of ASD with the probability of 99%, and positive results will be confirmed in 1–5 of 10 screen-positive kids [86].

In 2015, a pilot project for early identification of ASD was started in Novosibirsk, Volgograd, and Chelyabinsk regions. The main screening tool was a clinico-psychological questionnaire for parents worked out by the Mental Health Research Center. It is designed to identify mental disorders including the risk of ASD development in toddlers (under 2 years) [87].

Over the period of 2015–2016, 74,191 parents were questioned. The children's age at that time was 16–24 months. The group of ASD development risk comprised 7,680 (10.35%) kids. Part of them received consultation from psychiatrists (4,703 children, 61%). Evident clinical disorders (general disturbances of psychological development according to IDC-10 (F84.0; F84.1; F84.8)) were detected in 36 children (0.5%) from the risk group [88].

Currently (since 2019), this screening directed towards the identification of mental disorders has been implemented in the entire country based on the Order of the Ministry of Health of the Russian Federation of June 13, 2019, No.396n "On the alterations in the Order on the procedure of conducting preventive medical examinations of minors approved by the Order of the Ministry of Health of the Russian Federation of August 10, 2017, No.514n" and is performed within the frames of preventive medical examinations for minor children reached the age of 2 years.

ABA therapy (applied behavior analysis), training for development of social skills, cognitive behavior intervention techniques proved to be effective in rendering comprehensive correction help. Indications for the selection of these methods are formulated in a number of works of Russian and foreign authors. The key role in the treatment of patients with ASD is given to psychological and educational measures rather than medication therapy [89–93].

In Russia, unlike the majority of European countries and the USA, assistance to children with ASD is at the stage of formation, depends on the availability of the programs of interdepartmental interaction in the region.

Serious obstacles arise already from the time of establishing the diagnosis. Quite often patients avoid contact with psychiatrists and are under care of neurologists or do not seek medical help at all preferring to work with psychologists or speech doctors.

Absence of mass screenings and wide awareness of specialists about current diagnostic criteria, validated diagnostic methods restricts essentially the capabilities of our national public health service in relation to the persons with autistic disorders.

The developed programs of treatment and rehabilitation of patients are not universal enough and well-elaborated. The projects aimed at the improvement of help to patients with ASD are pilot.

No official documents on the choice of therapy have been presently found except for clinical recommendations of Simashkova and Makushin where psychological and educational technologies are listed [89]. It is explained by heterogeneity of autistic disorders, therefore, the decision on the use of appropriate correction methods should be made by a professional directly working with a patient.

The most effective validated methods will provide the quality and availability of medico-psychological assistance to patients with ASD across the lifespan.

Conclusion

High prevalence of autism spectrum disorders in the world requires improvement of help rendered to children with developmental challenges. First of all, it is necessary to implement screening programs at the governmental level allowing for the assessment of the true scale of the disease as well as the risks of developing cognitive and behavioral disorders in children [94, 95]. Numerous investigations confirm that medical rehabilitation must begin at an early stage of autistic disorders formation in the years physiologically favorable for an infant (from the age of 2 to 7 years).

The quality of life in patients with ASD and their relatives is lower than in population in general [96, 97] due to the absence of any complex etiopathogenetic treatment and preventive measures. The existing pharmacological therapy is based on the perceived risk factors for ASD development that results in the use of different groups of medications the efficacy of which is proved only in single works [98].

Investigations show that psychotropic agents may only alleviate symptoms accompanying the disease if integrated with psychological and educational intervention [99, 100].

Patients with ASD need special lifelong attitude. In this connection, it is necessary to create and implement country-wide the scientifically grounded and approved standardized system of routing this category of patients, and also to attach the resources allowing them to get secondary and higher education to the programs of medical assistance [101].

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