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Historical and Contemporary Scientific Data on the Problem of Schizophrenia

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Annotation. Publications were analyzed and the main stages of the historical development of the concept of late schizophrenia were described. Despite the continuing ambiguity of this concept, the possibility of both late manifestation of schizophrenia (after 40 years) and very late (after 60 years) is recognized. The issues of classification, diagnosis, clinic and course of late schizophrenia are considered. The results of modern paraclinical research methods are presented. The relevance and prospects for further study of schizophrenia spectrum disorders at a later age, their possible connection with organic changes in the brain are shown.

Key words: late schizophrenia; very late schizophrenia-like psychoses; elderly age.

Introduction. In recent years, there has been a change in the diagnostic criteria for schizophrenia. Recent studies, as well as the DSM-5 classification, cast doubt on the concept of E.Kraepelin (Emil Wilhelm Magnus Georg Kraepelin) about schizophrenia as a nosological entity. So, in DSM-5, the division of schizophrenia into forms (hebephrenic, catatonic, paranoid) is excluded and it is proposed to consider them as stages of one process, while some symptoms that were previously considered sufficient for establishing a diagnosis are currently not.

Much attention is paid to research using modern neurobiological and neuroimaging methods, which contributes to the expansion of knowledge in the field of etiology, pathogenesis and treatment of this disease.

The relevance of research on schizophrenia at a later age is due to the aging process of the population, an increase in the number of elderly patients with schizophrenia, which include both those who have survived to old age and those who first fell ill at a later age. The peculiarity of the clinical manifestations of schizophrenia at a later age was the reason for the allocation of its special forms - late-onset schizophrenia and very late-onset schizophrenia-like psychosis [1]. In view of the recent changes in the diagnostic boundaries of schizophrenia, the question of the legitimacy of distinguishing "late schizophrenia" as a separate diagnostic category, as well as the study of etiopathogenetic features, risk factors, clinical features and treatment options for various forms of the disease, still remain in highly relevant. Of particular importance is the study of the relationship of schizophrenia with cerebral organic pathology and age-dependent cognitive impairment in order to develop an effective treatment for these disorders.

Literature review. Despite the introduction by E.Krepelin of the term “dementia praecox” (“dementia praecox”), indicating the onset of the disease at a young age, in 1913 he revised his views on the age of onset of the disease and spoke about the possibility of developing the disease not only in adolescence and adolescence, but also in middle and late. Subsequently, M.Bleuler (Bleuler M., 1943) examined 130 patients in whom the disease began after 40 years, and developed the following diagnostic criteria for late schizophrenia:

1) age of onset of the disease - after 40 years;

2) the clinical picture of psychosis should not differ significantly from the clinical picture of schizophrenia at a young age;

3) in psychopathological and neurological symptoms, there should not be any signs that would speak of the organic nature of the disease.

In the future, the study of this issue continued, and in various psychiatric schools and international classifications, views on this problem differed. M.Roth (1955) proposed to use the term "late paraphrenia",

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referring to the definition of E.Kraepelin, which meant hallucinatory-delusional psychoses that do not lead to a pronounced personality and emotional defect. With the development of geriatric psychiatry, "late paraphrenia" was included in the ICD-9 as a separate diagnostic category.

In France, the concept of "chronic hallucinatory psychosis" is widely used, which implies a late psychosis that develops predominantly in women and is characterized by severe hallucinosis in the absence of dissociative disorders. It is based on the teachings of Gaetan Gasian de Clerambaut on mental automatisms (1923).

In the American literature, the problem of late-onset psychoses was ignored for a long time [2]. Only DSM-III-R introduced the category "late schizophrenia" for patients with the onset of the disease after 45 years, but in subsequent revisions and in ICD-9, -10 it was not included in the classification. The DSM-IV-TR removed the upper age limit for the diagnosis of schizophrenia. At the same time, the following features of schizophrenia, which began at a late age, were emphasized: the predominance of women among the sick; better social and family status of patients (many were married or previously married at the time of the disease), although they lived more isolated than the general population.

Research Methodology. Postmenopause and cerebrovascular diseases were considered as risk factors. The clinical picture was determined by the predominance of delusions of persecution and hallucinations, the rarity of symptoms of disorganized thinking and negative symptoms. It also pointed to smaller doses of antipsychotics needed for treatment. In recent decades, the study of this issue has continued - a number of studies have been carried out concerning the nosological affiliation of late schizophrenia, clinical and neuropsychological features, and possible risk factors for the disease at a later age. However, there is no clear answer to any of these questions yet.

Analysis and results. In generally accepted international classifications (DSM, ICD), the diagnosis of "late schizophrenia" is not singled out. In earlier revisions (DSM-I, ICD-6, ICD-7, ICD-8, DSM-II) there was no age limit for establishing a diagnosis of schizophrenia, however, in the case of late-life psychoses, the term "late paraphrenia" was used. Some of the researchers noted that schizophrenia can be diagnosed if the first symptoms appear only before the age of 40 [3]. According to ICD-9, the diagnosis of schizophrenia could only be established if symptoms occurred before the age of 40, while the category of delusional disorders was introduced, for which there were no age restrictions and only "paraphrenia" was designated as hallucinatory-delusional syndrome with onset at a late age. In DSM-II, the age of onset of schizophrenia was up to 45 years, and there was no age limit for delusional disorders. The DSM-III-R introduced the concept of "late schizophrenia", subject to the onset of symptoms, including prodromal ones, not earlier than 45 years. However, later, already in DSM-IV and ICD-10, this term was excluded, as well as the age limit for diagnosing schizophrenia.

In 1998, the International Late Schizophrenia Research Group, after examining the results of many studies, agreed that the age of distinction between early and late onset schizophrenia is 40 years. It has been noted that the disease, manifesting in the age range from 40 to 60 years, has a significant similarity with earlier-onset schizophrenia. Based on the results of clinical, neuroimaging, and neuropsychological data, it was proposed to classify the disease with an onset after 60 years as a schizophrenia-like disorder.

An agreement was also reached on the criteria for diagnosis, nomenclature, therapeutic recommendations and prospects for further research in late schizophrenia [1]. Although this event had a major impact on subsequent research, current classifications of diseases (ICD-11, DSM-5) lack age criteria or specifiers, although it is indicated that cases of late onset may meet the criteria for schizophrenia.

The results of domestic clinical and epidemiological studies have shown that the number of patients with disorders of the "schizophrenic spectrum" in the late age groups of the population is quite significant. Their occurrence varies from 0.9 [4] to 1.7% [5]. The prevalence of schizophrenia, according to foreign studies, is 0.6% among the population aged 45 to 60 years [6]. It has been shown that the number of patients with schizophrenia after 40 years is 15–23.5% of the total number of cases, and after 60 years it is about 3–4% [7], and the number of hospitalizations with schizophrenia-like disorders increases in patients older than 60 years by 11% every five years [8].

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Clinical cases of manifestation of schizophrenia at the age of 70 and 100 years have been described [9, 10]. Researchers emphasize the predominance of women among the sick, but the rates differ significantly - from 1.3:2 to 6.7:1 [11]. Among the clinical forms of late schizophrenia, the most common are recurrent and paranoid forms (19.1% versus 14.9% of cases at a younger age), the malignant form is extremely rare.

At the same time, the increase in the proportion of patients with paranoid schizophrenia reflects a general trend towards an increase in the incidence of this form among patients with schizophrenia with increasing age [2]. Also, among late-onset patients, there is a rather rare occurrence of sluggish schizophrenia, both psychopathic-like and neurosis-like [13]. The number of patients with late-onset schizophrenia who were ever married was comparable to that in the healthy control group, however among them, the number of divorced people prevailed, which ultimately led to the fact that the number of people who were married at the time of the survey among patients with late and early onset schizophrenia was approximately the same [4]. Other authors confirm these data, pointing out that among those who fell ill early, the number of married people is significantly lower compared to the control group [5].

As for patients with late-onset schizophrenia, according to this indicator, they are between these groups [6]. There was no significant difference in the level of education between the groups of late and early onset schizophrenia, but it was lower compared to healthy controls [5]. Also, among people with late onset schizophrenia, the majority of patients had permanent employment compared with patients with early onset schizophrenia [1].

Almost all studies on late-onset schizophrenia and other psychotic disorders in later life emphasize the predominance of women. It has been suggested that higher estrogen levels in premenopausal women may play a “protective” role against the development of psychosis [7]. An increased density of D2 receptors has been reported in patients with late schizophrenia [8], although a recent attempt to replicate this finding failed [9]. It is assumed that estrogen can modulate the sensitivity of D2 receptors in the brain, and according to some authors, it has antipsychotic properties [2].

Moreover, estrogen can reduce the concentration of dopamine in the striatum (Foreman M.M, Porter J.C, 1980), modulating the sensitivity and number of dopamine receptors (Koller W., Weiner W., 1980; Gordon J., Diamond B., 1981; Bediard P., Boucher R., 1984). Thus, estrogens may act as a protective factor, and menopause is a risk factor in women with a predisposition to the development of schizophrenia. At the same time, this hypothesis does not explain the development of late schizophrenia in men. In addition, these assumptions were not confirmed during hormonal therapy [1].

Despite the fact that views on the concept of "late schizophrenia" and the legitimacy of its allocation differ, researchers agree that the clinical picture of late schizophrenia should not differ significantly from that at an earlier age. At the same time, most authors emphasize some clinical features in patients with late schizophrenia. M. Bleiler (1943), after examining 130 patients after 40 years of age, concluded that in more than half of the patients the clinical picture is characteristic of advanced age. Most often, he described paraphrenic states and depressive-anxiety-catatonic states, while pointing to a group of patients with a clinical picture of confusion similar to amental states. In a minority of cases, the symptoms were similar to those in younger patients. W.Klages (Klages W., 1961), speaking about the age-related coloration of the psychopathological symptoms he discovered, emphasized the more specific and systematized content of paranoid disorders and noted the abundance of unpleasant bodily sensations, in which a “physiopathological substrate” was assumed, i.e. specific delusional coloration of existing somatic sensations. G.Huber (Huber G., 1975) emphasized that delusional perception, taste and olfactory hallucinations are more common in late schizophrenia, while “I” disorders, affective disorders, unpleasant bodily sensations and depersonalization syndromes are less common. In another study, half of the patients had affective disorders (sadness, fear, anxiety and dysphoria) [2]. A number of authors emphasized the great diversity of the clinical picture, with the frequent occurrence of delusions of persecution and hallucinations affecting different areas of perception [3], and the rare occurrence of incoherence, ideas of "foreign influence" and "openness of thoughts" [5]. M. Roth, on the contrary, emphasized the poverty of the clinical picture. No significant difference in the frequency of occurrence of symptoms of the first rank in patients with early and late onset schizophrenia was found [3], in general, symptoms of the first rank occurred in 39% of late cases [6]. In schizophrenia that began at a late age, associative "loosening" of thinking and inadequate affect and negative disorders, in particular, apatoabulic defect, were less common [4]. The opposite opinion was shared by researchers who

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found mental disorders in patients in the form of "breaks" of thoughts, poverty of associations and negative symptoms represented by affective flattening and inexpressive speech [7]

The predominance of the paranoid form of schizophrenia and the high frequency of schizoid and paranoid traits in a premorbid personality, which, however, did not reach the degree of psychopathy, were noted. The absence of a course determined only by negative symptoms was especially emphasized [1]. As an exception, a clinical case of a patient aged 50 years with negative (nuclear) schizophrenia was published [8]. Important are the works devoted to the features of schizophrenia in the elderly, carried out at the NCCH using a multidisciplinary approach. In domestic psychiatry, the possibility of a late manifesto is recognized by most authors [3]. Conducted clinical and epidemiological studies have made it possible to describe the features of the course of schizophrenia in elderly patients [2]. The study of the clinical features of late schizophrenia, the use of a comparative age approach made it possible to compare the features of schizophrenia in the elderly and senile age. In the study of hallucinatory-delusional psychoses of late age, a variety of clinical forms occurring with paranoid housing syndrome was revealed. Two main variants were identified - actually delusional (paranoid) with a predominance of delusions of a small scale and hallucinatory with a predominance of "elementary" (usually auditory) hallucinations. Late schizophrenia, occurring with housing paranoid syndrome, was less common and was diagnosed only in the presence of “first-rank symptoms”, which were usually limited to delusions of physical impact and auditory hallucinations of a commentary character.

A clinical genetic study revealed a commonality between schizophrenia, involutional paranoid and dementia with delusions (Medvedev A.V., Valova O.A., 1991). In the study of late paranoid psychoses, a similarity was shown between them and schizophrenia at a later age, which manifested itself in the generality of the clinical picture with the predominance of "small-scale" delusions, while indicating their nosological independence.

A.N.Pyatnitsky (1980) showed that the progression of late schizophrenic psychoses manifested itself in an increase in the severity of productive symptoms and, to a lesser extent, in an increase in negative changes. Summarizing the research data, V.A.Kontsevoi (1999) noted that patients who had become ill for a long time and lived to old age are characterized by a rarity of the malignant course of the disease, the predominance of paroxysmal forms over continuous ones, a tendency to mitigate the manifestations of the disease and stabilize the process. There was a "blurring" of the clarity of the boundaries between the forms of the course of schizophrenia. Paranoid symptoms predominated among continuously ongoing forms in the structure of the disease, incompleteness of symptoms typical of schizophrenia and a rarity of neurosis- and psychopathic-like disorders were noted. The “small scale” of delusional experiences, their ordinary nature with age-related themes (ideas of damage, oppression, jealousy) were characteristic. In paroxysmal schizophrenia, the frequency of occurrence of intermediate forms between recurrent and paroxysmal-progredient increased, the range of clinical manifestations narrowed, depressive-delusional attacks acquired a protracted character. In remission, residual hallucinatory-delusional symptoms, subdepressive and psychopathic disorders often persisted.

Conclusion. Improving the diagnosis of schizophrenia spectrum disorders at a later age creates prospects for the development of effective methods for their prevention and treatment. The use of biological (paraclinical) examination methods will provide new information about the etiology and pathogenesis of this pathology, which, in turn, will allow developing a personalized approach to managing patients with late schizophrenia, determining the severity of organic pathology and methods for its correction, as well as predicting the course and outcome of the disease.

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