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**Research Article**
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# Incidence of Delirium Tremens in Acute Poisoning by Psychopharmacological Drugs or Corrosive Substances and Its Prevention Using Intestinal Lavage: on the Pathogenesis of Delirium Tremens

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**RELEVANCE** In patients suffering from alcohol dependence admitted to hospital with an intercurrent disease, the probability of delirium tremens (DT) is high, so the search for means of its prevention is relevant.

**THE AIM OF STUDY** To study the incidence of DT in patients with poisoning by psychopharmacological drugs and corrosive substances, and to evaluate the effectiveness of intestinal lavage as its prevention.

**MATERIAL AND METHODS** We conducted a prospective study that followed 287 patients (observation group). Of these, 162 patients had psychopharmacological drug poisoning (PPDP) and 125 patients had corrosive substance poisoning (CSP), who underwent intestinal lavage (IL) for the purpose of detoxification and correction of metabolic disorders.

A retrospective analysis of the examination results of 211 patients with PPDP and 102 with CSP (a total of 313 patients — comparison group) who did not receive IL was conducted. The patients in the groups were comparable in terms of gender, age, and severity of the same poisonings.

The severity of PPDP corresponded to stage 2b, and the severity of CSP corresponded to 2nd-3rd degree chemical burn of the upper gastrointestinal tract, including the stomach. All the patients had metabolic disorders that required correction.

The study endpoints were the incidence of DT, and the duration of treatment in the intensive care unit (ICU).

**RESULTS** In the comparison group, DT in PPDP and CSP developed in 57.8% and 56.9%, respectively. In the observation group, with the same nosological forms of poisoning, DT developed in 6.8% and 12% of cases, respectively. The intergroup differences in the incidence of DT in the same types of poisoning were statistically significant ($p<0.05$; U curve).

The ICU stay of patients with DT in CSP who had previously underwent IL was 10 days shorter than in the comparison group, and in PPDP — 11 days shorter than in the comparison group. This difference was statistically significant ($p<0.05$; U curve).

**CONCLUSION** The obtained results showed the effectiveness of intestinal lavage as a method for preventing delirium tremens in individuals with alcohol dependence. The observed phenomenon of decreased risk of delirium tremens development in patients who underwent intestinal lavage suggests that the pathogenesis of delirium tremens is associated with morphological and functional disorders of the gastrointestinal tract, the key link of which is the excess proliferation of microflora, for the vital activity of which ethanol is necessary. The decreased risk of delirium tremens in the group of patients who underwent intestinal lavage in the complex treatment is obviously associated with the therapeutic mechanisms of the latter — detoxification of the body and correction of homeostasis disorders, including intestinal microbiota, by eliminating ethanol-dependent microflora and its toxins.

**FINDINGS** 1. In individuals suffering from alcoholism with poisoning by psychopharmacological drugs and corrosive substances, delirium tremens occurs in 57.8% and 56.9% of cases, respectively.

2. When using intestinal lavage in complex treatment for the same poisonings, the incidence of delirium tremens is 6.8% and 12.0%, respectively, which is 8.5 and 4.7 times less than in case of standard treatment. This difference is statistically significant ($p<0.05$).

3. The use of intestinal lavage in acute poisoning by psychopharmacological drugs and corrosive substances reduces the stay of patients with delirium tremens in the intensive care unit by 2.6 and 2.7 times, respectively. This difference is statistically significant ($p<0.05$).

**LIMITATIONS OF THE STUDY:** age from 28 to 55 years, clinical diagnosis of "Alcohol related disorders" (ICD-10 code F10) in patients with poisoning by psychopharmacological drugs or corrosive substances, intestinal lavage in a volume of at least 12 (9; 15) l.

**Keywords:** acute poisoning; intestinal lavage; delirium tremens prevention; pathogenesis of delirium tremens

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AP — acute poisoning
AWS — alcohol withdrawal syndrome
CNS — central nervous system
DNA — deoxyribonucleic acid
DT — delirium tremens
ES — enteral solution
ET — endotoxin of gram-negative bacteria
GABA — gamma-aminobutyric acid
GIT — gastrointestinal tract
IL — intestinal lavage
LPS — lipopolysaccharide
PAMPs — Pathogen-associated molecular patterns (LPS, bacterial DNA and RNA, flagellin, lipoteichoic acid, lipopeptides, peptides and (1→3)-β-D-glucan)
PCS — poisoning by corrosive substances
PPPD — poisoning by psychopharmacological drugs
RNA — ribonucleic acid
SCFA — short-chain fatty acids

## INTRODUCTION

In the practice of modern clinical toxicology, poisoning by psychopharmacological drugs (PPPD) and poisoning by corrosive substances (PCS) are the most common — in 65% and 14% of cases, respectively, of the total number of acute poisoning (AP). They are different in nature and clinical features, therefore, of the greatest interest for studying their various complications and comorbid conditions [1, 2].

In people suffering from alcoholism, AP can act as a trigger for delirium tremens (DT). Depending on the type of poisoning, this most often occurs in the somatogenic stage, but can also occur in the toxicogenic stage [3]. In any case, this event aggravates the course of the underlying disease, increases the risk of complications, the length of stay in a hospital bed and the cost of treatment [4]. In such a situation, an element of hopelessness is added due to the fact that there are no effective means of preventing and combating DT.

The incidence of severe forms of alcohol dependence, according to a number of statistical studies, is highest in medical and preventive institutions, and intensive care units [5, 6]. Severe alcohol withdrawal syndrome (AWS), manifested by a complex of vegetative, somatic, neurological and mental disorders, is observed in 15% of such

patients, and requires treatment in the intensive care unit, doubling the length of hospital stay [7, 8].

According to K. Salottolo et al. (2017), the length of hospital stay, the length of stay in the intensive care unit and mortality in patients with alcoholic mania are higher than in patients without alcohol dependence and DT [9]. The development of complications in DT, such as cerebral edema and severe forms of pneumonia, is the main cause of death in hospital. Mortality in the most severe forms of DT can reach 47% [10].

Alcoholics are characterized by homeostasis disorders and manifestations of endotoxicosis of varying degrees of severity [7, 8, 10].

The first mentions of alcoholic mania in literary sources date back to the 17th century, and a professional description of this condition was made by T. Sutton in 1813 under the name of delirium tremens. Alcohol as an etiological factor was established by Rayer in 1818. The patterns of DT development, its symptoms and main forms were studied by V. Magnan, C. Lasegue, Rose, K. Bonhoeffer, E. Kraepelin, S.S. Korsakov. However, as follows from literary sources, the pathogenesis of DT remains unclear [7, 8, 10].

Since the pathogenesis of DT remains unclear, the treatment is empirical and symptomatic. According to Z.I. Kekelidze et al. (1998): "More than 135 drugs and their combinations have been proposed for the treatment of delirium tremens. This is due to the fact that no drug meets the ideal criteria: the presence of a sedative effect without suppression of protective reflexes, an increase in the seizure threshold, suppression of autonomic hyperactivity, antipsychotic action" [cit. according to 10]. The listed requirements for an "ideal" drug may someday be met, but the use of such a drug, nevertheless, cannot be called pathogenetic, but rather, again, symptomatic.

Currently, clomethiazole is considered the drug of choice in Europe. It has sedative properties, stabilizes the autonomic system, has an anxiolytic and anticonvulsant effect, but the antipsychotic effect of the drug is not expressed. In Russia, as in the USA, the drugs of choice are benzodiazepines, and among them the most popular is diazepam [10]. Thus, at present, treatment of a patient with DT is limited to eliminating the symptoms of the latter.

The present study was motivated by two circumstances. Firstly, there is no information in the literature on the incidence of DT in PPPD and PCS. Secondly, we have noticed that DT, developed during AP, was easily stopped as a result of using enteral detoxification methods, in particular, intestinal lavage (IL). In addition, it appeared that patients after IL had a lower incidence of DT. The research of this phenomenon became the subject of the present study.

**Aim:** to study the incidence of DT in PPPD and PCS, and how IL influences the prevention of its development in these cases of poisoning.

Objectives:

1. To study how often does DT develop in people with PPPD and PCS who suffered from alcohol dependence.
2. To evaluate the effectiveness of IL as a means of preventing DT in PPPD and PCS.
3. To assess the impact of IL on the length of stay in the intensive care unit of patients with DT in PPPD and PCS.

## MATERIAL AND METHODS

A prospective analysis of the examination results of 287 randomized patients (observation group) was conducted, including 162 with PPPD and 125 with PCS, treated at the Department of Acute Poisoning and Somatopsychiatric Disorders of the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2023–2024, who, in the toxicogenic stage of poisoning, were given IL in a volume of 12 (9; 15) liters for PCS, and 18 (15; 21) liters for PPPD for the purpose of detoxification and correction of metabolic disorders.

For comparison, a retrospective analysis of the examination results of 313 patients (comparison group) treated at the same Department in 2019–2023 was conducted, including 211 with PPPD and 102 with PCS, who underwent standard therapy without IL. In terms of gender, age and severity of the same

poisoning, patients in the observation group and the comparison group were comparable.

Patients with PPPD were in a serious condition upon admission to the Department, due to profound depression of consciousness (3–5 points on the Glasgow Coma Scale), mixed-type respiratory failure, and hemodynamic instability. The severity of poisoning according to the classification of E.A. Luzhnikov (2007) corresponded to stage 2b.

The severity of the condition of patients with PCS was due to pain syndrome associated with the presence of a chemical burn of the mucous membrane of the oral cavity, pharynx, esophagus and stomach, which was recorded using endoscopic examination, and according to the classification of S.V. Volkov et al. (2005) corresponded to 2–3 degree.

All the patients with PPPD and PCS had electrolyte imbalance and acid-base imbalance in blood, other metabolic and functional disorders that determined the severity of the condition and required correction.

The endpoint of the study was a comparative assessment of the incidence of DT and the length of stay of patients of the study groups in the intensive care unit.

Table 1 shows the distribution of patients by type of poisoning, gender and age in the observation and comparison groups.

As can be seen from Table 1, the study groups were comparable in terms of the indicated characteristics.

The patients of the observation group (287 people) underwent IL using enteral solution (ES) according to the method of V.A. Matkevich (2012) [11]. The ES used for performing IL contains: sodium phosphate, sodium chloride, sodium acetate, potassium chloride, citric acid, $Na_2EDTA$ complexone, as well as calcium chloride and magnesium sulfate, and purified drinking water. ES is prepared from a set of mineral acid concentrates, which are produced serially. To do this, the concentrate is dissolved in a given volume of water according to the manufacturer's instructions. The osmolarity of the solution is 290–310 mOsm/l (depending on the volume of water used to dissolve the salts), pH ≈ 5.8 [11].

To administer the prepared solution, a two-channel silicone nasogastric tube with a diameter of 6 mm was inserted. Before installing the tube, patients with disorders of consciousness underwent tracheal intubation and were transferred to mechanical ventilation. To perform IL, one of the tube channels was connected to a suspended container with ES, the temperature of which was 37–38°C for patients with PPPD, and the ambient temperature for patients with PCS. The head of the patient's bed was elevated by 30–45 degrees. ES was administered in portions of 150–200 ml every 5 min or at an average rate of 40 ml/min in PCS and 60–100 ml/min in PPPD. After the administration of 2 (1.5; 2.5) l of the solution, liquid stool appeared. In cases of absence of stool after administration of 2.5 l of ES,

*Table 1*

**Distribution of patients by types of poisoning, gender and age in the compared groups**

| No | Type of poisoning | Patient groups | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Comparison group | | | | Observation group | | | |
| | | Total number of patients | Gender | | Age Me ($Q_1$; $Q_2$) | Total number of patients | Gender | | Age Me ($Q_1$; $Q_2$) |
| | | | M n (%) | F n (%) | | | M n (%) | F n (%) | |
| 1 | PPPD | 211 | 145 (68.7) | 66 (31.3) | 36 (28.0; 45.0) | 162 | 100 (61.7) | 62 (38.3) | 39 (31.0; 47.0) |
| 2 | PCS | 102 | 71 (69.6) | 31 (30.4) | 43 (34.0; 54.0) | 125 | 86 (68.8) | 39 (31.2) | 41 (34.0; 55.0) |
| Total: | | 313 | 216 | 97 | – | 287 | 186 | 101 | – |

Notes: PPPD — poisoning by psychopharmacological drugs, PCS — poisoning by corrosive substances; Me ($Q_1$; $Q_2$) — median, 25th and 75th percentiles

pharmacological stimulation of the gastrointestinal tract was started. IL was continued until the wash water was clear. The total volume of the solution was 12 (9; 15) l in PCS and 18 (15; 21) l in PPPD. The duration of the IL procedure was on average 5 (3; 6) hours. A rectal tube with a colostomy bag was installed to collect intestinal secretions.

### STATISTICAL PROCESSING OF RESULTS

Statistical processing of the material was performed using IBM SPSS Statistics 26.0. The normality of data distribution was assessed using the Shapiro–Wilk test (n≤50). Due to the abnormal distribution of the sample, the median (Me), 25th and 75th percentiles were determined as Me ($Q_1$; $Q_3$). Categorical data were presented as n (%). The Mann–Whitney U test (independent groups) was used to compare medians between the groups. The significance level was taken as p<0.05.

## RESULTS

As a result of the treatment, the patients' condition improved; patients with PPPD regained consciousness, and their vital functions were restored. In case of PCS, the pain syndrome was relieved, bleeding was stopped, and physiological constants were normalized. However, 65.5 (50.0; 70.0) hours after admission to the intensive care unit, 11 of 162 patients (6.8%) with PPPD and 15 of 125 patients (12%) with PCS developed DT.

A comparative analysis of the incidence of DT in the observation group and the comparison group of patients with PPPD and PCS is presented in Fig. 1.

Fig. 1 shows that with standard treatment, DT developed in 57.8% of patients with PPPD, and in 56.9% of patients with PCS. In patients, whose complex of detoxification and metabolic disorder correction measures included IL, the incidence of DT was 6.8% and 12.0%, which is 8.5 and 4.7 times less frequent, respectively, than as a result of standard treatment, with a statistically significant difference (p<0.05).

Table 2 presents the results of the study of the length of stay in the intensive care unit of patients in the observation group and the comparison group.


Fig. 1. Distribution of patients by types of poisoning and incidence of delirium tremens in the compared groups

Notes: [1] – statistically significant difference in indicators in the compared groups with the same type of poisoning (p<0.05; U curve)

*Table 2*

**Duration of intensive care unit stay of patients in the compared groups**

| Type of poisoning | Comparison group | | Observation group | |
|---|---|---|---|---|
| | Absence of DT | DT | Absence of DT | DT |
| PCS | 8 (6.5; 9.0)[1] | 16 (13.3; 19.3)[1,2] | 4 (3.0; 5.0)[1] | 6 (5.0; 7.0)[1, 2] |
| PPPD | 9.3 (8.5; 10.0)[1] | 18 (11.0; 19.0)[1,2] | 5 (4.0; 6.0)[1] | 7 (6.0; 9.0)[1, 2] |

Notes: [1] — statistically significant intragroup difference (p<0.05; U curve); [2] — statistically significant intergroup difference (p<0.05; U curve), DT — delirium tremens; PPPD — poisoning by psychopharmacological drugs; PCS — poisoning by corrosive substances

Table 2 shows that in cases of DT development, patients stayed in the ICU longer, which is consistent with the literature data. The analysis showed that patients with DT and PCS who received standard treatment stayed in the ICU on average 8 days longer, and with DT and PPPD - 8.7 days longer than patients without DT. This difference was statistically significant (p<0.05; U curve). A similar comparison in the observation group showed that in the case of DT in PCS and PPPD, patients stayed in the ICU only 2 days longer than patients without DT. The duration of treatment in the intensive care unit of patients with DT in PCS in the observation group was 10 days shorter than in the comparison group, and 11 days shorter in the case of PPPD. This difference was statistically significant (p<0.05; U curve).

Table 2 also shows that as a result of IL, the time spent in the intensive care unit for patients who did

not develop DT was 4 days less than in the comparison group.

## DISCUSSION OF RESULTS

An explanation for the apparent effect of reducing the risk of DT among patients who received IL should be sought in the processes that are triggered in the body as a result of this procedure. Studying these processes, in turn, may help understand the pathogenesis of DT.

On the one hand, it is known that in various forms of DT, in addition to specific ones, general clinical and laboratory manifestations characteristic of all its forms are distinguished, namely, dysregulation of catecholamine production and metabolism, endotoxicosis, disruption of homeostasis and functional state of organs and systems, including microbiota.

It is known that some intestinal microbes are involved in the synthesis of neurotransmitters such as glutamate, serotonin, norepinephrine, dopamine and γ-aminobutyric acid (GABA), as well as in their function and bioavailability both in the central nervous system (CNS) and in the periphery [13, 14]. For example, *Prevotella*, *Bacteroides*, *Lactobacillus*, *Bifidobacterium*, *Clostridium*, *Enterococcus*, and *Ruminococcus* gut microbes are able to modulate dopamine synthesis and metabolism by changing their own enzymatic activity [12]. Emerging evidence shows that the gut microbiota plays an important role in maintaining adequate dopamine concentrations through a complex bidirectional communication along the microbiota–gut–brain axis. The vagus nerve, immune system, hypothalamic–pituitary–adrenal axis, and microbial metabolites serve as important mediators of reciprocal microbiota–gut–brain signaling [15].

In addition to the vagus nerve-mediated interaction pathways between the gut and the CNS, a connection between intestinal microbes and the CNS via their secretion of serotonin [16], as well as translocation of their metabolites, for example, short-chain fatty acids (SCFA) from the intestinal lumen into the systemic circulation were described [17–19].

Together, these microbiota-gut-brain axis interactions link cognitive, emotional, and reward centers in the brain with visceral signals from the gut.

Along with physiological interactions between the intestinal microbiota and the central nervous system, pathological effects associated with the vital activity of the intestinal microbial community were also described. For example, when a population of gram-negative bacteria dies en masse and their membranes are lysed, there is a massive release of lipopolysaccharide (LPS), a structural element of the outer membrane of these bacteria, which enters the bloodstream from the intestines as an endotoxin (ET), initiating a systemic inflammatory reaction. Translocation of ET is facilitated by increased permeability of the intestinal wall to pathogens.

Thus, the following key positions can be identified that are involved in the pathogenesis of DT:

1. Disruption of catecholamine metabolism.
2. Existence of the microbiota-gut-CNS interaction axis.
3. Participation of intestinal microbiota in the synthesis and metabolism of neurotransmitters.
4. Intestinal dysbacteriosis.
5. Endotoxicosis with the participation of microbial endotoxin.
6. Disruption of homeostasis.

The presented pattern of cause-and-effect relationships in the pathogenesis of DT can hypothetically be fit into the following sequence of events, reflecting both the development of DT and its prevention or relief with the help of IL.

Chronic alcohol intake probably causes specific restructuring of the composition and qualitative changes in the microbiota, and the formation in the gastrointestinal tract of a community of microbes whose metabolism requires the use of alcohol, similar to acetic acid gram-negative bacteria (*Acetobacteraceae*), which are known to convert homemade wine into vinegar. These bacteria are from the family of Proteobacteria (*Pseudomonadota*), and they obtain energy by oxidizing ethanol to acetic

acid. There are 1534 known species, distinguished by a wide variety of biochemical, physiological and morphological properties, which are widespread wherever alcohol is present (overripe, spoiled fruits and berries, fermented milk and yeast products, low-alcohol drinks) [12]. Endogenous ethanol is formed in humans during the digestion process, namely, carbohydrate metabolism, and acetic acid bacteria are present in the gastrointestinal tract of all people. Their quantity is individual and depends on the nature of the diet. It is quite logical to assume that a person who regularly drinks alcohol, without suspecting it, grows inside himself a colony of microorganisms for which alcohol is vital.

It is known that altering the species of gut microbes and the metabolites they produce can modulate the activity of the afferent part of the vagus nerve through a variety of mechanisms. Microorganisms producing SCFAs were shown to activate and directly act on vagus nerve endings in the gastrointestinal wall [20]. The nature of the effects of gut microbes on brain structures via the vagus nerve depends on the characteristics of the particular strain. There is compelling evidence of how certain microbes alter brain neurochemistry and subsequent behavior related to the dopaminergic system. Indeed, the vagus nerve serves as a primary mediator in cross-talk between the gut and the brain, affecting central and peripheral dopamine concentrations. For example, it was shown that stimulation of the vagus nerve causes dopaminergic activation and affects the concentration of dopamine in the central nervous system [15]. Thus, the mass death of alcohol-dependent bacteria during the period of abrupt cessation of the patient's alcoholization, changes in the quantitative and qualitative characteristics of the gastrointestinal microbiota cause an explosion of biochemical, immunological and metabolic changes in the body, including catecholamine production and metabolism, which are realized in the form of specific and non-specific manifestations that fit into the picture of AWS and DT.

The proposed hypothesis of pathogenetic sequences characteristic of DT explains the phenomenon of decreased risk of its occurrence as a result of IL in individuals suffering from alcoholism. The sanogenetic mechanism of IL, which helps prevent DT, can be schematically represented as follows:

— detoxification (elimination of endotoxicosis, including excess of LPS and catecholamines);

— process of restoring clinical and biochemical constants, and the functional state of organs and systems;

— reduction in the number of opportunistic flora and restoration of the normal flora population.

Long-term study of the therapeutic effects of IL has shown that its sanogenetic mechanisms are universal. First of all, it is appropriate to talk about detoxification of the body in both exo- and endotoxicosis. In fact, in acute poisoning considered in this work, the detoxification process began with cleansing the gastrointestinal tract. As a result of IL, chemical substances of both exogenous origin and microbial toxins, including ET, as well as natural metabolites accumulated in excess quantities are effectively removed from all sectors of the body (enteral and internal) [11, 21]. Thus, as a result of IL, the concentration of ET and medium-molecular peptides in the blood decreases, and the ratio of pro- and antioxidant processes is normalized [11, 21]. The consequence of successful detoxification is the prevention of infectious and inflammatory complications, including pneumonia as a possible trigger of DT [22].

Another, no less important vector of IL action is the correction of imbalance of physiological constants and the functional state of organs and systems. Moreover, correction of water-electrolyte imbalance and acid-base imbalance occurs in the autoregulation mode, when the deficiency of macroelements, for example, magnesium ions, typical for DT, is replenished by the intake from the lavage solution; and the excess, for example, calcium or sodium ions, is removed against the concentration gradient along the following trajectory: cells →

interstitium → blood → gastrointestinal tract cavity → lavage solution and further on. Also, in the autoregulation mode, blood acidosis is leveled due to the absorption and metabolism of acetate, which is part of the ES [23]. Due to partial absorption of the solution during IL, the deficit in circulating plasma volume is replenished, central hemodynamics and microcirculation are improved [23].

In terms of DT prevention, an important point is the correction of intestinal microbiocenosis disorders. We have previously established that dysbacteriosis in patients with acute poisoning, in the form of a decrease in the titer of *Bifidobacterium* and *Lactobacillus* by 1–2 orders of magnitude, and an increase in the content of opportunistic, including gram-negative, LPS-producing flora, up to 105 CFU, was leveled with the help of IL [24]. As a result of washing out a part of the cavity flora, which includes opportunistic microorganisms, there was a rapid restoration of the populations of the mucosal flora, which includes *Bifidobacterium* and *Lactobacillus*, which, being producers of GABA, increase its content in the body, which could become an additional factor in the prevention of DT [12]. The hypothesis of a cause-and-effect relationship in the occurrence of DT, as well as understanding of the treatment and preventive mechanisms of IL provide grounds to position this method as affecting pathogenetic links and thereby preventing the development of DT in individuals suffering from alcoholism. Based on the obtained results, IL can be recommended to people with alcohol dependence in the first day of the post-aggressive period.

IL reduces the risk of DT in individuals suffering from alcohol dependence by almost 5 times in PCS and more than 8 times in PPPD. And in cases where DT did develop after IL, it was milder, as indicated by a shorter period of intensive treatment by 2.7 times in PCS and 2.6 times in PPPD compared to patients who did not undergo IL.

The high efficiency of IL as a preventive measure for DT and understanding of its therapeutic mechanisms suggest that the pathogenesis of DT may include some links associated with morphological and functional disorders of the gastrointestinal microbiota, for the metabolism of which alcohol is necessary.

In the last 20–30 years, the world medical science has seen a growing interest among researchers in the role of microorganisms in the pathogenesis of diseases traditionally considered non-infectious. On the agenda is the study of the nature of the involvement of microorganisms in the occurrence of diseases such as diabetes mellitus, obesity, hypertension, atherosclerosis, autoimmune diseases, Alzheimer's disease, Parkinsonism and many others that would seem to be in no way related to the gastrointestinal tract [25–30].

It is known that the gastrointestinal microflora is formed under the influence of external and internal factors [31]. The most significant of all factors is nutrition [32]. The composition of the gastrointestinal microbiocenosis depends on the nature and quality of the products consumed [33–35]. Thus, in meat-eaters, the intestinal microbiocenosis is dominated by proteolytic microflora, while in vegetarians, it is dominated by saccharolytic microflora [31]. Alcohol can significantly change the quantitative and qualitative composition of the intestinal microflora [36, 37]. It leads to excessive bacterial growth in the small intestine. Changes in the taxonomic composition of microflora in alcohol abusers consist of active growth of gram-negative bacteria [38]. These microorganisms include acetic acid bacteria [12]. In the presence of alcohol, their population increases rapidly. V.B. Dubinkina et al. (2017) note that the intestinal microbial community of patients with alcohol dependence is dysbiotic: it contains an increased content of Proteobacteria (which convert alcohol into acetic acid), namely, gammaproteobacteria and bacilli. Against this background, a decrease in the number of commensal taxa of *Clostridia*, *Bacteroidetes* and *Ruminococcaceae*, as well as *Lactobacillus* and *Bifidobacterium* is noted [36].

It is known that microorganisms are capable of controlling human behavior with the help of afferent

signaling [31]. Just as they periodically "signal" to a sweet tooth: "eat something sweet", so to an alcoholic, at first: "why not have a drink?", and then: "find it and drink it!" People perceive signals from the microbiota on a subconscious level and take them for their desires. But they know that when an irresistible desire (compulsive attraction) arises, it must be satisfied, otherwise bad things are going to happen. This is the nature of addictions, including alcohol addiction.

When microbial cohabitants lack "specific food," some of them die, releasing endogenous toxins into the environment in the form of patterns (PAMPs — Pathogen-associated molecular patterns), including such formations as: LPS, bacterial DNA and RNA, flagellin, lipoteichoic acid, lipopeptides, peptideglycan and (1→3)-β-D-glucan [39–41]. These patterns (and the bacterial cells themselves) penetrate into the lymph and blood, spread throughout the body and complementarily combine with specific cellular receptors, causing one or another reaction of the executive organ or individual cells (for example, the release of hormones, neurotransmitters, the production of free radicals, etc.) [42]. Moreover, they promote the development of neuroinflammation, which subsequently leads to psychiatric symptoms of alcoholism [43].

In this way, the microflora-intestine-CNS axis is realized, and, probably, the pathogenesis of diseases and conditions associated with alcohol dependence develops.

The proposed hypothesis of the involvement of gastrointestinal microorganisms in the pathogenesis of DT explains the high effectiveness of IL as a prophylactic agent.

Until now, the research of alcohol dependence syndrome has been focused on studying neurophysiological effects, as well as the influence of alcohol on the state of various organs. At the same time, the question of the influence of alcohol on the intestinal microbiota and, accordingly, its role in the formation of alcohol dependence syndrome remains poorly understood. Meanwhile, in this chain, the formation of a "vicious" circle can be seen: alcohol abuse → growth of specific microbiota → formation of alcohol dependence syndrome → alcohol abuse, in which the microbiota occupies a key (main) position.

## CONCLUSION

The obtained results showed the effectiveness of intestinal lavage as a method for preventing delirium tremens in individuals with alcohol dependence. The observed phenomenon of decreased risk of delirium tremens development in patients who underwent intestinal lavage suggests that the pathogenesis of delirium tremens is associated with morphological and functional disorders of the gastrointestinal tract, the key link of which is the proliferation of microflora above the norm, for the vital activity of which ethanol is necessary. The reduction in the risk of delirium tremens in the group of patients who received intestinal lavage as part of the complex treatment is obviously associated with the therapeutic mechanisms of the latter - detoxification of the body and correction of homeostasis disorders, including intestinal microbiota by eliminating ethanol-dependent microflora and its toxins.

The authors hope to attract specialists' attention to the topic of this publication both to discuss the details and confirm the provisions of the proposed hypothesis of the pathogenesis of delirium tremens, and to continue research in this direction.

## FINDINGS

1. Against the background of poisoning by psychopharmacological drugs and corrosive substances in individuals suffering from alcoholism, delirium tremens occurs in 57.8% and 56.9% of cases, respectively.
2. When using intestinal lavage in the complex treatment for the same poisoning, the incidence of delirium tremens is 6.8% and 12.0%, respectively, which is 8.5 and 4.7 times less than with standard treatment. This difference is statistically significant ($p<0.05$).
3. The use of intestinal lavage in acute poisoning by psychopharmacological drugs and corrosive substances reduces the stay of patients with delirium tremens in the intensive care unit by 2.6 and 2.7 times, respectively. This difference has statistical significance ($p<0.05$).

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