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NEUROVISCERAL DYSREGULATION AND SYSTEMIC AUTONOMIC DYSFUNCTION IN ALCOHOL DEPENDENCE

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The purpose of the study was to systematize modern data concerning the autonomic nervous system involvement in alcohol dependence and propose a multi-level integrative model of autonomic dysregulation. An analytical review of the literature was conducted using PubMed, Google Scholar, Web of Science and Scopus databases. Contemporary clinical and experimental studies were analyzed alongside fundamental research in neurophysiology, neuroendocrine, and neuroimmune regulation. A systems-based and pathophysiological approach was applied. The findings showed systemic autonomic dysfunction formation with multisystem involvement, including cardiovascular, gastrointestinal, respiratory, thermoregulatory, urogenital, metabolic-endocrine and immune systems as a result of chronic alcohol exposure. These alterations occur across multiple hierarchical levels of autonomic nervous system organization and are associated with impaired integration of neurovegetative, neuroendocrine, and immune regulatory pathways. The proposed model conceptualizes autonomic dysfunction as a systemic process and provides a framework for the development of targeted diagnostic, prognostic, and therapeutic strategies in alcohol dependence. Authors conclude that chronic alcohol exposure is associated with systemic autonomic dysfunction which results in regulatory systems generalized disruption. Autonomic dysfunction follows a continuum from subclinical regulatory disturbances to overt organ manifestations, determining disease progression. The proposed integrative model provides a conceptual basis for personalized diagnostic and therapeutic approaches in alcohol dependence.

Key words: alcohol dependence, autonomic nervous system, autonomic dysfunction, central autonomic network, neurovisceral integration, multisystem dysregulation, pathophysiological mechanisms.

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НЕЙРОВІСЦЕРАЛЬНА ДИЗРЕГУЛЯЦІЯ І СИСТЕМНА ВЕГЕТАТИВНА ДИСФУНКЦІЯ ПРИ АЛКОГОЛЬНІЙ ЗАЛЕЖНОСТІ

Метою дослідження було систематизувати сучасні дані про участь вегетативної нервової системи в алкогольній залежності та запропонувати багаторівневу інтегративну модель вегетативної дизрегуляції. Було проведено аналітичний огляд літератури з використанням баз даних PubMed, PubMed, Google Scholar, Web of Science та Scopus. Сучасні клінічні та експериментальні роботи проаналізовані поряд з фундаментальними дослідженнями в галузі нейрофізіології, нейроендокринної та нейроімунної регуляції. Було застосовано системний та патофізіологічний підхід. Результати показали формування вегетативної дисфункції внаслідок хронічного впливу алкоголю з ураженням багатьох систем, включаючи серцево-судинну, шлунково-кишкову, дихальну, терморегуляторну, урогенітальну, метаболічно-ендокринну та імунну системи. Ці зміни відбуваються на кількох ієрархічних рівнях організації вегетативної нервової системи і пов'язані з порушенням інтеграції нейровегетативних, нейроендокринних та імунних регуляторних шляхів. Порушення інтегративної функції центральної вегетативної мережі пропонується як ключовий механізм, що лежить в основі єдиного патофізіологічного континууму вегетативної дизрегуляції. Запропонована модель концептуалізує вегетативну дисфункцію як системний процес і забезпечує основу для розробки цілеспрямованих діагностичних, прогностичних та терапевтичних стратегій при алкогольній залежності. Автори висловлюють, що хронічний вплив алкоголю пов'язаний із системною вегетативною дисфункцією, наслідком формування якої є генералізоване порушення регуляторних систем. Вегетативна дисфункція є континуумом від субклінічних регуляторних порушень до явних органних проявів, що визначає прогресування захворювання. Запропонована інтегративна модель забезпечує концептуальну основу для персоналізованих діагностичних та терапевтичних підходів до алкогольної залежності.

Ключові слова: алкогольна залежність, вегетативна нервова система, вегетативна дисфункція, центральна вегетативна мережа, нейровісцеральна інтеграція, мультисистемна дизрегуляція, патофізіологічні механізми.

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The Ukrainian statistic data reported about each year progressive increase the number of registered persons with alcoholism in Ukraine [1, 25]. However, the real figure is significantly greater which indicates a national epidemic in the country. Today, the level of alcohol consumption in Ukraine is one of the highest in the world and is about 15 l of absolute alcohol per each person per year [31]. A sad fact is the consumption of stronger alcoholic beverages in Ukraine vs the same data in Moldova, Hungary and the Czech Republic. However, these data are considered contradictory [6]. It is known that almost

380 thousand people die every year in Ukraine from problems associated with alcohol and drugs. It is dangerous that about 40 % of Ukrainian teenagers (14-18 years) regularly consume alcoholic beverages [25, 31]. Thus, the organisms' pathology associated with excessive alcohol intake, which, according to fundamental data, develops after 6-9 months of abuse, is an important medical and social problem in the country, which solution requires the priority attention of specialists in different fields of medicine.

Autonomic nervous system (ANS) damage in alcohol dependence modifies and intensifies its clinical manifestations, changing the course of the disease (tolerance formation, exacerbation, withdrawal syndrome, relapses, etc.). At the same time, along with psychological and social factors, biological factors play an important role, in particular genetic predisposition, neuroanatomical and neuroendocrine rearrangements, immune changes, as well as biochemical disorders (neurotransmitter and metabolic imbalance, neuro- and organotoxicity). These processes contribute to the disruption of self-regulation mechanisms and the shift of ANS functioning towards the "alcohol-dependent" type [45].

"Autonomic dysfunction associated with alcohol abuse" is a broad concept that encompasses a complex of central and peripheral mechanisms of ANS regulation. The latter controls the vital functions of the body, while in the early stages, subclinical autonomic disorders are formed at the level of regulation, rather than subjective feelings.

The purpose of the study was to systematize modern data concerning the autonomic nervous system involvement in alcohol dependence and propose a multi-level integrative model of autonomic dysregulation.

Materials and methods. To achieve the goal of the review, three main literature searches were conducted in the databases PubMed, Google Scholar, Web of Science and SCOPUS was conducted, covering scientific articles in English from 01.01.2020 till 01.01.2025. The last search query was performed on July 14, 2025.

A meticulous and strategic search process was employed within each database utilizing a broad range of keywords relevant to the field of pathological physiology, clinical pathological physiology, neurology and vegethology such as alcohol dependence and autonomic dysfunction with an appropriate Boolean operators (i.e., AND, OR).

A bibliometric approach was adopted to meet this objective; it entailed quantitative and structural-analytical status of scientific publications. The used international scientometric databases allowed creating a representative set of publications to evaluate the current trends in science in the field of studying the chronic impact of alcohol on autonomic functions disruption in human organism and autonomic regulation complete breakdown. Current clinical and experimental work is analyzed alongside fundamental research in the field of neurophysiology, neuroendocrine, and neuroimmune regulation. A systemic and pathophysiological approach was used to analyze the selected scientific literature for review.

For explanation. Searching within the PubMed database the following verbatim search query was used: "alcohol dependence", "chronic alcohol intake", "alcohol impact", "alcohol abuse", "alcohol use disorder", "autonomic nervous system", "autonomic nervous system pathology", "autonomic dysfunction", "neuronal dysregulation", "central autonomic network", "central processing disorder", "neuroimmune disorder", "neuroendocrine disorder", "neurovisceral integration", "multisystem dysregulation", "pathogenesis", "treatment", "prophylaxis", "personalized diagnostic" and "pathophysiological mechanisms".

Similar search strategies were subsequently used in other databases - Google Scholar, Web of Science, and SCOPUS. This extensive collection of keywords ensured a broad and exhaustive search that captured the recent experimental trials, neurological clinical discoveries and advances and the newest fundamental data regarding the alcohol dependence and related alcohol-induced autonomic disorders pathogenesis, diagnosis, treatment and prophylaxis.

The inclusion criteria for the review were strictly defined to ensure high-quality and relevant studies. Only original research articles, systematic reviews, and meta-analyses published in peer-reviewed journals were considered for inclusion. Emphasis was placed on studies published in English, which were prioritized for their broader accessibility and relevance to the international scientific community. Studies published in Ukrainian were also included to reflect regional contributions to the field.

Exclusion criteria were also considered important. Conference abstracts, editorials, preprints, and non-peer-reviewed articles were excluded due to their inconsistency with the review objectives. Only studies that provided substantive information concerning theoretical explanation and clinical realization of the problem of chronic alcohol impact on biological organism, alcohol dependence and alcohol-provoked autonomic disorders pathogenesis, clinical manifestation, treatment, and possible prevention were selected for inclusion.

As this is a review article based on the analysis of publicly available literature, ethical approvals were not required for this study. The study protocol was performed in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Hence, a total of 531 articles were selected. After removing duplicates and those not meeting the inclusion criteria, a portion was selected for full-text review. Therefore, 50 manuscripts were determined to meet the inclusion criteria (Table 1).

Table 1

Simplified PRISMA Flow

Stage	Description	Number of Records/Studies
1. Identified	Total number of records identified through database searching and other sources	531
2. Duplicates Removed	Number of records removed before screening (e.g., duplicates)	103
3. Screened (Title/Abstract)	Number of records screened after duplicates were removed	428
4. Assessed for Eligibility (Full-text)	Number of full-text articles assessed for eligibility against the inclusion/exclusion criteria	108
5. Included in Review	Total number of primary studies finally included in the systematic review	50

Results of the study and their discussion. Chronic alcohol exposure leads to ANS central structures neurotoxic damage, autonomic neuropathy development and results in sympatho-vagal interaction imbalance with an organism' adaptive capabilities decrease. The cardiovascular system is most sensitive to these changes, where disturbances in cardioregulation, baroreflex sensitivity and sinus node modulation are noted, being accompanied by an increased risk of non-alcoholic, including fatal, events even in the absence of clinically expressed autonomic failure. The systemic disorders are formed meanwhile including metabolic and coagulation instability, chronic low-intensity inflammation and endothelial dysfunction [38].

It's necessary to take into account the multilevel ANS organization - the so-called "levels" or "floors" of regulation introduced by the Odesa School of neurovegetology [2]. They include central structures (hypothalamic-stem level), which ensure the adaptive reactions integration as well as ANS peripheral departments responsible for local regulation of vascular, metabolic and organ tone.

Different levels of regulation disturbances lead to diverse clinical picture formation. Higher (central or suprasegmental) levels damage is manifested by changes in general reactivity, autonomic tone and impaired interaction with the cerebral cortex, limbic system and endocrine regulation. The stem (middle or segmental) levels dysfunction is accompanied by impaired baroreflex sensitivity, regulation of cardiovascular activity and respiration. Peripheral parts of the ANS damage is manifested by local organ symptoms, in particular, changes in vascular tone, sweating, secretory function, thermoregulation, etc.

Such a multilevel nature of ANS and its connections involvement into pathophysiological mechanisms determines the variability and combination of clinical manifestations in patients even with the same degree of alcohol intoxication, forming a complex multiorgan phenotype of autonomic dysfunction [8].

The following question remains to be open - whether ANS dysfunction is a factor that precedes and contributes to alcohol dependence formation, or whether they develop secondarily, in parallel with intoxication, enhancing clinical manifestations and the risk of complications. At the same time, according to the multilevel concept [1, 24], a combination of these mechanisms is observed: in some individuals, subclinical ANS dysregulation may cause increased susceptibility to ethanol abuse, while in others, autonomic disorders are formed as a consequence of the toxic effect of alcohol on the central and peripheral levels of regulation.

The question of ANS both sympathetic or parasympathetic divisions dominance in alcohol dependence requires further clarification. This aspect is debatable, especially at the level of individual organs and systems, where their effects can be opposite, and the interaction can determine the nature and direction of functional disorders, their degree and variability of clinical manifestations [12]. It is assumed that sympathetic activity may dominate in certain organ systems - for example, vardiovascular system reacts in the fprm of tachycardia, increased vascular tone and decreased baroreflex sensitivity [7]. Gastrointestinal and genitourinary systems showed parasympathetic dominance mainly clinically manifested by impaired peristalsis, secretory function or decreased smooth muscle tone. It should be noted that cardiac autonomic innervation changes reflect a complex interaction of sympathetic and parasympathetic influences, but the mechanisms of these changes in conditions of chronic intoxications remain unclear yet [7, 8].

One concrete ANS department dominance is well known to determined not only by organ specificity, but also by individual characteristics (genetic predisposition, type of higher nervous activity, basic vegetative tone), the stage and duration of alcohol exposure, the functional state of the organism as well as the nature of the lesion of central and peripheral regulatory mechanisms. This necessitates both sympathetic and parasympathetic regulation differentiated analysis in various physiological and clinical contexts [49].

Such multidirectional activity causes autonomic dysfunction clinical manifestations high variability in individuals with the same level of alcohol intoxication. This determines the need for further studies aimed at comparative analysis of autonomic regulation mechanisms in different organic systems to develop the targeted diagnostic approaches, differentiated therapeutic strategies and to predict possible complications. It is expected that such

studies will allow to establish the ANS departments in different organs patterns of imbalance and to identify the most vulnerable links of regulation. This is of key importance for alcohol dependence pathophysiological mechanisms detailed understanding [8, 12].

The most studied are the indexes of cardiovascular system functioning due to their high informativeness, availability of objective registration and prognostic significance [35]. Heart rate variability parameters, blood pressure and baroreflex sensitivity, ECG indexes and other cardiovascular tests are easily standardized, reproducible and allow to perform the sympathovagal equatiob quantitative assessment. Additionally, standardized autonomic functional tests are used (Ewing battery, Valsalva test, orthostatic test, deep breathing test, etc.) [12]. The cardiovascular system is highly sensitive to autonomic regulation changes and quickly responds to toxic effects which is a convenient model for autonomic dysfunctions investigation [8]. At the same time, the illusion of their universality is created, while autonomic changes in other organ systems (despite their pathogenetic significance) may limit the ANS disorders systemic nature understanding [42].

Impaired sympathetic skin response (SSR) in alcohol abusers reflects sudomotor mechanisms dysfunction with postganglionic thin unmyelinated sympathetic C-fibers damage innervating sweat glands which is characteristic feature of alcoholic polyneuropathy [18]. It should be stressed that the subjective complaints of sweating disorders are often absent even in the presence of objective changes in alcoholic patients. Important that standardized assessment methods (evoked SSP, Quantitative Sudomotor Axon Reflex Test, thermoregulatory sweat test etc.) allow to detect subclinical sudomotor dysfunction which is considered to be an early marker of autonomic neuropathy and is associated with the risk of systemic ANS damage [42, 43].

The formation of the sudomotor reflex which is evaluated using the evoked SSR is provided not only by peripheral structures but also with the help of central regulatory mechanisms (hypothalamic-stem and cortical), which allows us to consider the SSR changes as an option of multilevel autonomic dysregulation. This is confirmed by the combination of sudomotor disorders with ANS other effector links dysfunction [43].

Given that alcohol is a systemic neurotoxin, SSR indexes can be considered as an integral marker of ANS different levels lesion including the Central Autonomic Network (CAN) components dysfunction - the ventromedial prefrontal cortex, the insular cortex and associated limbic structures. This outlines the altered autonomic and cardiovascular reactivity that characterizes the central regulatory mechanisms disruption in alcohol dependence [5, 21, 40].

The erectile dysfunction (ED) rate is known to be significantly higher than in the general population, with prevalence rates ranging from 60 % to 72 % or higher [30]. Its association with alcohol consumption remains controversial. Several studies have suggested that moderate alcohol consumption may be associated with a reduced risk of ED, whereas the effects of heavy, chronic alcohol abuse are mixed and generally tend to worsen function [23, 30]. While the available evidence suggests an association between alcohol consumption and ED, the results are highly variable, due to differences in the amount of alcohol consumed, duration of abuse, and assessment methods used, making their interpretation and statistical generalization difficult [3, 23].

At the same time, patients with alcohol dependence showed erectile function significant improvement within the first month of abstinence, indicating alcohol-induced ED partial reversibility in condition of alcohol consumption termination [23].

The ED cascade pathophysiological mechanisms include CNS depression by alcohol, normal erection neurohumoral activation disruption, both testosterone synthesis and sex hormone metabolism impairment, peripheral signaling damage. One should observe also the ED vascular component increased dysfunction (endothelial dysfunction, nitric oxide synthesis increase, cavernous bodies impaired vasodilation, free radical processes accelerartion), especially in case of comorbid (hypertension, diabetes, odesity etc.) and other somatic pathology [22, 23]. Physiological disorders are often aggravated by the following psychosocial factors: emotional disorders, cognitive deficits and quality of life in general. Resuming, there is an ED multicomponent pathogenesis including vascular, hormonal, neurogenic and psychogenic chains [22, 49].

Ethanol and acetaldehyde have a toxic effect on the gastrointestinal tract (GI): they damage the mucosa, disrupt the intestinal barrier function, promote the development of inflammation and dysbiosis, and also change the gastrointestinal motility [4]. These processes are under the ANS control which provides the intestinal motor, secretory and barrier functions regulation as well as their coordination with central (hypothalamic-stem) mechanisms [27, 47].

Chronic alcohol consumption leads to autonomic nerve fibers damage with alcoholic polyneuropathy development which frequency reaches 25–50 % and depends according from alcohol consumption duration and dose [32]. The visceral form of autonomic neuropathy is clinically manifested by gastroparesis, impaired peristalsis, chronic diarrhea or constipation, secretion disorders, and dyspeptic phenomena in the absence of organic pathology [27].

Alcoholic gastroparesis (15–40 % of cases) is manifested gastric emptying delay, nausea, early satiety, and vomiting. Pathogenetically, these symptoms are due to vagus damage, degeneration of neurons (mainly intermuscular - Auerbach's, as well

as submucosal - Meissner's plexuses), impaired NO-ergic regulation, interstitial Cajal cells damage, gastric smooth muscle (decreased contractility, mitochondrial dysfunction) structural and functional changes as well as due to thiamine deficiency. The visceral autonomic fibers crush can be indirectly detected using standardized cardiovascular autonomic tests (assessment of heart rate variability, Valsalva maneuver, orthostatic test, deep breathing test etc.) which could evaluate the systemic autonomic dysregulation [10, 19]. They are closely correlated with the degree of delayed gastric emptying, which indicates the systemic nature of alcoholic autonomic neuropathy and the commonality of pathogenetic mechanisms [48].

Predominant esophageal motility disorders with dyscoordination, lower esophageal sphincter dystonia, gastroesophageal reflux and esophageal atony in cases of severe autonomic neuropathy are possible. These changes are likely related to vagal nerve damage and due to ethanol toxicity toward distal esophageal smooth muscle [11].

Enteropathies with malabsorption syndrome, increased intestinal wall permeability, chronic diarrhea which is associated with mucosal damage, dysbiosis, and dysregulation of motility, are distinguished. At the same time, the ethanol direct toxic effects and autonomic dysfunction contribution to these disorders remains controversial [15, 41]. Constipation (20–40 % of cases) is also considered to be the autonomic neuropathy manifestation and is associated with colonic peristalsis decrease due to parasympathetic innervation destruction together with both distal esophagus smooth muscles tone [34] and intestinal reflexes impairment [36].

The gallbladder atony is manifested by a decrease in its contractile function and may be accompanied by biliary dyskinesia as motor coordination violation. In particular, there is a decrease cholecystokinin-induced contractile response and the gallbladder with sphincter apparatus interaction dyscoordination. These changes are due to autonomic dysfunction, alcohol hepatotoxic effect and the impaired neurohumoral regulation. Symptoms can persist even after 12 months of alcohol abstinence, which indicates a long-term effect of alcohol on gastrointestinal motility and autonomic regulation [13, 17, 28].

Thus, systemic autonomic (visceral) neuropathy is formed, which in its clinical and pathogenetic characteristics resembles diabetic autonomic neuropathy and is formed under the influence of chronic alcohol intoxication and with the participation of various levels of regulation disorders - central (hypothalamic-stem), peripheral (vagus and sympathetic), intramural (enteric neuronal plexuses) as well as effector (interstitial cells of Cajal and smooth muscles) [32, 41, 45].

Chronic alcohol consumption is accompanied by respiration impaired autonomic regulation, manifested by respiratory pattern changes, decreased sensitivity to hypercapnia and hypoxia and central regulation of ventilation instability [21, 50]. The respiratory centre within the medulla oblongata, as a component of the central autonomic network, ensures the chemoreceptor signals integration and the formation of an adequate ventilatory response. Hence, sensitivity to CO_2 is realized through central chemoreceptors that respond to cerebrospinal fluid pH changes which in turn mediated by CO_2 diffusion, with subsequent respiratory neural networks activation [37]. Brainstem structures depression and impaired vagal afferentation occur which cause rhythm disorganization and respiratory regulation instability reflecting the autonomic dysfunction systemic nature [50].

Metabolic and endocrine regulation disorders are formed in conditions of prolonged exposure to ethanol. They are manifested by insulin resistance, changes in appetite, body weight imbalance and hormonal disorders [9, 44]. Pathogenetically, these changes are associated with hypothalamic-pituitary axis dysfunction, impaired insulin secretion and sensitivity as well as dysregulation of appetite hormones (leptin, ghrelin and other peptide regulators) that are under the autonomic control [16].

The hypothalamic-pituitary axis activation plays an additional important role with cortisol secretion changes and chronic stress response development. Violation of neurohumoral integration leads to energetical homeostasis disorganization and reflects the systemic nature of autonomic dysfunction in alcohol dependence.

Long-term alcohol exposure leads to immune-inflammatory processes activation which is manifested by the formation of chronic low-intensity inflammation and impaired immune homeostasis [14, 39]. Pathogenetically, these changes are associated with innate immunity activation, pro-inflammatory cytokines excessive release, oxidative stress as well as increased intestinal barrier permeability and bacterial endotoxins translocation (in particular lipopolysaccharide) [46]. The interaction between immune and autonomic regulation (neuroimmune axis) leads to dysregulation of autonomic functions and supports the systemic nature of the pathological process in alcohol dependence. Regulation of immune-inflammatory processes is performed by both parasympathetic (vagus-mediated anti-inflammatory) and sympathetic influences interaction, which balance determines the immune response nature and intensity. One could note this balance shift towards vagal activity decrease and sympathetic mechanisms relative predominance in conditions of chronic alcohol intoxication [29].

Alcohol dependence causes vascular tone dysregulation outside the cardiovascular system which is manifested by changes in microcirculation, tissue perfusion and regional bloodflow, particularly in the gastrointestinal tract, liver, and peripheral

tissues [14, 26]. These changes pathiphysiologicla mechanisms include endothelial dysfunction, decreased nitric oxide bioavailability, oxidative stress and vascular tone neurovegetative regulation imbalance [29]. Disruption between local vascular mechanisms and the ANS interaction leads to regional bloodflow disorganization and reflects the systemic nature of autonomic dysfunction in alcohol dependence.

Chronic alcohol consumption disrupts thermoregulation which manifested by body temperature instability, decreased tolerance to heat and cold stress and sweating disorders [33]. The sudomotor disorders described above should be considered not only as a diagnostic marker of small sympathetic fibers damage but also as a functional component of thermoregulation disorders, reflecting then ANS central and peripheral mechanisms interaction impairment. Pathogenetically, these changes are associated with hypothalamic centres of thermoregulation dysfunction, sympathetic (mainly cholinergic) sudomotor fibers damage and the impaired vascular tone and heat exchange neurohumoral regulation [7, 49]. Central and peripheral thermoregulatory mechanisms interaction disorganization outlines the systemic nature of autonomic dysfunction and correlates with other autonomic neuropathy manifestations in alcohol dependence, reflecting a single continuum of thermoregulation, microcirculation, and vascular tone autonomic regulation disorders.

Finally, one should conclude that chronic alcohol consumption leads to the systemic autonomic dysfunction formation with organs and regulatory circuits' multisystemic damage. These disorders involve the cardiovascular, gastrointestinal, sudomotor, thermoregulatory, respiratory, urogenital, metabolic-endocrine and immune-inflammatory systems into clinical manifestation, which reflects the alcohol impact universality as a neurotoxic and stress-associated factor.

The interrelated disorders are formed at different levels of regulation - central (hypothalamic-stem), peripheral (sympathetic and parasympathetic), intramural (enteric nerve plexuses) as well as effector (smooth muscle, endothelium, interstitial cells of Cajal) leading therefore to organism' functional systems disorganization.

The central autonomic network dysfunction plays a key role in this process, which ensures the autonomic, neuroendocrine and immune regulatory mechanisms integration. As a result, a single pathophysiological continuum of autonomic dysregulation is formed, which determines the variability of clinical manifestations, their organ specificity and alcohol dependence progression.

Limitations. The following limitations were applied when reviewing the selected literature sources: Russian-language sources and works published in journals of the Russian Federation and the Republic of Belarus were excluded. Literature sources not published in Ukrainian, English or Italian were also excluded. When analyzing the selected literature sources, cases of terminal or borderline states with loss of consciousness and associated organ and system dysfunction, primarily the nervous system, were excluded; cases of alcohol-induced neurological disorders due to ischemic and/or hemorrhagic cerebral blood flow disruption; and cases of neuropathological syndromes (epileptic, parkinsonian, and similar) due to the formation of determinant lesions in brain structures were excluded.

Conclusions

1. Chronic alcohol intoxication is associated with systemic autonomic dysfunction, which goes beyond the isolated organ disorders and reflects the generalized nature of regulatory systems damage.

2. Autonomic disorders are implemented as a multi-level process involving central (central autonomic network), peripheral and effector links, which determines the heterogeneity of clinical phenotypes.

3. The central autonomic network integrative function disturbance is a key mechanism that provides a connection between the neurovegetative, neuroendocrine and immune-inflammatory components of the pathological process.

4. Autonomic dysfunction has the character of a continuum - from subclinical changes in regulation to clinically significant organ manifestations, which determines the variability of alcohol dependence clinical manifestation and progression.

5. The sympathetic and parasympathetic influences imbalance has context-dependent and organ-specific nature which requires a differentiated assessment within individual functional systems.

6. An integrative view of alcohol dependence pathogenesis is formulated on the modern scientific data background analysis. It creates a theoretical basis for autonomic disorders personalized approaches to diagnosis, risk stratification and targeted correction.

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