Hepatic encephalopathy: definition, etiology, pathogenesis factors, clinical picture, diagnostic and treatment methods

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Definition. There are many definitions of the syndrome of hepatic encephalopathy.
Here are two, in our opinion, most successful ones.
1. *Hepatic encephalopathy* (hepatic encephalopathy) — a potentially reversible infringement of functions of the brain, resulting from acute liver, chronic liver disease and/or portosystemic shunting on vie flowing with reversible metabolic encephalopathy, cerebral edema, and chronic structural changes in the brain, mental, neuromuscular disorders and changes in the electroencephalogram [18].
2. *Hepatic encephalopathy* — a complex potentially reversible neuromuscular disorders of mental e Sgiach brain functions that occur when hepatocellular adequacy in patients with chronic liver diseases, with acute hepatitis and portosystemic bypass blood-forming character and decline of intellectual functions of the brain, personality RA stroystvami, disturbance of consciousness and changes in α-rhythm on the EEG [23].
Synonyms. Besides the term *"Hepatic encephalopathy"* — HE, sometimes use the term *"hepatargia"* and *"portosystemic encephalopathy"*.
Types of HE. It is proposed to distinguish several types of HE:
Type A. Acute form of HE, associated with acute hepatic insufficiency.
Type B. HE, due to the portosystemic bypass Blood (in the absence of liver diseases).
Type C. Chronic HE, liver cirrhosis develops, flowing from p tal of hypertension and portosystemic bypass of the blood [4].
Etiology. One of the etiologic factors HE is acute liver and insufficient accuracy, which develops in acute *fulminant hepatitis* due to Nogo massi necrosis of hepatocytes accompanied by severe impairment sudden sic tions liver, parenchymal failure with the result of endogenous hepatic coma.
Another cause of *cirrhosis* is HE (CPU) of various etiologies, when the cat is observed for combination of rum chronic hepatic failure and *portosystemic of th bypass Blood* — portosystemic HE (SSPE) having more suitable tech and e of the prediction which in some cases may also be terminated endogenous coma.
Mixed coma arises in those cases where patients with liver cirrhosis and expressed Kollath e eral circulation m assivnye developing necrosis in liver tissue [15, 18].
Pathogenesis. The pathogenesis of HE has not been sufficiently studied, there are a number of controversial positions and contradictions.
The main scientific hypothesis (theory) of the pathogenesis of HE is a *"theory of glia"* in Basic Island which is a violation of homeostasis astrocytes.
With the development of hepatocellular insufficiency and port system bypass cr on vie produced *neurotoxins* developing amino acid imbalance, there are functional disorders and astroglial swelling, and therefore *increases e pronitsa Axle blood-brain barrier* (BBB), disturbed *neurotransmission processes,* increases the activity of ion channels and ensuring reduced brain neurons and other ATP makroenergeticheskimi compounds [15].
The most valid theories of the pathogenesis of HE are:

1. toxic theory; 2. The theory of false neurotransmitters and 3. The theory of violations of exchange used γ-am inomaslyanoy acid — GABA [28, 37, 42, 50].

I. *Of End ogen neurotoxins* leading role in the pathogenesis of HE belongs *ammonia* to about tory formed mainly in the colon, kidney, and muscle tissue (with p and phe- loads) and the portal vein to the liver,joining ornithine in the urea cycle. About 50% of the ammonia produced in the liver L in the disintegration baa postglacial substances. Normally ammonia binding

(neutralization) occurs in the liver *during the synthesis of urea and the formation of glutamine.* Ammonia partially trapped in the liver tissue of claim ulyatsiey perivenous hepatocytes, where under the influence of *the enzyme glutamate* from amino acids (glutamate, ketoglutamat) *mod* involving ammonia *and glutamine zuetsya* [18] prepyats m Vuia thus its penetration in common to the first bloodstream. In addition, glutamine is synthesized in the muscles and in the brain strobitises [4, 15, 18, 28, 42].

In various acute and chronic liver diseases and Gluth synthesis of urea from ammonia and mine decreases and *develops hyperammonaemia.* Similar changes occur in the case of a port system shunting of the blood [4].

In connection with increased permeability of the BBB ammonia easily penetrates into the brain, causing a violation of the processes of neurotransmission, an increase in the activity of ionic kan and fishing and decreased ATP synthesis and provide neurons.

However, it should be noted that the most pronounced changes in HE upd and exhibits a not in neurons and astrocytes (in astroglial), accompanied by their proliferative and tion with the appearance of abnormal cells with a large nucleus, marginatsiey chromatin and nak of captive glycogen [28]. A direct relationship between the clinical severity of HE and the concentration of ammonia in the blood (hyperammonemia) was established [4, 15, 28, 30, 31, 42].

II. In addition to ammonia, *mercaptans* (methyl mercaptan), formed from methionine, as well as *short-chain fatty acids and slots* and *phenols* that are detoxified in the liver, act as neurogenic endotoxins, and in CP participate in the inhibition of Na^+/K^+ ATPase in membranes of the nervous cells. When the HE processes them obezvr e zhivaniya broken, and therefore the enzyme synthesis inhibition occurs Na^+/K^+ ATPase in the membranes of nerve cells [31, 51].

Mercaptans are formed in the large intestine as a result of bacterial hydrolysis of sulfur — containing amino acids (methionine, cysteine, etc.) and in norm are rendered harmless in the liver. With an increase in blood mercaptans in patients with HE appears *to hara lattice constant a "smell of liver"* (foetor hepatica) from the mouth. The toxic effect of mercaptans is due not only to the inhibition of the enzyme Na^+/K^+ ATPase in neuronal membranes g of the nerve tissue, but also an increase in transport of aromatic amino acids in the brain [4, 15, 18, 28].

Increasing concentrations of short chain fatty acids (SCFA), produced in the intestine from dietary fat under the action of colonic bacteria and/or p e result of incomplete breakdown of fatty acids in hepatic failure causes neurotoxic effect due to the decrease of urea synthesis in the liver and decel and it neuronal Na^+/K^+ ATPase [1, 4, 31, 38, 51].

Phenols, which are derivatives of tyrosine and phenylalanine are also formed in Kish h nick under the influence of intestinal microbiota, and their increased concentration in blood contributes to the development of hepatic coma [4, 15].

III. An important role in the pathogenesis of HE performs *an amino acid imbalance* manifests itself increase the level of aromatic amino acids (tyrosine, phenylalanine, tryptophan), which are precursors of false neurotransmitters, and the reduction of amino acids with branched chain (valine, leucine, isoleucine) [3, 4, 15, 19].

In chronic liver disease, especially with portocaval occurring anastomoses, the level of aromatic amino acids significantly increased, but contains amino acids and of a branched network, in contrast, is reduced, which leads to a reduction of the coefficient to Fisher.

K Fisher coefficient = valine + leucine + isoleucine/tyrosine + phenylalanine + tryptofan = < 1, 0 (at the rate of 3 — 4.5) [4]. In these conditions there is an excessive intake of holo hydrochloric brain in the aromatic amino acids that serve as starting material for the synthesis of false neurotransmitters (α-phenylethanolamine and oktapamin) differing susches m venno lower activity. Furthermore, these amino acid changes in the composition due vayut and decrease *dopamine* synthesis *enzyme,* which also promotes the formation of neurotransmitters [1, 22, 37, 50].

In chronic progressive liver disease increases the content three to claim Tofana in the blood and in the brain and reduces the density of postsynaptic serotonin receptors and new and serotonin levels.

IV. Another hypothesis of pathogenesis HE can serve as a *GABA-ergic theory* with a publicly which participates in the development of HE γ-aminobutyric acid (GABA), serving as the inhibitory neurotransmitter systems. Its concentration in patients with HE is increased due to a decrease in the activity of hepatic *transaminase GABA-I-governing* in the main enzyme reactions of neutralization of GABA.

Formed in the intestine, GABA enters the general bloodstream and through the BBB penetrates into the brain, where due to the swelling of astroglial has a toxic effect on the brain tissue on-hand, causing a decrease in the content of neurotransmitters and their true retse n tori and decreased levels of serotonin and 5-HT $_1$ receptor regulating sleep and dressings e-agency reaction.

Simultaneously increased content inhibitory neurotransmitter — γ-aminobutyric acid (MHA K) and GABA-ergic receptors capable Activate about Vat endogenously generated or coming from outside*benzodiazepines which* exist improve clinical manifestations HE, especially when applied trankviliz and tori [3, 4, 15].

Thus, in the pathogenesis of HE involved complex pathological factors vozdeys t vuyuschih on the brain: the endogenous neurotoxins, before all of the ammonia; aminoki with a lotus dysbi lance; a disorder in the functions of neurotransmitters and their receptors, and the accumulation of γ-aminobutyric acid — GABA, as well as an increased concentration of fatty chain fatty acids.

Clinic. When HE affects all parts of the brain, due to which its Klinichev e tion pattern observed various neuropsychiatric disorders [19, 24].

I. On the part of the psychic sphere tsya note:

1. *sleep disorders (drowsiness);* disturbance of the normal rhythm of sleep and wakefulness;
2. *disorders of consciousness:* symptoms resembling delirium; disorientation in sp e Meni and space; paranoid-hallucinatory and soporous disorders consciously and Nia; general inhibition, apathy;confusion of consciousness. With hepatic coma, consciousness is completely absent;
3. *personality disorders:* childishness, euphoria, accentuation of personality; annoyed and telnost, loss of interest; degradation of the person;
4. *intellectual disorders:* decreased attention; violation of the letter (change of the draft); loss of ability to account; inability to draw a five-pointed star; violation of the optico-spatial orientation; lengthening the execution time of Reitan's test for the combination of numbers;
5. *speech disorders:* delayed, slurred, blurred speech; monotony of voice;
6. *behavior change:* its inadequacy [9, 24, 29, 47, 49, 52].

The *Glasgow Consciousness Scale* (GCS), developed below, was developed [23].

The Glasgow Consciousness Assessment Score (GCS)

Symptom	**Severity of symptom**	**Score**
Consciousness	Oriented	5
	Confusion/confusion	4
Verbal pe action	The answer is not right	3
	Inaudible sounds	2
	No answer	1
	Executes commands	6
	A targeted reaction to pain	5
	Non-directional reaction to pain	4
The motor Reaction	Flexion reaction to pain	3
	Extensor pain reaction	2
	No reaction	1
	Spontaneous	4
Eye reaction	To vote	3
	To the pain	2
	No	1

Evaluation: a total score of 10 *to* 15 points is a sopor; 5 — 10 points — precommission; 0 — 5 points — a coma.

I. *Neuromuscular disorders:*

1. "Clapping " tremor (asterixis); increased deep tendon reflexes and muscle tone; propensity to spasticity;
2. A change in the initial increase in reflexes for areflexia ; neuromuscular disorders of the type of hepatocerebral degeneration.

II. The appearance of an unpleasant *"liver" odor* from the mouth; Respiro hyperventilation and iterated origin (due to respiratory stimulation).

It is necessary to clarify that asterixis — a "flapping" tremor bent in the dorsal n the decomposition of the brush when trying to hold a brush. The basis of the mechanism of asterixis lie violations of afferent impulses from the musculoskeletal system into the reticular formation of the brain [6, 33, 35, 36, 40, 41, 45].

Classification. A *distinction is made between the course of HE in stages* (West scale H a ven):

I. *Subclinical (latent) a step* in which a distinct clinical and simptomat ka absent, but there is a violation of standardized psychomotor tests (test connection numbers; line test).

II. *The first stage:* apathy, agitation, irritability; anxiety, euphoria; b s Stra fatigue; violations the rhythm of sleep and wakefulness; slight tremor; violation of coordination of movements; asterixis.

III. *The second stage:* drowsiness; lethargy; disorientation in time and space; neadekv m in the behavior; asterixis; dysarthria; ataxia.

IV. *The third stage:* sopor; pronounced disorientation; fuzzy speech; hyperreflexion; the presence of pathological reflexes (Gordon, Zhukovsky); myoclonia; hyperventilation.

V. *Fourth stage:* hepatic coma; Decerebrate rigidity; okulotsefalichesky ^ e nomen; no response to any stimuli.

The *International Classification of Diseases* and Related Health, 10th revision (ICD-10), published by the WHO in 1995, mention of HE not, but there are headings *"liver failure, acute and subacute"* (code K72 and K72 0.)And *"chronic hepatic untill with tatochnost"* (K72,1 cipher) [23].

Diagnostics. At early (subclinical) stage HE there are no reliable (special and physical) methods of its diagnostics.

Among the diagnostic methods, an important role is assigned to the clinical symptomatology of HE, detailed above.

In the initial stage, HE can be used for diagnostic purposes *Psi-tachometer and optic methods* (tests) [29, 47, 52], the sensitivity of which reaches 70 — 80%.

We can conditionally identify 2 groups of psychometric tests:

1. test the connection of numbers;
2. the test line and the test for the formation of dotted figures [4, 15].

1. The test of the connection of numbers is carried out by connecting groups of numbers from 1 to 25 as soon as possible (in healthy people this process takes less than 30 seconds, and at HE it is significantly longer).

2. Line test: it is necessary to draw a line in a "corridor" bounded from two sides, without touching the outside lines.

3. The test for tracing dotted figures consists in the fact that it is necessary to circle the various figures, indicated by a dotted line, in a solid line.

The test of the connection of numbers reflects the speed of the cognitive activity of the brain, and

the test line and the test of dotting figures — the precision of fine motor skills [4, 6, 15, 29, 41, 47].

II. *Laboratory and instrumental methods for the diagnosis of HE:*

1. It is advisable to examine the biochemical diagnostic test reflecting hepatic sic tion, which are determined: decrease in albumin and cholinesterase; factors of blood coagulation (prothrombin, proaccelerin, proconvertin) — in 3-4 times; increased activity of cytolysis enzymes (ALAT, ASAT), indicating necrosis in the hepatic tissue, and enzymes of cholestasis (APF, γ- GTP, LAP).

2. To establish the presence of high content of ammonia in the blood (hyperammonemia), which is determined in 80 — 90% of patients with HE.
3. Investigate the spin and nasal fluid (lumbar puncture); HE detected at a high content of s in it glutamine (more accurate technique).
4. A simple method for determining in stool and serum of short chain fatty acids (SCFA) — intestinal flora metabolites (MD Ardatskaya) with pom about schyu *GLC* cirrhotic patients, prot e repentieth with HE syndrome [1, 10, 11]. It has been established that the absolute and relative content of CLC in various biological fluids (feces, blood, cerebral fluid) with HE is significantly increased, especially long-chainCLC with more than 3 ˣ carbon atoms, and more than this index correlates quite accurately with the HE stage [31]. The method is simple enough, and its carrying out takes a little time.
5. *Method of electroencephalography* (EEG) in HE allows to set the characteristic frequency of a slowing and increasing the alpha rhythm amplitude already at the initial stage — 0.5-3 cola b/sec, and the appearance of δ-activity, starting from the 2nd stage HE.
6. *Magneto-resonance spectroscopy* (MR-C) can be considered the most reliable method of instrumental diagnostics of HE, but it is far from accessible to all. For x and HE acteristic increase signal intensity T1 basal ganglia and white matter of the brain; decrease in myoinositol/creatine ratio; and increase the peak Gluth mine in gray and white matter of the brain (sensitivity of 95 — 100% [4, 15].
7. Some authors consider it justified to use in diagnosis of HE *computer f p tomography* and *magnotno resonance tomography that* allow e opred casting presence atrophy lesions in the brain [4].
Differential diagnosis of HE should be carried out primarily with alcohol s nym delirium, subdural hematoma and Wernicke-Korsakoff syndrome.
Treatment. Therapeutic possibilities in the syndrome of HE, complicating various chronic liver disease, primarily CP, and acute liver failure, for example, with acute fulminant hepatitis, are still very limited and imperfect.
Among the factors that provoke the development of HE in diseases of the liver, it is necessary to name: 1. bleeding from varicose veins of the esophagus and stomach; 2. Portocaval shunting; 3. massive therapy with diuretics ; 4. Alcohol abuse; 5. reception of tranquilizers; 6. Various infectious processes.
Therapeutic nourishment. The main principle of diet therapy for HE is the restriction of proteins in the diet. The amount of proteins should not exceed 1-1.5 g/kg m. The total caloric intake of food is 1500-1800 kcal/day, mainly due to the consumption of fats (70-140 g/day) and carbohydrates (280-325 g/day).
Pharmacotherapy for chronic hepatic insufficiency, which occurs with the syndrome of HE.
The main thrust of therapeutic measures is the maximum reduction in the production of endogenous neurotoxins, primarily ammonia, with bacterial intestinal microflora. For this purpose, pharmacological preparations with a different mechanism of action are used.

1. *Lactulose* (dyufaklak, n ortilik) — a synthetic disaccharide, which in the thin (ileum) gut has a retarding effect on the production of the *enzyme glutaminase* in enterocytes and participates in blocking the*capture of glutamine*, thereby preventing the formation of ammonia.

   In the large intestine, lactulose inhibits the production of ammonia by bacteria, and ammonia, which has already penetrated from the intestine into the bloodstream, returns back to the lumen of the gut due to diffusion and is excreted with feces.

   In addition, lactulose causes acidification of the colon, reducing the pH from 7 to 5, which inhibits the growth of proteolytic bacteria (Clostridium, Enterobacter, Bacteroides, etc.) and stimulates the growth of endosymbiont bacteria (Bifidobacterium, Lactobacillus).

   Under the influence of lactulose, the passage of intestinal contents through the intestines is shortened due to its laxative osmotic action, which contributes to the elimination of ammonia in the urea composition.

An important effect of lactulose is the fact that it serves as a source of carbohydrates and energy of saccharolytic (useful) intestinal bacteria that break down carbohydrates.

Dose of lactulose varies from 30 to 120 ml/day. In severe cases, HE is prescribed in enemas at a dose of 300 ml in 700 ml of water. With a hepatic coma, lactulose is injected through the nasode-duodenalprobe [4, 7, 12, 15, 17, 18, 20, 32].

Instead of lactulose, *lactitol*, which is *β- galactosidosorbitol*, can be assigned, which to a lesser degree causes diarrhea and flatulence. Its dose is 30 g/day.

2. *Rifaximin (alpha-normix*) *is a* nonabsorbable antibiotic that inhibits the ammonogenic proteolytic bacterial intestinal microflora. It is prescribed in a dose of 200-400 mg 2-3 times/day (1200 mg/day) for 5-7 (up to 14) days [4, 15, 17, 34, 43]. According to the indications, other antibiotics of general desorbtion may be prescribed, preferably from the group of fluoroquinolones (ciprofloxacin in a dose of 500 mg 2 times/day, 5-7 days) for the administration of the pathogenic microflora of the large intestine.
3. The most effective of the existing modern means of treating HE and neutralizing ammonia is *L-ornithine L-aspartate (Hepa-Merz preparation*). Hepa-Merz is involved in the activation of the *key enzyme ornithine cycle — carbomoyl phosphate synthetase*, which provides urea synthesis in periportal hepatocytes as a substrate in the ornithine cycle. Aspartate stimulates the *enzyme glutamyl synthetase*in the liver, muscles and brain and serves as a substrate for the synthesis of glutamine by participating in the binding of ammonia in perivennous hepatocytes, in muscles and the brain, ensuring its utilization [2, 13, 15, 16, 26, 39, 44, 46, 53].

   In addition, Hepa-Mertz reduces the activity of cytolysis- aminotransferase enzymes (ALAT, A cAT); has anti — catabolic effect; increases tolerance to food proteins. Clinically, there is a normalization of psychometric tests and an ammonia equation in the blood.

   When HE Hepa-Merz is prescribed sequentially: first — intravenously drip 20 *to* 40 g/day in 500 ml isotonic solution (7 days); then — take inside at 9-18 g/day (another 7 days). Further treatment with thisdrug may be prolonged up to 6 months at a dose of 9 g/day [4, 15, 16, 39].

   The clinical efficacy of Hepa-Mertz in the treatment of HE has been fairly proven in controlled studies [13, 15].
4. In some cases instead of Hepa-Merz can be appointed *ornitsetil* (α-ketoglutarate ornithine) at a dose of 3-6 g/day orally after a meal or intravenously drip 10-50 g/day, but it is less effective.
5. Another pharmacological preparation, similar in mechanism of action to Hepa-Merzu, is *glutargin* (L — aspartate — L — glutamate), binding ammonia due to the formation of urea and glutamine ; In addition, it stabilizes the cellular membranes of hepatocytes [4].
6. The drug *flumazenil* is an antagonist of benzodiazepine receptors; reduces the severity of inhibitory processes in the brain in HE.

   Assigned intravenously drip in a dose of 0.4-1 mg in a 5% solution of glucose or

   0.9% solution of sodium chloride. Under the influence of flumazenil, the symptomatology of HE for 2-3 hours decreases, but it does not influence the frequency of side effects and the survival of patients [4, 9, 26].
7. *Glutamic acid* increases the stability of the macroorganism to hypoxia, reduces the activity of free radical lipid oxidation (SPOL) processes in hepatocytes ; stimulates the transmission of excitation in the synapses of the central nervous system.

   Dose: 150 ml of 1% solution in the form of intravenous drip injections.
8. *Gepasol-A* — farmakopreparat consisting of amino acids; has immunomodulatory and antioxidant effect; contributes to the regression of clinical manifestations of HE, primarily the disappearance of neurological symptoms.

   Assigned intravenously drip at a speed of 30-35 cap./m in., which corresponds to 0,08-0,1 g of amino acids per kg of mt per hour [2, 21, 26].
9. *Sodium benzoate* — krovyanosnom binds ammonia in line to form hippuric acid; activates the exchange of *"glutamate-benzoate"* in perivenic hepatocytes. Dose: 10 g/day.

Auxiliary agents for the treatment of HE:

The use of zinc as a food additive, providing an antioxidant effect in HE, is a cofactor of urea synthesis; but its therapeutic significance is small [48].

With regard to the appointment of hepatoprotectors (ademethionine — heptral) in HE, recommended by some authors [8, 27], as well as corticosteroids, then we consider their use as insufficiently justified.

In acute liver failure with the development of hepatic coma and cerebral edema, treatment is performed in the intensive care unit using the same pharmacological drugs as in chronic liver failure, but at higher doses.

Additionally, the following treatment options can be recommended:

1. Intravenous drip of 5% glucose solution with vitamins (ascorbic acid) and electrolytes (potassium chloride, calcium gluconate).
2. Intravenous injection of lyophilizate Ornithol in a dose of 15-25 g/day in an isotonic solution of sodium chloride or glucose.
3. High cleansing enemas for cleansing the colon.
4. To correct the acidosis, intravenous injection of 5% sodium hydrogencarbonate is used, and for the control of alkalosis, intravenous injections of *gelatin* (250-500 ml colloidal 8% solution) and ascorbic acid.
5. Other drugs (according to indications: mannitol ; polarizing mixture).
6. The only effective method of treating acute hepatic insufficiency is *liver transplantation* [5, 14, 25, 48].

Successful therapy of HE with various liver diseases requires continuous and prolonged use of effective and safe therapeutic agents.

References:

1. Ардатская М. Д. Печеночная энцефалопатия: определение, вопросы патогенеза, клиника, методы диагностики и принципы лечебной коррекции / М. Д. Ардатская, Л. В. Баркалова, О. Н. Минушкин // Фарматека. — 2011. — № 12. — С. 23–28.
2. Буеверов А. О. Рациональное ведение больных с печеночной энцефалопатией / А. О. Буеверов // Русск. мед. журн. — 2003. — № 14. — С. 7–12.
3. Гастроэнтерология. Гепатология / Под ред. Н. А. Бука, Н. Р. Колледжа и Б. В. Уолкера / Пер. с англ. — М., 2009.
4. Губергриц Н. Б. Основы практической гепатологии / Н. Б. Губергриц. — М., 2015. — С. 161–189.
5. Иванов А. Г. Оптимизация терапии больных циррозом печени с энцефалопатией / А. Г. Иванов, В. В. Трусов // Клин. мед. — 2008. — № 6. — С. 62–66.
6. Клинические аспекты печеночной энцефалопатии у больных хроническими заболеваниями печени / Л. Ю. Ильченко, О. Н. Топчеева, Е. В. Винницкая [и др.] // Consilium medicum. — Прил.: Гастроэнтерология. — 2005. — № 1. — С. 23–28.
7. Лактулоза в лечении печеночной энцефалопатии / И. С. Шулятьев, Л. Ю. Ильченко, Е. В. Винницкая [и др.] // Экспер. и клин. гастроэнтерол. — 2003. — № 5. — С. 38–41.
8. Маев И. В. Лечение и профилактика печеночной энцефалопатии гепатопротекторами / И. В. Маев, К. Г. Гуревич // Российск. журн. гастроэнтерол., гепатол. и колопроктол. — 2001. — № 4. — С. 41–45.
9. Майер К. П. Гепатит и последствия гепатита / К. П. Майер // Перев. с нем. — М., 1999. — С. 341–353.
10. Минушкин О. Н. Короткоцепочечные жирные кислоты в диагностике печеночной энцефалопатии и оценке эффективности препарата лактулозы (дюфалака) / О. Н. Минушкин, М. Д. Н. А. Ардатская, Елизарова // Клинич. фармакол. и тер. — 2001. — № 10 (5). — С. 9–12.
11. Минушкин О. Н. Метаболиты кишечной микрофлоры и печеночная энцефалопатия: использование в диагностике, прогнозировании течения и оценке лечения / О. Н.

Минушкин, М. Д. Ардатская, Н. С. Иконников // Российск. журн. гастроэнтерол., гепатол. и колопроктол. — 2001. — № 4. — С. 33–40.
12. Минушкин О. Н. Фармакоэкономическая эффективность длительного применения дюфалака при циррозе печени, осложненном печеночной энцефалопатией / О. Н. Минушкин, М. Д. Ардатская, Н. А. Елизарова // Клин. перспективы гастроэнтер., гепатол. — 2004. — № 4. — С. 22–26.
13. Надинская М. Ю. Гепа-Мерц (орнитин-аспартат) в лечении печеночной энцефалопатии при циррозе печени / М. Ю. Надинская, С. Д. Подымова // Российск. журн. гастроэнтерол., гепатол. и колопроктол. — 1998. — № 1. — С. 53–58.
14. Надинская М. Ю. Лечение печеночной энцефалопатии у больных циррозом печени с позиции доказательной медицины: мифы и реальность / М. Ю. Надинская // Consilium medicum. Прил. Гастроэнтерология. — 2007. — № 1. — С. 17–28.
15. Надинская М. Ю. Печеночная энцефалопатия // М. Ю. Надинская / В кн.: Болезни печени и желчевыводящих путей / Под ред. В. Т. Ивашкина. — М., 2002. — С. 177–189.
16. Опыт применения препарата «Гепа-Мерц» в лечении хронической печеночной энцефалопатии / И. С. Шульпекова, Л. Ю. Ильченко, Е. В. Винницкая [и др.] // Клинич. перспективы гастроэнтерол., гепатол. — 2005. — № 6. — С. 17–23.
17. Оценка эффективности комплексной терапии печеночной энцефалопатии у больных циррозом печени / И. В. Маев, Е. С. Вьючнова, Е. Г. Лебедева [и др.] // Клин. мед. — 2002. — № 5. — С. 42–45.
18. Подымова С. Д. Болезни печени: руководство для врачей / С. Д. Подымова. — М., 2005. — С. 109–127.
19. Подымова С. Д. Гепатогенная энцефалопатия / С. Д. Подымова // Российск. журн. гастроэнтерол., гепатол. и колопроктол., 1997. — № 1. — С. 88–92.
20. Подымова С. Д. Печеночная энцефалопатия. Клинические особенности. Диагностика. Лечение / С. Д. Подымова // Consilium medicum: Хирургия. — 2001. — С. 19–22.
21. Родченко В. Г. Гепасол-А в лечении хронических заболеваний печени с проявлениями системной печеночной энцефалопатии / В. Г. Родченко, О. Н. Родченко // Российск. журн. гастроэнтерол., гепатол. и колопроктол. — 2002. — № 2. — С. 73–76.
22. Родченко В. Г. Печеночная энцефалопатия / В. Г. Родченко, О. Н. Родченко. — СПб. ; М., 2005.
23. Циммерман Я. С. Классификации гастроэнтерологических заболеваний и клинических синдромов / Я. С. Циммерман, И. Я. Циммерман. — 5ое изд. — Пермь, 2016. — С. 127–131.
24. Шерлок Ш. Заболевания печени и желчных путей / Ш. Шерлок, Дж. Дули // Пер. с англ. — М, 1999.
25. Шульпекова Ю. О. Возможности коррекции метаболических нарушений при печеночной энцефалопатии / Ю. О. Шульпекова, В. Т. Ивашкин // Русск. мед. журн. — 2005. — № 7 (2). — С. 77–81.
26. Шульпекова Ю. О. Печеночная энцефалопатия и методы ее коррекции / Ю. О. Шульпекова // Consilium medicum. — 2005. — № 1. — С. 26–31.
27. Эффективность различных гепатопротекторов при печеночной энцефалопатии / О. В. Любшина, В. Е. Гречко, Ф. Л. Вертнин, И. В. Маев // Клин. мед. — 1999. — № 10. — С. 17–20.
28. Albert N. Ammoniainduced depolarization of calturedrat cortical astrocytes / N. Albert, H. Koller, M. Siebler // Brain. Res. — 1998. — Vol. 782, No 1–2. — P. 261–270.
29. Attention deficits in minimal hepatic encephalopathy / K. Weissenborn, S. Heidenreich, J. Ennen [et al.] // Metab. Brain Dis. — 2001. — Vol. 16, No 1–2. — P. 13–19.
30. Butterworth R. E. Portal-systemic encephalopathy: a disorder of neuron- astracitic metabolic trafficking / R. E. Butterworth // Dev. Neurosci. — 1993. — Vol. 15. — P. 313–315.

31. Clausen M. R. Serum levels of short chain fatty acids in cirrhosis and hepatic civa / M. R. Clausen, P. B. Mortensen, F. Bendsen // Hepatology. — 1991. — Vol. 14. — P. 1040–1045.
32. Comparison of refaximin and lactulose for the treatment of hepatic encephalopathy : a prospective randomized stady / Y. H. Paik, K. S. Lee, K. N. Han [et al.] // Yonsei Med. J. — 2005. — Vol. 46, No 3. — P. 399–407.
33. Diseases of the liver and biliary tract. Standartization of nomenclature, diagnostic criteria and prognosis / Eds. M. Carol, S. Levi [et al.]. — N. Y. : Raven Press, 1994. — 205 p.
34. Evalution of the efficacy and safety of rifaximin in the treatment of hepatic encephalopathy : a doube-blind, randomized, dose-finding study, multi-centre study / R. Williams, O. F. James, T. F. Warnes [et al.] // Eur. J. Gastroenterol., Hepatol. — 2000. — Vol. 12. — P. 203–206.
35. Ferenci P. Hepatic encephalopathy / P. Ferenci // Abstracts. New trends in Hepatology. Falk symposium No 92. — St.-Peterburg, Russia, 1996. — P. 46–47.
36. Fight R. D. The neurogical disorder associated with acute and chronic liver diseases / R. D. Fight // Liver Intern. — 2004. — Vol. 12. — P. 23–24.
37. Fischer J. E. Falsche neurotransmitter and hepatic failure / J. E. Fischer, R. J. Baldessarini // Lancet. — 1971. — Vol. 11. — P. 75–80.
38. Geroc W. Ammonia detoxication by the liver: new concepts of glutamin and urea synthesis / W. Geroc, D. Haussinger. — Brunner H. Thaler Hepatology. — N. Y., 1985. — P. 211–221.
39. Grundreiff K. Efficacy of L-ornithine-L-aspartate granules in the treatment of chronic liver disease / K. Grundreiff, J. Lambert-Baumann // Med. Welt. — 2001. — Vol. 52. — P. 2019–2026.
40. Hepatic encephalopathy — definicion, nomenclature, diagnosis and quantification: final report of the working party at the 11th World Congress of Gastroenterology, Vienna, 1998 / P. Ferenci, A. Lockwood, K. Mullen [et al.] // Hepatology. — 2002. — Vol. 35. — P. 716–721.
41. Hepatic encephalopathy: syndromes and therapies / Eds. H. O. Conn, J. Bircher. — Bloomington, Illionis : Medi- Ed. Press. — 1994. — 243 p.
42. Hindfelt B. Effect of acute ammonia intoxication on cerebral metabolism in rats with portocaval shunts / B. Hindfelt, F. Plum, T. Duffy // J. Clin. Invest. — 1977. — Vol. 59. — P. 386–396.
43. Levy C. Hospitalization during the use of rifaximin versus lactulose for the treatment of hepatic encephalopathy / C. Levy, J. Phillips // Dig. Dis. Sci. — 2007. — Vol. 52. — P. 737–741.
44. L-ornithine-L-aspartate vs. placebo in the treatment of hepatic encephalopathy : a meta-analysis of randomized placebo-controlled trials using individual data / A. Delker, R. Jalan, M. Schumacher, G. Comes // Hepatology. — 2000. — Vol. 32, No 2. — P. 310A.
45. Neuropsichological abnormalites in cirrhosis include learning impairment / M. Ortiz, J. Cordoba, C. J. Jacas [et al.] // J. Hepatol. — 2006. — Vol. 44. — P. 104–110.
46. Oral L-ornithine-L-aspartate therapy of chronic hepatic encephalopathy: results of placebo-controlled double-blind study / S. Stauch, G. Kircheis, G. Adler [et al.] // J. Hepatol. — 1998. — Vol. 28. — P. 856–864.
47. Patients with minimal hepatic encephalopathy have poor insight into their driving skills / J. S. Bajaj, K. Salian, M. Hafeezullah [et al.] // Clin. Gastroenterol., Hepatol. — 2008. — Vol. 6. — P. 1135–1139.
48. Role of zinc in subclinical hepatic encephalopathy: comparison with somatosensory-evoked potentials / S. S. Yang, Y. C. Lai, T. R. Chiang [et al.] // J. Gastroenterol., Hepatol. — 2004/ — Vol. 19. — P. 375–379.
49. Sandhir S. Portal-systemic encephalopathy / S. Sandhir, H. Ir. Weber // Cur. Pract. Med. — 1999. — Vol. 2. — P. 103–108.
50. Schafer D. F. Hepatic encephalopathy and the γ-aminobutiric acid neurotransmitter sestem / D. F. Schafer, E. A. Jones // Lancet. — 1982. — Vol. 16. — P. 18–20.

51. Sinergism between ammonia and fatty acids in the produccion of coma inplications for hepatic coma / F. J. Zieve, L. Zieve, W. M. Doizaki [et al.] // J. Pharmacol. Exp. Ther. — 1974. — Vol. 191. — P. 10–16.
52. Subclinical hepatic encephalopathy impairs daily functioning / M. Groeneweg, J. Quero, I. Bruijn [et al.] // Hepatology. — 1998. — Vol. 28, No 1. — P. 45–49.
53. Therapeutic efficacy of L-ornithine-L-aspartate infusions in patients with cirrhosis and hepatic encephalopathy: results of placebo-controlled double-blind study / G. Kircheis, R. Nillius, K. Held [et al.] // Hepatology. — 1997. — Vol. 25, No 6. — P. 1351–1360.

Hepatic encephalopathy: definition, etiology, pathogenesis factors, clinical picture, diagnostic and treatment methods

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Key words: hepatic encephalopathy, etiology, pathogenesis, diagnosis, treatment

The review presents modern information on such an actual clinical problem as hepatic encephalopathy syndrome upon acute and chronic hepatic insufficiency: its definition, etiology, detailed description of pathogenesis factors, clinical features, classification, diagnostic methods (clinical and laboratory-instrumental). The possibilities of treatment are fully highlighted: dietotherapy and pharmacotherapy of hepatic encephalopathy upon acute and chronic hepatic insufficiency.