Review
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Modern Approaches to Enteral Nutrition in Intensive Care

M.M. Potskhveriya[1, 2], Yu.S. Goldfarb[1, 2]✉, V.A. Matkevich[1, 2], A.A. Ryk[1]

Department of External Scientific Relations
[1] N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department
3 B. Sukharevskaya Sq., Moscow, 129090, Russian Federation
[2] Russian Medical Academy of Continuing Professional Education of the Ministry of Health of the Russian Federation
2/1 bldg 1 Barrikadnaya St., Moscow, 125993, Russian Federation

✉ **Contacts:** Yuri S. Goldfarb, Doctor of Medical Sciences, Professor, Head of the Department of External Scientific Relations of N.V. Sklifosovsky Research Institute for Emergency Medicine.
E-mail: goldfarb@mail.ru

ABSTRACT

The analysis of the literature data allowed us to establish that today enteral nutrition (EN) is unanimously recognized by specialists as the preferred method of nutritional therapy, which significantly affects the course of critical conditions (CC). The use of EN now affects almost the entire nosology that forms the cohort of such patients. To the least extent, the scientific analysis of the possibilities of EN touched acute poisoning, where, given the special danger to life of their severe forms, there are great prospects for further research of this kind. It is especially emphasized that EN mainly in the first 24-48 hours from the onset of the disease mostly affects the achievement of positive results of treatment of CC, accompanied by an improvement in metabolic processes in organs and tissues. There is great interest in studying the pathogenesis of CC by assessing changes in homeostasis indicators using modern laboratory and instrumental control, which strengthens the scien-tific basis of EN. At the same time, it also contributes to the disclosure of his sanogenesis. Considering that, along with immunological shifts, the formation of oxidative stress and hemorheological disorders is of particular importance in the pathogenesis of CC, being to a large extent involved in the development of endogenous intoxication and their irrevers-ibility, studies on EN in this field are promising, which, in our opinion, are still are very limited, and in relation to hemorheology, according to the data available to us, are not represented at all. There are also no generalized up-to-date data on the economic compo-nent of EN. Further improvement of EN, as well as the corresponding organizational measures, it seems, can bring this method to a higher level of efficiency and, accordingly, safety, which, combined with the economic advantages of EN, will expand the possibilities of its implementation in clinical practice.**AIM OF STUDY** Standardization of staged treatment of patients with severe concomitant closed abdominal trauma.

Keywords: enteral nutrition, intensive care, critical conditions, acute poisoning
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Affiliations

Mikhail M. Potskhveriya	Candidate of Medical Sciences, Head of the Scientific Department of Acute Poisoning and Somatopsychiatric Disorders, N.V. Sklifosovsky Research Institute for Emergency Medicine, Associate Professor of the Department of Clinical Toxicology, Russian Medical Academy of Continuing Professional Education; https://orcid.org/0000-0003-0117-8663; potskhveriya@mail.ru; 30%: research idea, suggestions for improving the quality of work, editing the text of the article
Yuri S. Goldfarb	Doctor of Medical Sciences, Professor, Head of the Department of External Scientific Relations, Researcher of the Department of Acute Poisoning and Somatopsychiatric Disorders, N.V. Sklifosovsky Research Institute for Emergency Medicine, Head of the Department of Clinical Toxicology, Russian Medical Academy of Continuing Professional Education; https://orcid.org/0000-0002-0485-2353; goldfarb@mail.ru; 30%: research idea, search and selection of publications on the topic of the article, writing work papers on the version of the article and its revision
Viktor A. Matkevich	Doctor of Medical Sciences, Scientific Consultant of the Department of Acute Poisoning and Somatopsychiatric Disorders of the N.V. Sklifosovsky Research Institute for Emergency Medicine, Associate Professor of the Department of Clinical Toxicology, Russian Medical Academy of Continuing Professional Education; https://orcid.org/0000-0001-6765-6619; matkevich@mail.ru; 20%: the idea of the research, editing the text of the article, entering the results of one's own research
Alla A. Ryk	Candidate of Medical Sciences, Senior Researcher, Department of General Rehabilitation, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-3968-3713, rykaa@sklif.mos.ru; 20%: suggestions for improving the quality of work, editing the text of the article

PEM – protein-energy malnutrition
DC – diene conjugates
GIT – gastrointestinal tract
AVL – artificial ventilation of the lungs
IC – intensive care
CC - critical conditions
MDD – malonic dialdehyde
NS – nutritional support
NT – nutritional therapy
DAIC – Department of Anesthesia and Intensive Care
ICU – intensive care unit
AP – acute poisoning
DRIC – Department of Reanimation and Intensive Care
PN – parenteral nutrition
IIS – intestinal insufficiency syndrome
SAP - severe acute pancreatitis
TBI – traumatic brain injury
EI – endogenous intoxication
EN – enteral nutrition

BRIEF HISTORY OF THE ISSUE

Enteral nutrition (EN) was used as one of the therapeutic agents already in the 1500s. BC in Ancient Egypt and Ancient Greece. The current stage in the development of EN as a scientifically grounded system for prescribing nutritious matters (mixtures) introduced through the stomach or small intestine is largely due to the appearance in the second half of the 20th century intensive care units (ICU), when the attention of resuscitators was drawn to the need to eliminate energy disorders in patients. This was the reason for the development of technologies of parenteral nutrition (PN) and EN, the use of which made it possible to significantly improve the results of treatment of severe patients [1, 2].

In our country in 1975 at the Institute of Nutrition of the USSR Academy of Sciences under the leadership of academician A.A. Pokrovsky, the first domestic mixtures for EN - "enpits" were created, and subsequently their industrial production was launched; more than 300 mixtures for EN are currently used [3, 4].

The creation of the scientific basis for EN is largely due to the discovery of A.M. Ugolev in 1959, intestinal membrane digestion and studies by Yu.M. Halperin and his school, performed at the N.V. Sklifosovsky Emergency Medicine Research Institute (RI) and led to the discovery of heterophase digestion in the intestinal cavity and the conduct of fundamental researchs related to the homeostation of the enteric environment, as well as the development of the concept of intestinal insufficiency syndrome (IIS). On this basis, a whole class of solutions and nutritional mixtures was created that had mimicked the composition of chyme, intended for programmed EN in the early postoperative period, which made a great contribution to further research in the field of EN, as well as the formation of EN priority over PN in subsequent years. In this regard, the physiological nature of EN is fundamental, with the help of which, in contrast to PN, it is possible to ensure the rate of intake of nutrients from the enteral into the internal environment of the patient's body, which is identical to that during natural digestion, since it is regulated by the body itself [3, 5–10, 11].

USE OF EP IN INTENSIVE MEDICINE

Currently, EN is actively used in many diseases requiring emergency care. Definition of indications for it is paramount. So, in critical conditions (CC) caused by acute lung injury and acute respiratory distress syndrome by assessing the dynamics of the level of serum proteins (albumin, transferrin and transthyretin) in the blood, it was found that such for nutritional support (NS) is the impossibility of self-sufficiency of the body's energy requirements. [12]. The onset of EN within 48 hours is associated with a positive outcome of cardiopulmonary resuscitation. In 259 patients, EN was also accompanied by a statistically significant decrease in the need for vasopressor therapy and its timing [13, 14].

Among acute surgical diseases, EN is recognized as the most important component of treatment for severe acute pancreatitis (SAP), as a result of which the risk of developing early multiple organ failure and septic complications is significantly reduced. In the latter case, against the background of early EN in the immediate postoperative period, there was a more pronounced decrease in mortality (from 28.6 to 15.6%), the frequency of sepsis (from 17.1 to 6.25%), pulmonary complications (from 40 to 15, 6%), suppuration of postoperative wounds (from 68.6 to 28%) and gastrointestinal bleeding (from 25.7 to 3.1%) than with the use of PN and the "standard surgical diet". In a study conducted on 500 patients, it was found that with EN, the duration of hospitalization, the risk of developing pancreatic infection and associated complications, as well as organ failure and [the need for] surgical intervention were statistically significantly less than with PN [15-17]. There is a good compatibility of EN with other methods of treatment: the combination of regional arterial infusion with early EN in 100 patients with SAP was accompanied by the best statistically significant indicators for assessing the severity of their condition according to the APACHE II scale and the concentration of glucose, serum amylase, leukocytes, C-reactive protein in the blood, tumor necrosis factor-□, interleukins (IL) -6, IL-10 and IL-17, as well as the level of albumin and serum calcium; there were shorter periods of relief of abdominal pain, the first defecation in IIS, as well as the duration of hospitalization and the frequency of complications compared with the results of traditional treatment [18].

When used in the complex of treatment of early EN with widespread peritonitis, the restoration of intestinal motility and indicators of protein metabolism was accelerated, and infectious complications developed less often; the frequency of deaths has decreased - from 19.5 to 14.3%. The benefits of early EN are also confirmed by the results of a retrospective study conducted in the intensive care unit (ICU), which included 88 adult patients with abdominal trauma who received EN within 72 hours after admission (28 patients) or later (60 patients). At the same time, there were statistically significantly lower incidence of infectious complications (17.9% versus 40%) and the duration of DRIC and hospital stay in general. Deaths on the 28th day against the background of early EN were not observed, whereas with its delayed onset, it was 5%, although statistically insignificant [19–21].

Early EN from day 1 promoted the restoration of the main functions of the transplanted small intestine and its preparation for the assimilation of polysubstrate mixtures and natural food products. In general, during abdominal operations, the importance of prescribing EN in the early postoperative period is emphasized, as it is a more physiological method of NS, contributing to the patient's adaptation to this period and a reduction in ICU stay, as well as in the hospital in general [22, 23].

The use of EN is recognized as necessary and effective in severe craniocerebral (TBI) and concomitant trauma. When it was included in treatment with 58% of the calculated energy and 53% of the calculated protein requirement, higher rates of their consumption were achieved, which contributed to the acceleration of patient recovery [24, 25].

The use of various NS programs, including EN, in severe non-traumatic intracerebral hemorrhages had a positive effect on the parameters of immunity, as well as on the severity of protein-energy malnutrition (PEM) present in this case, as in other CC, which contributed to the prevention of pulmonary infectious complications with a significant decrease in their frequency (from 70 to 40%) and the rate of development of pneumonia, the duration of artificial lung ventilation (AVL) and treatment in the DRIC; it was noted that the presence of PEM in stroke reaches 40%, and in neurosurgical patients - more than 60% [26-28].

In severe polytrauma on the background of EN, the length of stay of patients in the department of anesthesia and intensive care (DAIK) was reduced by an average of 3 days (from 19.9 ± 1.2 to 16.9 ± 1.4). It was also noted that the first 3-5 days of intensive therapy (IT) according to the PEP uP protocol can reduce the risks of developing multiple organ failure, which follows from a decrease in the total score when assessed on the SOFA scale from 4-7 to 1-4. Early EN with extended protein-caloric supply allows to improve the adequacy of the protein-energy resource requirements in the acute period of polytrauma, which can affect the decrease in the incidence of complications and the duration of patients' stay in DAIC. A study including an assessment of the effectiveness of EN in trauma in 126 people showed that earlier EN was accompanied by a significant decrease in mortality [29, 30].

However, doubts are expressed about the effectiveness of EN in sepsis, where, at the same time, the replenishment of energy inputs and nutrients is very important [31, 32].

In the case of thermal injury, the positions of the EN in recent years have been seriously revised in favor of the EN before the PN. As a result of the analysis of the literature data, it was concluded that the prevention of complications from the gastrointestinal tract (GIT) can be achieved only by ensuring its functioning, and therefore the recommendations of EN and its early onset (no later than 24-48 hours) were supported [33].

We have met only an occasional reports about the use of EN in acute poisoning (AP). For example, in AP with corrosive substances, EN is recognized as one of the most important therapeutic links. Correction using various methods of EN PEM in these cases significantly promotes faster healing of upper GIT injuries, stabilization of biological, immunological and metabolic parameters and, due to active influence on the nature of inflammatory infiltration, prevention of perforations and progressive fibrosis, esophageal and gastric stenosis with subsequent reduction of the treatment time in a hospital. In this case, it is recommended to assess the dynamics of serum levels of total protein, albumin, transferrin and the absolute number of lymphocytes [34–36]. In severe AP with organophosphate pesticides, it was demonstrated in 50 patients that early EN, started within 24 hours, was accompanied by a statistically significantly faster improvement in their condition, assessed by the APACHE II scale, than when EN was used after 24–72 hours [37].

Analysis of the EN results use in CC has led to the conclusion that early EN, contributing to a decrease in the risk of complications and mortality, especially after 96 hours of admission to the DRIC, is possibly a necessary condition for the patient's subsequent survival. It is also emphasized that even when some components of NS can only be administered parenterally, the use of EN is desirable [38–40].

It was also noted that PN may be accompanied by such complications as hyperglycemia, hypertriglyceridemia, impaired pulmonary function and increased thrombus formation. Conducting EN in such cases turned out to be favorable: for example, the use of mixed artificial nutrition (EN and PN) in severe concomitant TBI did not lead to hypertriglyceridemia - the concentration of triglycerides in the blood 2 hours after the start of the infusion was normal, and did not cause disturbances in pulmonary gas exchange - the ratio of oxygen tension in arterial blood to the fraction of oxygen in the inhaled mixture (PaO2 / FiO2) was also normal, which made it possible to achieve the goals of nutritional therapy (NT) [41, 42]. Similar results were obtained against the background of mixed artificial nutrition in CC caused by non-traumatic intracranial hemorrhages - only the development of minor hyperglycemia was noted 2 hours after the onset of PN [43].

The advantages of EN are confirmed by in-depth statistical analysis of its results. A review of seven randomized controlled trials in 527 patients with burn injuries, including 958 full-text articles, showed that, compared with all other types of nutritional support, early EN was accompanied by statistically significant reduction in mortality, frequency of the gastrointestinal bleedings, sepsis, renal failure, and hospitalization duration. In another study, which included an analysis of 699 full-text articles and sixteen randomized controlled trials in 3225 seriously ill patients, it was found that the onset of EN within 24 hours was accompanied by a decrease in mortality and the likelihood of pneumonia compared with delayed EN [44–48].

IMPROVEMENT OF THE METHODS AND COMPOSITION OF EN WITH ITS USE IN INTENSIVE MEDICINE

One of the most important issues in the use of EN is its energy reserve. Thus, with isolated TBI, the daily energy requirement was calculated as 25–30 kcal / kg, and with concomitant injuries - up to 35–50 kcal / kg (the volume of injuries was taken into account). The target level of daily calorie intake was achieved on average in 2.8 and 4.1 days when using continuous and intermittent EN, respectively; more rare stool in the first case indicated that with continuous delivery the nutrient mixture was absorbed better than with intermittent one [25]. When correcting PEM using ET, it is recommended to use indirect calorimetry, since the calculation methods, according to the authors, do not provide reliable information. In the absence of the possibility of indirect calorimetry, the Penn State formula is considered preferable, and not the Harris – Benedict equation, when using which the correct introduction of ET by caloric was achieved only in 24.3% of cases [49–52].

With SAP, the delivery of nutritional mixtures to the patient was realized in three ways: fibrogastroduodenoscopic insertion of a probe into the initial section of the small intestine, suboperative nasogastrointestinal intubation and formation of a suspension jejunostomy according to Witzel, while official nutritional formula was used in combination with probiotic Saccharomyces boulardii (I-745) and metabolic corrector - malate citrulline. The results were an accelerated recovery of peristalsis and a positive dynamics of

microstructural changes in the mucous membrane of the small intestine, as well as faster cleansing of the purulent-necrotic focus during programmed relaparotomies.

Taking into account the fact that conservative methods - the installation of a nasogastric or nasoenteric probe, are used for short-term EN (up to 4 weeks), for a longer NS, surgical methods are used - gastro- and jejunostomy. Recently, percutaneous endoscopic gastrostomy has become popular, which, due to its technical simplicity, safety and good tolerance, provides ample opportunities in the treatment of various categories of critically ill patients [40, 53, 54].

The important questions are the definition of the beginning moment of the EN and the tolerance to it. The use of a water evacuation gastric sample by intragastric probe introduction of distilled water with fixation by means of ultrasound examination of of the beginning time of its evacuation from the stomach into the duodenum, if it does not exceed 20 minutes, allows one to proceed to EN [55], and to determine the tolerance to EN , intra-abdominal pressure measurement through a urinary catheter is suggested before its onset, the most typical value of which for EN intolerance was 14 mm Hg. [56].

For practical purposes, the evacuation of gastric contents during EN is also measured by direct (scintigraphy) or indirect (absorption of drugs and carbohydrates, breath samples using isotopes) tests. This demonstrated that the use of "energetically dense formulas" to increase calorie intake in severely ill patients does not achieve its goal due to the slower evacuation from the stomach. However, a prospective, randomized, double-blind, parallel-group and multicenter study in 112 patients in 5 DRIC by using AVL showed that an increase in the caloric content of thesolution for EN from 1.0 to 1.5 kcal / ml led to an increase in calorie delivery by 46% without side effects [57-59].

The adaptation of nutritional mixtures for solving the EN problems is of great importance. Low-carbohydrate EN may serve as a non-insulin alternative for the treatment of stress hyperglycemia in critically ill patients. At the same time, in 52 patients, its use was accompanied by a trend towards a moderate but statistically significant decrease in the average blood glucose level (7.8 ± 1.0 versus 8.4 ± 1.1 mmol / L) and a significantly lower need for insulin administration in terms of compared with the results of standard EN, which may be important in diabetes mellitus. Attention is paid to adding fiber to nutritional mixes. Examination of about 120 patients on the background of AVL and probe EN revealed that with "cellular" EN (fibrinized food mixture), gastrointestinal complications (45% and 73%, respectively), mainly diarrhea, develop much less frequently. This makes it possible to avoid frequent interruptions in nutrition, which cause protein-energy deficiency [60, 61].

Thanks to the accurate definition of the pharmacological role of individual nutrients in metabolism and immunomodulation (amino acids - glutamine, arginine, taurine, including branched-chain ones - leucine, isoleucine, valine; lipids - □-3-fatty acids, medium-chain triglycerides; nucleotides, etc.) mixtures have been developed, which include these metabolically important compounds, which in fact are indispensable components of nutrition. □-3-fatty acids are precursors of the synthesis of a number of leukotrienes and prostanoids, which have anti-inflammatory effects in sepsis and purulent-septic complications, and therefore (primarily eicosapentaenoic acid) are included in the mixtures of this group as an essential component. Mixtures containing one or more of these nutrients were called "immune" - given the important role of the included nutrients in the process of immunomodulation, or "stressful", that is, designed for use in the most severe CC. These mixtures may contain glutamine, arginine, taurine, carnitine, selenium, chromium, molybdenum, yeast ribonucleic acid, soluble dietary fiber, and □-3 fatty acids [62].

From this point of view, the introduction of enteral glutamine into the composition of the mixture for immune nutrition "Intestamin" in CC caused by intracranial hemorrhages contributed to the early onset of EN, a significant decrease in the frequency of pneumonia and effective elimination of the antigenic load. In the main group, where 'Intestamin' was used, in contrast to the comparison group, there was no increase in the blood content of circulating immune complexes of a small size - the most difficult to remove complexes that contribute to the maintenance of the inflammatory process due to endothelial alteration. In addition, in the main group there was a clear tendency to an increase in the absolute and relative content of T-lymphocytes in the blood, in contrast to a decrease in these indicators in the comparison group [28].

In similar cases, the use of EN with the inclusion of alanine-glutamine prevents the development of severe forms of nutritional deficiency, aggravation of the initial depression of cellular and humoral immunity, which makes it possible to reduce the development frequency of pneumonia, postpone its development, reduce the

duration of AVL and the duration of treatment in the intensive care unit. It was also noted that EN with the traditional scheme using a multicomponent mixture was accompanied by a high incidence of nutritional deficiency, which may result in a statistically significant decrease in the level of immunoglobulins G in the blood with an increase in the incidence and severity of purulent-septic complications and therefore requires additional PN [26, 63].

Positive clinical results (a decrease in mortality from 30 to 20%) were also obtained in cardiac surgery using the "Nutrikomp Immune Liquid" immune mixture (1.3 kcal / ml) containing 6.67 g / 100 ml of protein, including 2 g / 100 ml of glutamine, and the blood level of prealbumin and transferrin is regarded as a highly sensitive marker of the effectiveness of EN. A study in 1056 patients with trauma confirmed the significance of transthyretin in this regard, the changes in blood levels of which were associated with enteral calorie intake [64, 65].

Recognizing the priority of EN in NS of patients with long-term impairment of consciousness, who are on AVL , it is recommended to take into account the absorption capacity of the GIT, and in case of its violations, preference should be given to semi-element enteral mixtures with the addition of digestive enzymes and PN. A positive effect after transplantation of the small intestine was also noted when using a monomeric-saline enteral solution and a mixture containing pharmaconutrients (glutamine, antioxidants, and tributyrin), as well as a half-element mixture from day 5, polymer mixtures and dietary food [66, 22].

In case of thermal burns, the results of treatment are improved when glutamine is included in the EN, increased doses of trace elements (copper, selenium and zinc), as well as EN is carried out in accordance with the data of indirect calorimetry. The active participation of calcium and manganese, which promotes its absorption, in enteral metabolism has been established. EN with the addition of vitamin C, thiamine and corticosteroids also shows promising results. With the development of CC in 30 patients, taking into account the violation of the composition of the intestinal ecoculture, a microbial cell preparation was included in the EN, which was accompanied by a more rapid recovery of intestinal function and required a shorter duration of AVL and treatment in the DRIC [33, 67–70].

In 106 patients with sepsis, isocaloric, isonitrogenic probe EN was used with the addition of eicosapentaenoic and β-linolenic acids, which have anti-inflammatory effects.

When compared with the results of the comparison group, in the evaluated group, as a rule, statistically significantly less pronounced manifestations of sepsis / septic shock (26.4 and 50.9%) were observed, as well as a rarer development of cardiovascular disease (20.7 and 37.7%). and respiratory (26.4 and 39.6%) failure, a decrease in the need for AVL (17.5 and 34.5%), the duration of DRIC stay (14.3 and 20.8 days) and further hospitalization (10.3 and 19.5 days); however, there were no significant differences in the 28-day mortality rate (26.4% and 30.18%, respectively) [71]. Taking into account the above-mentioned ambiguous view at EN in sepsis [31, 32], a differentiated approach to it is recommended: with its moderate manifestations (APACHE II score is less than 15 points) - immunocorrective nutrition, while in severe sepsis, where no advantages have been found enriched immune EP, it is not recommended, since it does not exclude an increase in mortality [32, 68].

In 144 patients in the DRIC of 7 hospitals, medium-chain triglycerides, carnitine and taurine were added to the EN formulawith a view to improve the digestion and absorption of fats. As a result, the frequency of cases of EN intolerance in relation to the comparison group decreased from 65.7 to 42.3%, including abdominal distention - from 49.3 to 32.9%. The addition of micronutrients - iron, copper, chromium, manganese, selenium and zinc to nutritional mixtures is also positively evaluated, which can help to eliminate, along with nutritional deficiencies, inflammatory processes, oxidative stress, immune dysfunction and anemia in burns, trauma and septic shock [72, 73].

In general, in recent years, there has been an opinion that NS, oriented to a relatively large amount of protein with a lower amount of energy, entails an earlier weakening of hypercatabolism inherent in CC, and the transition of metabolic processes to the anabolic stage. This, in turn, leads to the speedy restoration of the visceral pool of proteins, elimination of lymphocytopenia and leukocytosis, and a decrease in the manifestations of the systemic inflammatory response and signs of multiple organ dysfunction [74].

HEALING MECHANISMS OF EN

With the development of IIS in CC in surgical patients, EN is recognized as an important component of complex treatment. At the same time, there is a minimization of energy and protein losses, as well as muscle tissue, the support of the organs function and tissues, especially the immune system, and elimination of metabolic disorders. It has been established that the GIT not only provides other organs with the necessary nutrients, but also that its own mucous membrane needs these nutrients to the same extent to maintain its functional activity. Moreover, only the intraluminal influx of nutrients stimulates the maintenance of the vital activity of epithelial cells and contributes to the preservation of the intestinal barrier [75].

When assessing the effect of EN on nutritional disturbances in SAP, a statistically significant regression of leukocytosis was found already on the 3rd day (from 11.7 ± 0.4 to 8.1 ± 0.6 × 109 / L), while in the comparison group this practically did not happen; the protein content in the blood in the main group increased significantly on the 7th day (from 58.4 ± 3.2 to 68.6 ± 2.8 g / l), while in the comparison group only slight changes were noted [53].

According to available data, when assessing the barrier function of the small intestine against the background of early EN in 21 patients after gastric resection, the content of alpha-1-antitrypsin resistant to degradation in the intestine in fecal samples and its clearance (37.03 ± 1.52 mg / dL and 66.33 ± 4.55 ml / day, respectively) were statistically significantly higher than during PN also in 21 patients (22.84 ± 1.84 mg / dL and 43.14 ± 4.16 ml / day). In case of poisoning with organophosphate pesticides against the background of positive results of early EN, a distinct improvement in the function of the intestinal barrier, however, was not observed. There are also proposed two more biomarkers of the state of enterocytes responsible for the barrier function - plasma citrulline, a biomarker of functionally active enterocytic mass, and plasma or urinary intestinal fatty acid-binding protein, a marker of enterocyte damage [35, 76, 77].

Based on the experience of examination after surgical treatment of 596 patients with pathology of the stomach and duodenum using tensometry and measurement of intraintestinal pressure in response to EN, it was shown that probe EN is the leading component in the treatment and prevention of postoperative complications associated with impaired motor-evacuation function of the GIT - anastomositis and atony of the resected stomach. At the same time, contractile waves on the 1st day after the operation appeared 20 seconds after the start of the infusion, while on the 4th day - after 6-10 seconds, and the duration of the period of strong contractions on the 1st, 2nd and 4th the day after the operation was 6.5–7.0 minutes, corresponding to the analogous parameters of the small intestine in healthy individuals [78]. The restoration of the myoelectric activity of various parts of the GIT was also noted, measured using the 'Gastroscan-GEM' ("Гастроскан-ГЭН") electrogastroenterograph [75, 79].

Based on the above data, it was believed that EN should be prescribed as early as possible and regarded as a therapeutic factor in the normalization of the metabolism of the intestinal structures, the preservation of the mucous membrane of the small intestine and the rehabilitation of the GIT functions, especially motor-evacuation. This is extremely important, given that GIT, mainly dysfunction of its motility, develops in 80% of critically ill patients and is associated with an increased incidence of complications and mortality [80].

The inhibitory effect of EN on microbial translocation in the case of SAP was established in the form of a decrease to 32.3% of the seeding rate of microorganisms (E. Coli, Enterobacter, Ps. Aeroginosae) from intestinal contents, pus from the zone of pancreatic necrosis and parapancreatic areas, systemic blood flow, organs and tissues ... Thus, the enteral route of generalization of infection is interrupted as the most important mechanism of infection of the necrotically altered pancreas and surrounding tissues, as well as the development of a systemic inflammatory reaction, multiple organ failure and sepsis; mortality at the same time decreased from 28.6 to 15.6%. In the same cases, the role of EN as a method of selective intestinal decontamination is positively assessed [81, 82].

In our opinion, before the start of EN, the GIT should be prepared by decontamination with intestinal lavage with a chyme-like solution according to our methodology. Total cleansing of the GIT simultaneously detoxifies the enteral and parenteral media, corrects water-electrolyte, acid-base, hemorheological and oxidative disorders, as well as the microbiome, which contributes to the restoration and normalization of the propulsive function of the GIT. Such a preliminary sanitation of the enteric environment can contribute to an increase in the assimilation of nutrient media and the prevention of EN complications in the form of flatulence, constipation or diarrhea [83, 84].

In acute purulent pancreatitis, among other disorders, there were signs of severe immunological deficiency in the form of absolute lymphocytopenia (below 1200 cells in 1 mm3) by reducing in lymphoid subpopulations CD3 +, CD4 + and CD8 + (T-helper type 1 and cytotoxic lymphocytes).

The EN with the use of complete balanced lactose-free nutritional mixtures (Nutrizon, Fresubin, Nutricomb, Isocal) in 32 patients was accompanied by positive dynamics of immunological parameters, as a result of which the content of T-lymphocytes, active T-lymphocytes, B-lymphocytes, T-helpers and secretory immunoglobulin A turned out to be statistically significantly higher than similar indicators in the comparison group, not differing also from those in the donor group. At the same time, the mortality rate decreased from 28.6 to 15.6%, the frequency of pulmonary complications - from 40 to 15.6%, gastrointestinal bleeding - from 25.7 to 3.1%, and the hospitalization period decreased from 67 ± 3, 7 to 42 ± 2.5 days; the formation of intestinal fistulas was not noted [16].

In 24 severe patients with acute thromboembolic cerebrovascular events, it was found that early EN can cause an improvement in cellular immunity in the form of a statistically significant increase in the content of T-helpers and T-regulatory cells in the blood and a decrease in the level of T-cytotoxic cells. This was associated with a decrease in the susceptibility to infections (10% versus 40%) and the median length of DRIC stay (10 days versus 15 days) [85].

In a significant part of cases, CC are accompanied by the development of oxidative stress with a decrease in the antioxidant capacity of the blood and an increase in the level of protein carbonyl in it as a measure of its oxidation; the blood level of prooxidants - diene conjugates (DC) and malondialdehyde (MDA) - increases significantly. The peroral use for EN of the balanced mixture "Shipa" ("Шипа") ("Nutrilon Pep TSC"/"Нутрилон пепти ТСЦ" mixture, modified with soy protein hydrolyzate, corn oil, rosehip syrup, orange juice, dry strains of lactic acid and bifidobacteria, water-soluble forms of vitamins A, E and C, selenium, folic acid and iron lactate) with a caloric value of 798.3 kcal / 100 g of the product was accompanied by a decrease in the content of DC and MDD in the blood and an increase in the activity of antioxidant enzymes - superoxide dismutase and catalase. A decrease in the degree of acute lung injury in such cases is also reported when vitamin D, which has antioxidant properties, is included in the mixture for EN. Attention is drawn to the maintenance of normoxia when using EN during cardiopulmonary resuscitation [13, 86–88].

The development of peritonitis and enteric insufficiency is accompanied by manifestations of endogenous intoxication (EI), which is in direct connection with the degree of suppression of the intestinal motor function; at the same time, more than 2–3-fold increase in such indicators of EI as the content of average weight molecules in the blood and the value of the leukocyte index of intoxication was determined. At the same time, the favorable effect of EN on homeostasis indices contributes to a decrease in the manifestation of EI, as evidenced by the fact of a greater than in the absence of EN, a decrease against its background in the neutrophil / lymphocyte ratio, also used to assess the EI level, and the duration of DRIC stay (9 days versus 16 days), treatment in general (18 days versus 22 days) and, finally, lower hospital mortality (13% versus 41%) [89, 90].

COMPLICATIONS OF EN

Among the complications of EN, there are technical ones caused by a violation of the method of installing a nasogastric (nasoenteric) probe: erosion of the mucous membrane of the nose, pharynx, esophagus, pulmonary aspiration and pneumonia, blockage of the probe. Quite often (up to 10-15% of cases) there are gastrointestinal complications: nausea, vomiting, diarrhea and constipation. Metabolic complications occur in 10–20% of patients in the form of hyper- and hypoglycemia, hyper- and hypokalemia, etc. At the same time, it is noted that in terms of severity and danger to life, complications of PN significantly exceed those in EN, although the latter are more common [1].

In 23 patients (76.7%) with TBI, gastrointestinal dysfunction began on average 5th (1-13th) days from the moment of injury. In 13 cases (56.5%), impaired tolerance to EN was manifested in the form of gastroparesis, in 6 cases (26%) - in a combined form, and in one (17.5%) diarrheal syndrome was observed. Statistically significant correlations were obtained between the timing of the development of impaired tolerance and systemic inflammatory response syndrome (positive), as well as between the occurrence of gastrointestinal dysfunction and the outcome of trauma (negative). Cases of nasogastric tube blockage were reported in 68 patients with isolated TBI and concomitant trauma - more often with continuous EN than with intermittent

EN. However, the time spent by medical personnel for intermittent EN during the day was 43 ± 3 minutes, and for continuous - 35 ± 2 minutes, or 18.6% less. Another reason for EN intolerance in these patients is a high residual stomach volume, which was found in 20 out of 32 patients even with the systematic use of metaclopramide to stimulate intestinal motility from the very beginning of EN. At the same time, the introduction of erythromycin through a nasogastric tube gave a positive result. In 24 patients with severe non-traumatic intracerebral hemorrhage, who received the calculated amount of enteral mixture, among the complications of probe EN, diarrhea developed in 29.2% of patients, abdominal distension - in 12.5%, vomiting - in 16.7%, hyperglycemia - in 37 patients. 5%, and gastroduodenal bleeding - in 4.2% [25, 26, 91, 92].

It is noted that EN in CC better supports the structure and function of the GIT mucosal than PN. At the same time, complications such as aspiration and reflux are distinguished, recommending the initiation of EN with a small amount of nutritional mixture and a gradual increase in its volume, raising the head end of the bed (from 30 to 45 °), switching to continuous EN administration, and the use of prokinetics or narcotic antagonists to increase the motility of the GIT and switch the EN to the post-pyloric pathway. To diagnose diarrhea as a complication of EN associated with impaired GIT motility, the frequency of defecation is used more than 3-5 times a day or the volume of defecation is more than 200-300 g / day. This avoids volemic, acid-base and electrolyte disturbances, infection of surgical wounds and pressure ulcers, and increased mortality. It is important to establish the causes of diarrhea associated with EN, which are complex and multifactorial, but mainly dependent on the formula of probe EN, and to take measures to prevent it: switching from intermittent to continuous infusion, changing the feeding route from post-pyloric to gastric, selection of drugs that improve peristalsis of the GIT, the use of herbal medicine or antidiarrheal agents, the introduction of dietary fiber, a hypoosmotic solution, a peptide as a source of nitrogen into the EN formula, the exclusion of fat, lactose or milk protein from it. If diarrhea is not resolved with appropriate treatment, EN should be discontinued and PN initiated. Intolerance of EN, the most common form of artificial nutrition, remains a complex problem, therefore, taking into account its development in 33% of 754 patients, it is necessary to further study its causes and treatment optimize on this basis [93–95].

As a rare observation, 10 cases of toxic epidermal necrolysis with involvement of the intestinal mucosa have been reported, which was complicated by small bowel intussusception, resolved conservatively. This occurred against the background of vomiting with an admixture of bile, diarrhea, and significant abdominal distention that developed during EN, and required a temporary cessation of EN [96]. Perforation complications are also possible when attempting to insert a nasogastric probe [97].

Compliance with contraindications contributes to the prevention of EN complications. When recommending the use of early EN in most CC, it is suggested to delay it in case of uncontrolled shock, hypoxemia, acidosis and bleeding from the upper GIT, gastric aspirate volume more than 500 ml / 6 h, intestinal ischemia, intestinal obstruction, the development of abdominal compartment syndrome and the presence of substantial fistulas without the possibility of feeding distal to their localization [98].

DEVELOPMENT OF EN PROGRAMS

The prospect of further research is the creation of programs aimed at optimizing the EN in order to implement the concept of an individualized approach to NT. Such programs can contain modules corresponding to the EN stages, and automate standardized algorithms that eliminate the doctor's error in calculating the risks of NT, choosing the correct method for delivering nutrients to the patient based on metabolic monitoring using metabolographs, and thereby determine the positive effect of treatment, greater than before the empirical choice used [98–104].

Errors in determining schemes of nutritional correction, leading to an unfavorable course of the disease, are still quite frequent, and it is even proposed to highlight their analysis in such a direction as errology (erratology) - the doctrine of errors. However, it is they that make it possible to judge the limits of the possibilities of artificial nutrition [98, 105].

Also topical are the issues of organization and legal basis for EN, supply of equipment and drugs for it [106]. In this regard, there is no doubt, for example, the benefit for the introduction of the EN of the order of the Moscow HD (health department) No. 1144 dated 24.10.2012 [107].

ECONOMIC ADVANTAGES OF EN

The use of EN has a positive effect on the cost of treatment. It was noted that the appointment of EN is accompanied by a decrease in the consumption of expensive medias for PN. The introduction of EN with the help of ready-made mixtures in the Minsk Regional Clinical Hospital made it possible to reduce the costs associated with IC, as well as improve the basic statistical indicators. It was also found that timely initiated adequate NS allows saving expensive antibiotics, blood preparations, consumables and dressings by reducing the frequency and severity of infectious and inflammatory complications [26, 108, 109]. Analysis of the results of EN in 409 patients and PN in 393 patients in the process of an open, multicenter, parallel-group randomized controlled study with a comprehensive economic assessment revealed a lower cost of EN, which subsequently also had a positive effect on the material situation of patients. A study of 859 critically ill children from two hospitals showed that daily hospital costs for more than 96 hours in the ICU were significantly lower when using early EN than when not using it [110, 111].

CONCLUSION

As can be seen from the presented data, selected by us from more than 5,000 literary sources, in recent years, serious efforts have been made to study enteral nutrition, which today is unanimously recognized by specialists as the preferred method of nutritional therapy that significantly affects the course of critical conditions. These efforts now affect almost all nosology that forms the cohort of such patients. It should be noted that the least scientific analysis of the possibilities of enteral nutrition concerned acute poisoning, where, given the special danger to life of their severe forms, there are great prospects for further search in this direction.

In the above studies, the role of early enteral nutrition in intensive care is particularly emphasized, since its implementation mainly in the first 24–48 hours from the onset of the disease has the greatest influence on the achievement of positive results in the treatment of critical conditions, accompanied by an improvement in metabolic processes in organs and tissues.

There is great interest in the study of the pathogenesis of critical conditions by assessing changes in homeostasis indicators using modern laboratory and instrumental control, which strengthens the scientific basis of enteral nutrition. At the same time, this also contributes to the disclosure its sanogenesis.

It is generally accepted that, along with immunological changes, the formation of hemorheological disorders and oxidative stress has particular importance in the pathogenesis of critical conditions, being in no small part involved in the development of endogenous intoxication and their irreversibility [112]. Therefore, in relation to enteral nutrition, research of this kind is promising, which, in our opinion, are still very limited in nature, and from the side of hemorheology, according to the data available to us, are not represented at all.

The current assessment of the economic component of enteral nutrition is also interesting.

Further improvement of enteral nutrition, taking into account the above information, as well as appropriate organizational measures, it seems, can bring this method to a higher level of efficiency and, accordingly, safety, which, combined with the economic advantages of enteral nutrition, will expand the possibilities of its implementation in clinical practice.

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