REPUBLIC OF UZBEKISTAN

MINISTRY OF HEALTH

FERGANA MEDICAL INSTITUTE OF PUBLIC HEALTH

Isaqova N.R.

Djurabayev A.A.

FEATURES OF ENZYMATIC HOMEOSTASIS IN BLOOD AND SALIVA IN ALIMENTARY OBESITY

(monograph)

Fergana – 2024 y.

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"APPROVED"

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DMSc, professor _____ A.A.Sidikov

“____” _____ 2024 y.

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The scientific work was carried out at the Fergana Medical Institute of Public Health

Authors:

Isaqova N.R.	Senior Lecturer, Department of Normal Anatomy, Operative Surgery and Topographic Anatomy
Djurabayev A.A.	Assistant, Department of Normal Anatomy, Operative Surgery and Topographic Anatomy

Reviewers:

Madaminov S.M.	Head of the Department of Normal Anatomy, Operative Surgery and Topographic Anatomy, Professor
Ulug'bekova G.J	ASMI , Associate Professor, Department of Anatomy and Clinical Anatomy, Ph.D.

The monograph presented for review is devoted to one of the most important problems of modern man - obesity, its causes, symptoms, analysis of enzymatic changes in blood and saliva.

Obesity, especially in young people, has been steadily increasing in prevalence over the past three decades, becoming an epidemic throughout the world. This raises some concerns, since obesity-related metabolic, cardiovascular complications, as well as metabolic syndrome, are especially common in young, able-bodied patients.

The monograph was approved by the Expert Council of the Fergana Public Health Medical Institute by the protocol No. "____"_____ of 2024 and was approved for publication and recommended for approval by the Scientific Council.

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Secretary of the Expert Council of the Fergana

Public Health Medical Institute PhD: A.R. Muradimova

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INTRODUCTION

The relevance of the problem. The relevance of the problem of obesity is that it undoubtedly occurs at any age. Researchers around the world associate obesity, first of all, with the fact that most people are not accustomed to a healthy eating culture and their sedentary lifestyle. The problem of excess weight is caused not only by the lack of somatic status, but also by the lack of self-esteem and psychological self-control of a person. Obesity, which has been steadily increasing over the past three decades, especially among young people, is becoming a global epidemic. Because the complications of metabolic and cardiovascular diseases associated with obesity concern us, as well as metabolic syndrome, which appears long before its clinical manifestations, especially in working-age and young patients [2]. Obesity is a metabolic disorder in adults, as well as in children and adolescents, characterized by the accumulation of excess fat in the body and an increase in body mass.

In our opinion, the formation of obesity among young people is of primary importance due to the fact that the diet of adolescents consists mainly of fatty foods (excessive fatty, fried foods) and light carbohydrate (for example, sweets, pastries) products, and the lack of an elementary culture of nutrition. As noted in the social network "Virtual Life", the development of computerized technologies is causing the formation of a sedentary lifestyle in people. A growing organism, that is, during adolescence, requires adequate physical activity of a certain level, appropriate for age.

Undoubtedly, the hereditary factor is of great importance, therefore, according to most researchers, the absence of the first two factors is of less importance.

It is clear that changes in the ratio of protein, fat, and carbohydrates consumed in the diet, as well as an imbalance between energy intake and expenditure, lead to an increase in body mass [3, 4]. The combined effect of these factors often leads to obesity [5].

It is known that the gut microbiota plays a crucial role in the development of disease and the formation of health in humans. The gut microbiota is a “microbial organ” located in the intestines. Recent research data indicate that changes in the gut microbiota affect energy storage and metabolism in the human body [6, 7].

This may play a more important role in maintaining human health than previously thought. In recent years, researchers have provided new evidence that the reasons for the increase in the prevalence of obesity may not be due solely to changes in the human genome, eating habits, or physical activity in daily life [8]. In this regard, it is necessary to take into account this important new environmental factor, namely the gut microbiota.

Today, scientists are considering an important question: obesity or diabetes? Because the practices carried out to prevent and treat such diseases control the formation of the microbiota. This has opened a new scientific direction. Several studies on the current problem of obesity have shown that the intestinal microflora also affects the overall energy balance of the body [9, 10]. The metabolic change scheme, that is, the mechanism of obesity, presented today, appears as a result of dysbiotic changes in the human body. As a result, the accumulation of fat mass and increased fat synthesis are observed [6]. After the formation of a new complex from triglycerides formed as a result of the digestion of plant products in the intestine, the association of several types of microflora can lead to obesity [11]. Experimental studies show that changes in the intestinal microflora lead to energy accumulation and, as a result, obesity.

Currently, approximately 2 billion people on earth live with the problem of obesity or overweight. Of these, more than 200 million are men and almost 300 million are women. In economically developed countries, about 30% of the population has an excess body mass, and every tenth child suffers from obesity. Obesity reduces life expectancy by 3 to 5 years. The number of people suffering from obesity is growing every year, and this figure is increasing by 10% every decade. In May 2004, the World Health Assembly adopted a global strategy on

health, physical activity and nutrition. It is based on the need to promote regular physical activity and healthy eating. The strategy called on all interested countries to take action at the global, regional and local levels to increase physical activity and improve nutrition. In 2013, the World Health Assembly adopted a major global plan for noncommunicable diseases (NCDs) for 2013-2020. Noncommunicable diseases (NCDs), mainly cardiovascular diseases, cancer, chronic respiratory diseases and diabetes, are the leading causes of death worldwide. The Global Plan for the Prevention and Control of Noncommunicable Diseases (NCDs) adopted at the 66th World Health Assembly was reviewed globally and important criteria were developed.

The Global Action Plan provides a roadmap for Member States and other stakeholders and provides a set of policy options, interventions and a monitoring framework. Member States can choose policy options based on their specific context and resource availability. The set of interventions presented in the Global Action Plan includes cost-effective interventions that can be implemented sustainably in all countries with moderate resource allocation. In addition, the 25 indicators included in the global monitoring framework can be adapted to national contexts to measure the achievement of voluntary targets.

The aim of our research is to investigate the specific nature of the enzymatic composition of oral fluid and blood and its changes in relation to different levels of alimentary obesity and weight gain. Therefore, we set ourselves the following tasks:

- to study the significance of the amylolytic activity of oral fluid and blood in groups of patients with different degrees of obesity and excess body weight;

- to study the significance of the lipolytic activity of oral fluid and blood in groups of patients with different degrees of obesity and excess body weight;

- to study the correlation indicators of enzymatic analysis of oral fluid and blood.

Scientific novelty of the study

As a result of our scientific research, it was found that there is a significant difference in the enzymatic composition of oral fluid and blood in the manifestation of obesity or overweight, which is expressed in different degrees of metabolic disorders. It is known that obesity can lead to the development of a number of diseases of the digestive system, such as non-alcoholic steatohepatitis, gallstone disease, gastroesophageal reflux disease, functional disorders of the digestive tract [3, 5, 8, 15, 19, 24]. As a result of these diseases, changes in the enzymatic composition of the blood and, accordingly, changes in the composition of the oral fluid are observed. The phenomenon of "deviation" of enzymes in the blood was studied in conditions characterizing the exocrine function of the pancreas, as well as in terms of lipase and α-amylase activity in the oral fluid and blood. The results of our studies showed that there is a correlation between the level of lipase and amylase in the oral fluid and blood in overweight and obesity. Based on these data, it can be used as a non-invasive method for the diagnosis of alimentary obesity and its various stages. At the same time, it is useful to detect and treat various diseases resulting from alimentary obesity at an early stage.

Methods and objects of examination.

During 2016-2018, we took 78 people under control at the RShTYoIMFF. They were distributed as follows: the control group consisted of 20 people and the experimental group of 58 people. People in the experimental group had varying degrees of obesity. The average age of the patients was 41 years.

People in the control group were taken in a 1:1 ratio, that is, 10 men and 10 women. The experimental group consisted of 30 women and 28 men. Accordingly, their percentage ratio was 52% and 48%, respectively. All patients were divided into groups according to body mass index. Also, all patients underwent general clinical and special examination methods. Statistics of the results obtained were prepared. Data from clinical trials were entered into the statistical analysis program

STATISTICA 5.0. STATISTICA When the distribution of variables followed a normal law, comparisons were made using the Student's t test. Otherwise, non-parametric rank-sum tests were used to identify significant differences: Wilcoxon and Mann-Whitney tests.

Differences between groups were considered significant at $p < 0.05$ (95% probability of difference) and $p < 0.01$ (99.9% probability of difference).

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When analyzing the correlation of data, Pearson linear correlation was calculated. The obtained data were interpreted as follows: if the correlation coefficient is greater than 0.4, then there is a linear relationship between the parameters. A negative value of the correlation coefficient indicates the presence of an inverse relationship between the parameters, a positive value indicates the presence of a direct relationship.

Practical significance of the work

Materials on the polymorphism of alimentary obesity are of direct importance for the clinical diagnosis of the disease and its secondary diagnosis. Despite the fact that a lot of data has already been published indicating the unusually high potential of saliva for diagnostic purposes, the fact that work on the study of works published on this problem by many authors is still ongoing allows us to draw the main conclusion that the study of the salivary proteome is at the stage of completion.

The lack of standardization of material collection, analysis methods, as well as the requirements for the representativeness of samples from which conclusions are drawn, leads to discrepancies in the data obtained by different researchers and creates obstacles to their practical use.

In addition, at present, the importance of the interaction of salivary proteins with oral microorganisms, as well as the biochemistry and physiology of the salivary

glands and saliva, has not been sufficiently studied. The developed approaches and principles of pathogenetic-based diagnostics of alimentary obesity and comprehensive assessment of the effectiveness of treatment can be used in practical health care for optimal therapy and primary medical examination.

Implementation of research results

The recommended methods for studying the enzymatic activity of blood and oral fluid and the obtained research results were introduced into the practical work of the departments of the ADTI clinic and the educational process at the departments of normal and pathological physiology.

Issues put forward for defense

1. Specific changes in the enzymatic homeostasis of oral fluid and blood accompany the clinical polymorphism of alimentary obesity.

2. The shift in the amylolytic activity of blood and oral fluid is significantly determined relative to the lipolytic activity of the corresponding fluids and is associated with the degree of obesity.

3. Substantiation of the correlation analysis of the relationship between alimentary obesity and changes in the enzymatic homeostasis of oral fluid and blood.

4. Comprehensive assessment of the effectiveness of the treatment of alimentary obesity and pathogenetic substantiation of its diagnosis using a non-invasive method that can be used in healthcare practice to bring the primary link of the medical base under dispensary control and conduct optimal therapy.

CHAPTER I.

Modern Imaging Monitoring Of Alimartary Obesity Problems

1.1. The problem of alimentary obesity and a modern interpretation of the fight against it.

Obesity is a chronic progressive metabolic disease, which is manifested by excessive accumulation of adipose tissue and recurs after discontinuation of treatment.

Obesity increases the risk of type 2 diabetes and cardiovascular diseases, negatively affects the musculoskeletal system and reproductive function, and also increases the risk of developing certain types of cancer. Obesity negatively affects the quality of life, sleep and mobility.

Etiopathogenetic classification of obesity:

Primary obesity:

- alimentary-constitutional (almost 95%);

- hypothalamic.

Secondary (symptomatic) obesity:

- endocrine-metabolic (Cushing's syndrome, etc.);

- cerebral (brain pathology).

Classification by type of adipose tissue deposition:

- abdominal (android, central, "high" type);

- gynoid (buttock-thigh, "lower" type);

- mixed.

Alimentary obesity is considered a serious disease, and it is fully proven that a number of complications can even lead to death. In 1989, the World Health Organization first declared that alimentary obesity is not a cosmetic defect, but a disease.

Indeed, alimentary obesity, which begins with bad habits such as overeating, upbringing, and food preferences in adolescence, can gradually spread in society and lead to fatal diseases diagnosed as "metabolic syndrome" [1]. Although no psychosomatic component has been observed in alimentary obesity, attempts have been made to treat it by somatic effects on excess body weight.

According to the World Health Organization (WHO), in 2008, 700 million people were obese, and by 2015, approximately 2.3 billion adults had increased body mass.

According to the Journal of the American Medical Association (JAMA) for 2003-2006:

• 11.3% of children and adolescents aged 2-19 years were at the 97th percentile or higher (severe obesity) for the 2000 age group on the TVI scale

• 16.3% - at the 95th percentile or higher (obese)

• 31.9% - at the 85th percentile or higher (overweight)

• Prevalence varies by age and ethnic group

• Analysis of changes in TVI by age did not reveal statistically significant fluctuations between boys and girls in four periods (1999–2000, 2001–2002, 2003–2004, and 2005–2006).

Today, the average TVI has increased and obesity has become more prevalent in patients, so the distribution curve has shifted to the right.

• WHO data for 2005 show that 1.6 billion adults (aged 15 and older) were overweight, and at least 400 million adults suffered from obesity.

• In 2005, at least 20 million children under the age of 5 worldwide were overweight.

• Obesity is becoming an epidemic.

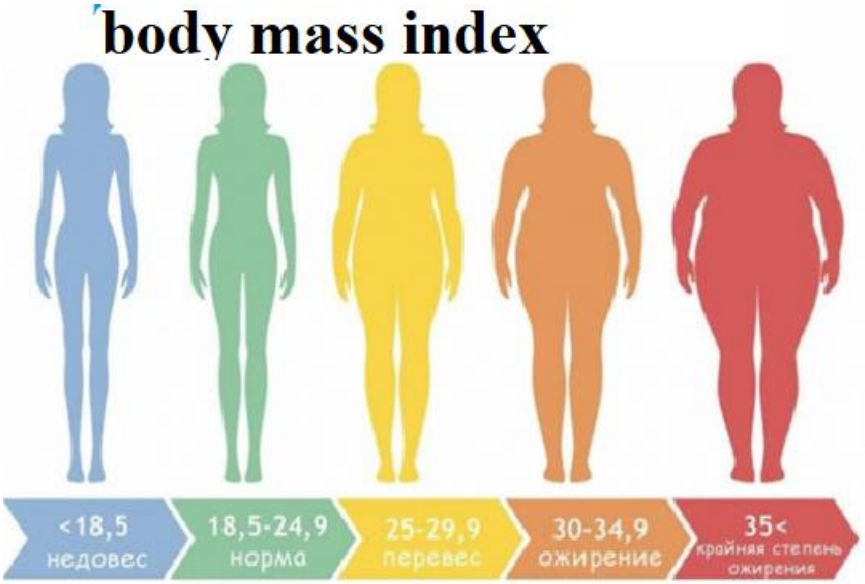
• In the United States, obesity among adults increased from 15.3% in 1995 to 23.9% in 2005.

Table 1

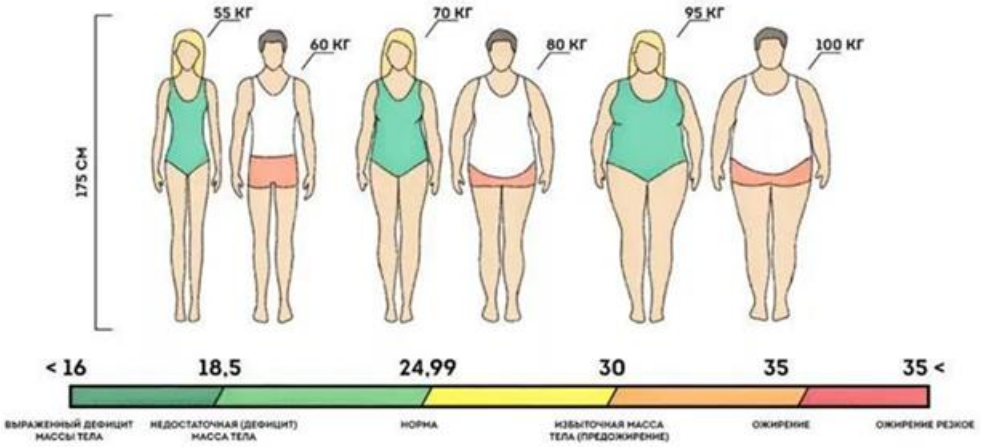
Data from the International Classification of Underweight, Overweight and Obesity for Adults by Body Mass Index (BMI)

Classification	Basic limit of TVI (kg/m²)
Underweight	< 18.50
Pronounced underweight	< 16.00
Moderate underweight	16.00–16.99
Mild underweight	17.00–18.49
Normal weight	18.50–24.99

Overweight	≥ 25.00
Pre-obesity	25.00–29.99
Obesity	≥ 30.00
Class I	30.00–34.99
Class II	35.00–39.99
Class III	≥ 40.00



body mass index = weight (kg) / height (m)



According to the World Health Organization, in 2022, one in eight people in the world was obese. At the same time, 2.5 billion adults (aged 18 and over) were overweight, of whom 890 million were obese.

The prevalence of overweight varies by region, from 31% in Southeast Asia and Africa to 67% in the Americas.

Since 1990, obesity rates among adults have doubled and among adolescents have quadrupled. According to WHO forecasts, the lack of adequate measures to address the problem of overweight and obesity will lead to significant economic losses, reaching 3 trillion US dollars by 2030 and more than 18 trillion US dollars by 2060.

In this regard, at the 75th World Health Assembly in 2022, WHO Member States approved the rapid action plan to combat obesity and developed new recommendations for the prevention and treatment of obesity (A75_REC1), which include encouraging and supporting countries' efforts to overcome the growing obesity crisis. It is known that drugs such as metformin and orlistat have been marketed as very popular weight loss drugs, but from the point of view of the currently presented data, it is necessary to change the drug when used for a long time. People have been led to believe that if they use this drug for a long time, it will cure the disease. This is not the essence of the problem. Indecisive people think that they need to reduce body mass to look good, take orlistat, but this drug leads to a violation of eating habits and impaired absorption of fats in the intestines. Such patients, despite the inconclusive evidence, without understanding the cause of the disease, form a highly conditioned reflex in themselves when treated with orlistat. It plays the role of a “whip” in the process of reducing body weight. Naturally, as a result, orlistat is used as a very good “banquet drug” according to their needs [2]. Metformin affects one of the mechanisms of the formation of excess body weight - insulin resistance. Since this mechanism is considered one of the leading mechanisms in the climacteric period, when diabetes mellitus is accompanied, long-term treatment with metformin can have an effective effect [3, 4]. Sibutramine shows itself well in obesity, which is formed under the influence of serotonin and

noradrenaline. However, sibutramine is currently not available on the pharmacological market, since in patients with a high risk of cardiovascular pathology, the side effects of the drug have been identified from the cardiovascular system.

Surprisingly, serotonin reuptake inhibitors - antidepressants with similar pharmacological properties to sibutramine (and therefore are used to combat "eating" emotional disorders), although the instructions for use clearly state that caution should be exercised when prescribing them for heart disease, are still available on the market for drugs used for eating disorders. Great difficulties await both the patient and the doctor who are trying to "swim" in the sea of biologically active food additives.

Of course, eating behavior affects the metabolism of not only a single biologically active substance, but also the control of a complex of regulatory substances. The role of noradrenaline (increased energy expenditure for thermoregulation) has long been known, this phenomenon was used in the mechanism of action of sibutramine.

The old rule: do you want to lose weight? - wear thin clothes, cool down, wash in cold water.

Cannabinoid receptors are a group of cellular receptors that belong to the G-protein membrane receptor superfamily, which is coupled to endocannabinoid ligands (anandamide and 2-arachidonoylglycerol) and exogenous ligands (true cannabinoids and their synthetic analogues) [1]. They were first discovered in 1988 by a group of scientists from St. Louis University Medical School in the USA using the synthetic cannabinoid CP-55,940 labeled with tritium in the rat brain [2].

It is currently known that there are two types of cannabinoid receptors found in mammals: CB-1 (in the central and peripheral nervous system) and CB-2 (mostly in immune and hematopoietic cells). The highest concentration of the CB-1 receptor is found in the following parts of the central nervous system: the cerebral cortex, hippocampus, cerebellum, caudate nucleus of the corpus callosum, reticular formation of the substantia nigra. CB-1 receptors are also found in lower

concentrations in the peripheral nervous system, as well as in the peripheral ganglia, pituitary gland, adrenal gland, and heart. In the natural state, the receptor is activated by anandamine and helps to inhibit the processing of excess dopamine, hyperactivity. The introduction of exogenous cannabinoids (for example, tetrahydrocannabinol) into the body has an effect similar to that of SV1 analogues, although much less intensively.

SV-2 receptors were first found in the spleen and later in other glandular tissues (stomach, ovaries, etc.). They differ from SV-1 receptors in that they bind exogenous cannabinoids well, but they show less anandamine-like properties. Recall that receptors are ionotropic and metabotropic. When ionotropic receptors are activated, the channel opens and allows charged ions to pass into or out of the cell, and a charge exchange occurs in the membrane, allowing an electrical impulse to pass along the neuron. Ionotropic receptors transmit the impulse quickly and easily. Metabotropic receptors, on the other hand, transmit chemical processes that occur in the cell due to changes in the cell membrane. These receptors transmit the impulse very slowly, but its activation can be varied. In particular, cannabinoid SV-receptors are typical metabotropic G-protein-coupled receptors.

Cannabinoids are also involved in the formation of hunger and food behavior. Anandamide increases the amount of food eaten, increases appetite, is one of the keys to the “hunger peptide”. This is the same in humans and animals. So, newborn mice are injected with the cannabinoid receptor blocker rimonabant and removed from their mother’s milk, and they die within four to five days. Cannabinoids also facilitate the release of dopamine from the ventral tegmental area (VTA, the ventral zone of the forebrain, where the dopamine pathway begins, the most important participant in the corresponding systems).

It has a synergy with opiate receptors, which explains the analgesic effect of cannabis. That is, as mentioned above, they do not seem to do anything directly, but indirectly affect everything and everyone.

The endocannabinoid system is composed of endogenous cannabinoids (endocannabinoids [ECBs]), metabolic enzymes responsible for the breakdown and formation of ECBS, and cannabinoid receptors [4, 5]. Endocannabinoids are responsible for several physiological processes in the body, including peripheral glucose homeostasis and lipid metabolism, analgesic and metabolic effects, modulation of synaptic function in the central nervous system, and retrograde signaling [6, 11]. Indeed, several therapeutic effects associated with the endocannabinoid system have been reported, including: pain management, emotional and neurodegenerative disorders, gastrointestinal disorders, metabolic disorders associated with obesity, cardiovascular diseases, and liver diseases [12, 13].

The work of T.V. Reshetova et al. shows that the appetite-regulating drug Dietressa sensitizes type I cannabinoid receptors through allosteric modulation mechanisms, which is accompanied by an increase in its sensitivity to endogenous cannabinoid neuropeptides. As a result of these processes, the endocannabinoid regulation of the mesolimbic system is normalized. Experimentally, when the drug is administered to animals, the lateral hypothalamus is inhibited from self-stimulation, indicating a satiety of the positive emotional reinforcement system and a decrease in the euphoric value of food. Taking the drug is accompanied by a decrease in food intake and weight loss without an inhibitory or stimulating effect on higher nervous activity. Previous studies have studied and analyzed the effects of Dietressa in various dosage formats on patients with different degrees of obesity [7].

Despite significant progress in the study of obesity in recent years, the problem of treating this disease remains unresolved due to the complex pathology of obesity, as well as the high rate of relapse after therapy. In this regard, an active search for new highly effective and safe treatment methods, taking into account the pathogenetic mechanisms of the development of this disease, continues.

One of the important directions of modern medicine is the study of the pathogenesis of impaired lipid metabolism and the development of methods for

reducing and stabilizing body weight, eliminating associated risk factors, adequately controlling associated diseases, and achieving positive changes in the quality of life and life expectancy of patients.

The generally accepted strategy for the treatment of nutritional obesity is the use of a comprehensive program of non-drug therapy, often in combination with medical and surgical methods of treatment [1, 2, 3].

Clinically significant and of real health benefit to these patients is a 5-10% reduction in body weight from baseline over 4-6 months, accompanied by significant improvement in comorbidities [4, 24].

The diet (3 main and 2 intermediate) is considered a necessary program for maintaining body weight within the norm. The daily caloric intake is divided as follows: breakfast - 25%, 2nd breakfast - 10%, lunch - 35%, 2nd lunch - 10%, dinner - 20% [5, 7, 12].

To reduce body weight, it is necessary to create a negative energy balance, in which the accumulated fat begins to be used as an energy form to compensate for the existing deficit. In this regard, various diets with a certain ratio of proteins, fats and carbohydrates are used to treat obesity [9, 14].

Although chronic diseases are a growing problem in low- and middle-income countries, there is limited data on the incidence in these regions and the developing world is largely ignored in global health policy. A recent systematic review found that Eastern Europe and the Middle East have the highest rates of childhood obesity. The lowest rates are in India and Sri Lanka. Studies in developing countries have shown a significantly higher prevalence of metabolic syndrome in adolescents. Developing countries are facing high rates of childhood obesity and new cases of metabolic syndrome in children. In the near future, the poorest countries could face major socio-economic challenges and strain on health systems. The WHO warns that the estimated number of new cases of diabetes could cost hundreds of millions of dollars over the next 20 years.

Globalization can exacerbate dietary disparities between the rich and the poor: higher-income groups can benefit from more dynamic market diversity, while lower-income groups can be forced to eat lower-quality diets. Many developing countries are in the midst of a "nutrition transition," as evidenced by the rapid increase in obesity and diet-related chronic diseases worldwide. While developing countries still struggle with malnutrition and micronutrient deficiencies, they are also increasingly consuming foods high in fat and sugar. This transition is driven by globalization processes that are changing the nature of agricultural and food systems, as well as the quality, variety, price, and appeal of the products they consume.

Some of the structural causes of obesity and diet-related chronic diseases worldwide may be linked to global nutrition and health policies, particularly among groups in lower socioeconomic backgrounds.

According to WHO, many low- and middle-income countries are now facing a "double burden" of disease:

• While they continue to struggle with infectious diseases and malnutrition, they must also contend with rapidly increasing risk factors for chronic diseases, such as obesity and overweight.

• Malnutrition and obesity can now coexist in the same country, in the same community, and even in the same family.

• This double burden in the prenatal period stems from inadequate nutrition during infancy and early childhood, followed by diets high in energy, high in fat, micronutrient deficiencies, and low physical activity.

1.2. Morphofunctional properties of adipose tissue

Adipose tissue is located in the connective tissue with its own characteristics. The cells of adipose tissue are adipocytes. They are responsible for the accumulation and synthesis of fat. During the first year of life, their number increases threefold and continues to grow until the age of five. Later, in most people, the mitotic activity of fat cells disappears, and only their size increases. In adults, their number is strictly individual and genetically determined. Adipose tissue is distributed throughout the body. In women, it normally makes up 20-25% of body mass, while in men this

figure is 15-20% of body mass. The absolute mass of adipose tissue is normally 10-20 kg. These figures can vary relatively in different cases. At different degrees of obesity, this tissue can increase from 40 kg to 100 kg. In starvation and anorexia nervosa, the volume of this tissue can decrease to 3% of normal levels. In humans, adipose tissue consists mainly of white adipose tissue. It performs a thermoinsulating and endocrine function, being the most necessary energy source for the body. Brown adipose tissue plays an important role in thermoregulation in newborns. It is found in very small quantities in adults and its function is still unknown. Adipocytes respond quickly to changes in endocrine and metabolic situations. In these cells, the processes of lipolysis and lipogenesis are constantly in balance. Adipose tissue has the following important functions: 1) energetic; 2) supporting, plastic, protective; 3) thermoinsulating; 4) depot (vitamins A, E, K, D and steroid hormones); 5) endocrine (leptin, visfatin, estrogens).

It is known that adipose tissue synthesizes and secretes a large number of biologically active peptides, called adipokines, which act in a local (autocrine and paracrine) framework. Among adipokines, the most studied are leptin, adiponectin, visfatin, which are synthesized by adipose tissue, which affect metabolic disorders and the development of insulin resistance (IR). In addition, adipose tissue, along with a number of receptors, provides the opportunity to quickly respond to afferent signals from the central nervous system and internal organs. Thus, adipose tissue participates in the coordination of many biological processes, including neuroendocrine and immune processes, energy metabolism.

A number of studies confirm the existence of a relationship between the level of gene expression in adipose tissue, the content of adipokines in blood serum, as well as these indicators, age and basic anthropometric characteristics. Data have been obtained on changes in the content of adipokines in the blood during obesity in children and the degree of its development. The relationship between the content of serum adipokines and metabolic diseases associated with obesity has been established.

The utilization of adipose tissue and the release of energy are regulated by catecholamines. Adipocytes have two types of receptors sensitive to catecholamines. ß-ı-receptors are lipolytic and respond to lipase synthesis. α-2 receptors block lipolysis and form a typical fatty deformed figure in functionally active zones: the upper outer surface of the thigh, the inner surface of the knee joint, the groin area, the abdomen, and this information is transmitted at the genetic level, just like hair and eye color, and due to the distribution of adipose tissue, fat can accumulate in these areas with physical exertion and various diets. Low-calorie foods and exercise can help to lose fat in such problem areas.

The distribution of fat in the body depends on gender. The accumulation of fat in the lower parts of the body, the iliac region, the inner and outer areas of the upper thighs is typical for women. On the contrary, in men, fat accumulates evenly throughout the body, including (android prevalence) the body, nape and neck thicken, the abdomen enlarges. Visceral type fat accumulation increases the retroperitoneal cavity, abdominal fat, and abdominal fat. Naturally, liposuction is not observed in this type of obesity. The accumulation of fat under the skin worries all women. The subcutaneous fat layer consists of two layers (superficial and deep) on the anterior wall of the groin and the upper part of the leg, where liposuction is often performed. The superficial fat layer consists of dense and thick fat, well connected with the fibrous shell. On the contrary, the deep fat layer consists of very soft fat, located under the fibrous membrane. In addition, there are “densely attached zones” located under the fascia, which are connected to the skin, and they are: the back surface of the lower third of the thigh, the iliac folds, the lateral area of the iliac crest, the inner surface of the middle thigh. These zones are called “taboo zones”. Liposuction is performed in these areas, as this can lead to a violation of the relief of the skin surface after the operation.

In large mammals, the bulk of adipose tissue is composed of adipocytes*, which are embedded in loose fibrous connective tissue. (Figure 1). They are located in the periphery, adjacent to the organelles and nucleus in the cytoplasm.

The intercellular substance of both white adipose tissue and brown adipose tissue is composed of a small amount of collagen and elastin fibers, and the main substance is proteoglycans and glycosaminoglycans.

The fat content of white adipose tissue can be up to 85%, of which 99% consists of triglycerides (triacylglycerides). Although white adipose tissue is less important in blood vessels than brown adipose tissue, each fat cell is connected to at least one capillary. During fasting, blood circulation in adipose tissue increases.

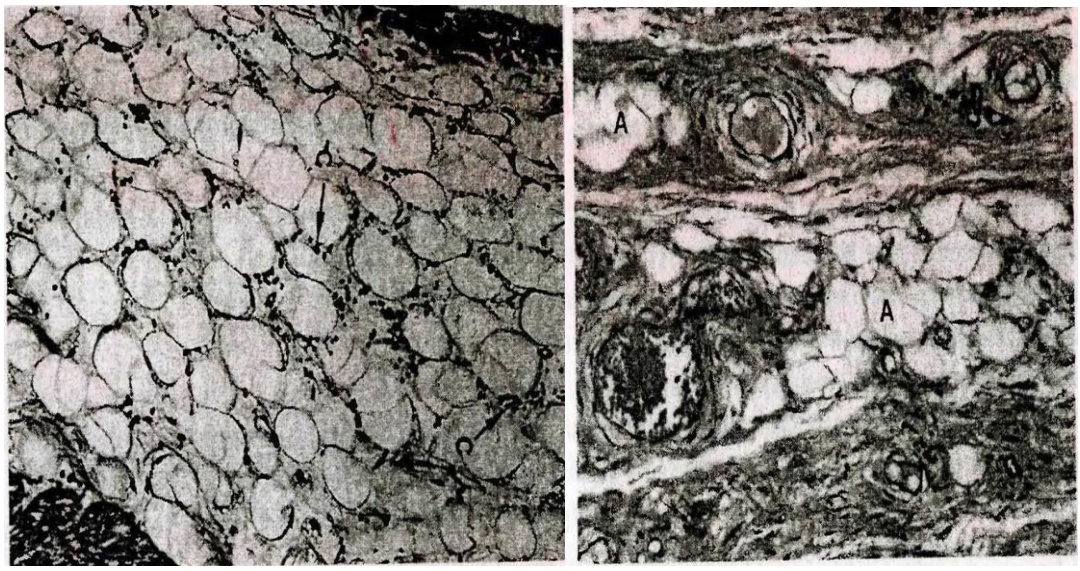


Figure 1. Adipose tissue.

The nucleus of brown adipocytes is located in the center of the cell, and small fat granules (the size of which is 60 μm) are located in the cytoplasm along with numerous mitochondria and other organelles. In addition to adipocytes, adipose tissue consists of fibroblasts, leukocytes, macrophages and preadipocytes.

It is known that the state of adipose tissue depends on age and gender. For example, in a healthy 25-year-old man, adipose tissue accounts for 15% of the total body mass, and in women, on the contrary, 25%. After 40, this figure changes accordingly: it changes to 22% in men and 32% in women. After 55 years, it increases to 25% in men and 38% in women. There are cases when a person may develop obesity due to a decrease in bone and muscle mass, even if their total weight does not change. Due to functional changes observed in old age: glucose absorption decreases, the composition and intensity of triglyceride metabolism increase. In addition, under the influence of hormones, the reaction in adipose tissue slows down,

and the lipolysis process begins to occur at a faster rate, respectively, the inhibitor is insulin and its stimulants are adrenaline, glucagon. Scientific studies have shown that when hormones are administered to old rats as a result of physical exertion, lipolysis can return to its original state under hormonal control depending on age. These data have been shown to be promising in the treatment of obesity in old age.

1.2. Modern methods of prevention and diagnosis of alimentary obesity.

The standard examination algorithm for a comprehensive examination of patients with obesity is as follows:

− blood lipid spectrum

− fasting blood glucose

− HbA1c

− ALT, AST, GGT

− uric acid, creatinine

− abdominal ultrasound

− ECG

− blood pressure changes

In all patients, fasting glucose and glucose tolerance should be determined to determine the presence of impaired carbohydrate metabolism. This is also important in the diagnosis of diabetes mellitus. In diabetes mellitus, its compensation and subcompensation may be increased. [31, 32]. In all patients, thyroid function can be assessed by determining the level of thyrotropic hormone. In thyroid dysfunction, its compensation may be increased.

All patients underwent the following less important procedures: salivary cortisol levels, the classic Liddell test, the overnight test with 1 mg dexamethasone, and 24-hour urinary cortisol excretion.

All patients were advised to have their total and ionized calcium levels measured, as well as serum 25(OH)D and PTG levels to screen for vitamin D deficiency [31, 32]. In addition, all patients were required to undergo a cardiological examination to assess cardiovascular risk factors.

It has now been reported that salivary proteome analysis has yielded surprising results in the diagnosis of many diseases.

At the same time, other conclusions can be drawn from these publications, in particular, the study of salivary proteome is currently at the stage of data collection and the lack of standardization of methods of analysis and requirements for representativeness in the collection of material, samples created on the basis of the authors' conclusions, which leads to inconsistencies in the results obtained by different researchers.

In addition, the specific aspects of the interaction between microorganisms in the oral cavity and proteins in saliva, as well as the biochemistry and physiology of the salivary glands and saliva, have not yet been sufficiently studied.

All this creates obstacles to the use of advances in the study of salivary proteome in diagnostic practice.

Solving these problems makes saliva an ideal biological tool for diagnosing diseases and predicting their course.

1.2. Anatomical and physiological properties of the salivary glands and the composition of the oral fluid

Saliva Chinese doctors used blood and saliva together in clinical diagnostics 2000 years ago [3]. In the 20th century, saliva examination became widespread and a special science called “salivology” emerged. Based on this, it was proven that saliva has a strong connection with blood and is of great importance in ensuring general homeostasis [4, 5, 6]. Recently, with the emergence of a new biological science, a new era in saliva examination has begun. “Salivology” is a branch of science that studies all biochemical and physiological processes occurring in the body, including the digestive process, and is based on accurate data on the gradual breakdown of nutrients entering the body with the participation of digestive enzymes and the effect of the composition of nutrients on the quantity and quality of these enzymes. Many problems of hereditary pathology in humans and animals are

associated with the lack or complete absence of synthesis of specific enzymes. Cellular growth and development, differentiation, and the occurrence of physiological functions are largely associated with the work of biocatalysts.

Recently, a new stage in the study of saliva has begun due to the emergence of a number of new biological sciences (the so-called "omics") based on various methodological approaches and using more sensitive methods (primarily mass spectrometry). Proteomics and bioinformatics are now of great importance in the study of saliva as a diagnostic biological fluid [7, 8], since great progress has been made in the study of the protein and peptide composition of saliva.

Saliva is an exocrine secretion, produced by three pairs of major salivary glands (pre-parotid, sublingual, and submandibular) and many minor glands. The oral cavity produces mixed saliva, or oral fluid, which differs in composition from saliva produced by the glands, as it contains bacteria and their metabolic products, fluid from the gingival crevice, blood plasma components, and decay products. Mixed saliva is very convenient for diagnostic purposes, since the method of obtaining it is simple, non-invasive, has minimal cost, and requires minimal processing [1, 2]. The methodological basis for proteomic studies of saliva is the methods of two-dimensional electrophoresis (2D electrophoresis) and mass spectrometry. By combining these methods with each other, as well as with chromatography, droplet electrophoresis, gel filtration, and other methods, it was possible to achieve unprecedented results in studying the protein composition of saliva. The basics of the methodology for proteomic studies of saliva are presented in a number of published works [9, 10, 11]. Due to the development of bioinformatics and the accumulation of data, existing databases on salivary proteome, such as the Salivaomics database, have been created.

1.4.1.Structure and functions of the salivary glands

All salivary glands are derived from the stratified squamous epithelium of the oral cavity. In the second month of intrauterine development, large paired salivary glands are formed: preauricular, sublingual and submandibular, and in the third

month - minor salivary glands: salivary glands of the labia, uvula, palate. Epithelial cells proliferate, they grow into the underlying mesenchyme, form branched epithelial outgrowths with expanded ends, giving rise to the excretory ducts and terminal secretory departments of the glands. Connective tissue is formed from the mesenchyme. The mesenchyme has a stimulating effect on the epithelium of the glands, determines the branching of the ducts and the direction of their growth. The type of salivary gland is determined even before the interaction of the epithelium with the mesenchyme begins. At birth, the salivary glands are not fully formed, their differentiation is completed between 6 months and 2 years. The growth and development of the salivary glands continues until 16-20 years of age, and the nature of the secretion they produce also changes: for example, the parotid salivary gland produces a mucous secretion in the first years of life, and by the age of 3 it becomes serous.

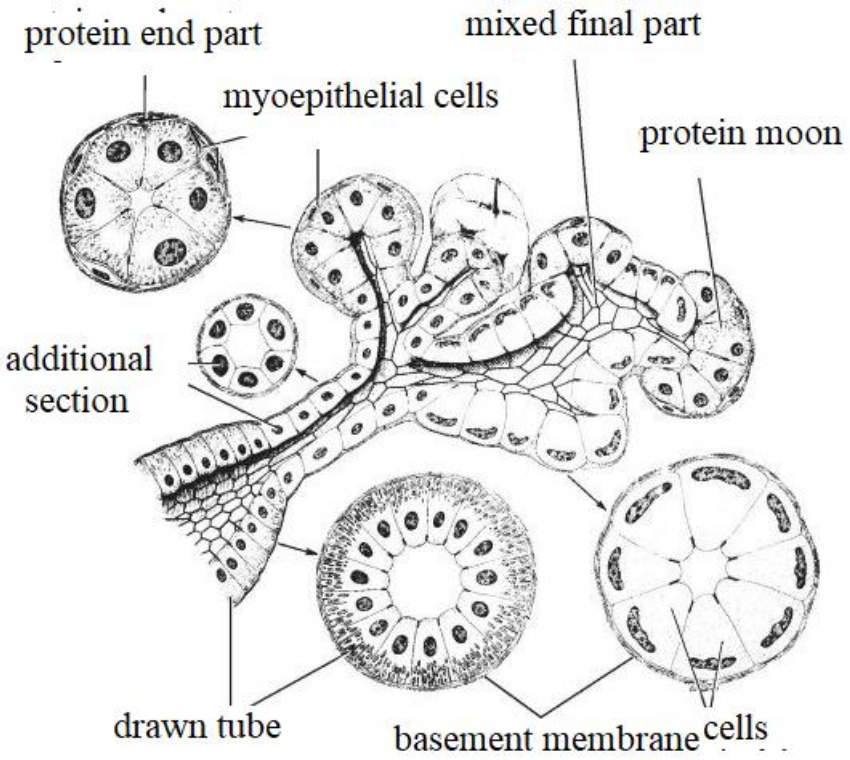


Figure 2. Structure of the salivary glands.

As mentioned, food undergoes initial chemical breakdown in the oral cavity. The main task in this is performed by the salivary glands. These salivary glands begin their function immediately after birth, and saliva begins to be secreted intensively in children aged 9-12 months. On average, children secrete about 800 cm3 of saliva per day. 99% of this saliva consists of water. The mass of the parotid

gland decreases to 23 g at the age of 30, 19 g at the age of 60-70, and to 15 g in the elderly. It is known that the average size of the salivary glands is larger in men than in women. After the age of 40, signs of age-related involution of the gland appear. In elderly and middle-aged people, changes occur in the last section of the excretory tract, that is, in one third of the total volume of the gland. In the terminal sections, the secretory granules in the gland cells decrease and lysosomal activity increases, and the shape and size of the gland cease to grow. In old age, the relative volume of the terminal section cells decreases by 1.5-2 times, its atrophy occurs, and its place is taken by fibrous connective tissue. Usually, the proteinaceous terminal sections decrease in size. The mucous sections increase in size and secretion accumulates there.

In people over 80 years old, the parotid salivary gland, as in early childhood, is mainly composed of mucous cells. The walls of the ducts often show signs of degeneration and atrophy, the content of cambial elements decreases, and the ability of the glands to regenerate decreases. In abnormally dilated interlobular excretory ducts, stones often have an oxyphilic color and a layered structure, containing calcium salts; Small stones are often found in the parenchyma and ducts of the major and minor salivary glands (1.2%), which is not considered a sign of pathology. On the contrary, the formation of large stones (salivary stones) leads to impaired salivary flow and is a pathology called salivary stone disease or xialolithiasis. With age, the amount of stroma and collagen fibers in it increases. The number of adipocytes increases in the interlobular layers, which can later replace the terminal sections and appear in the lobules of the glands. This process is most clearly manifested in the parotid salivary gland, about 50% of its terminal sections are replaced by periductal and subepithelial accumulations of lymphoid tissue; The above processes occur in the major and minor salivary glands. The salivary glands function from birth, but the onset of salivary secretion is unknown. At 20-24 weeks of the postnatal period, salivation increases, up to physiological salivation. After 12-14 years of age, due to hormonal changes in the body, the secretory process in the salivary glands increases intensively. After 60-70 years of age, due to the

development of dryness of the oral mucosa, atrophic processes occur in parts of the gland. The ducts of the salivary glands expand, the nucleus deforms and shrinks. The diameter of the excretory ducts of the gland decreases. The intersegmental and intrasegmental arteries of the submandibular gland undergo sclerosis and hyalinosis, as blood circulation deteriorates, changes in salivation are observed, and arthropathy and hyposecretion are observed in the salivary glands. Initially, Academician I.P. Pavlov, in all his experiments, linked the functions of the digestive system with the salivary glands, studying their physiology and pathology. At the same time, many scientists in their studies noted that the salivary glands are not only involved in digestion, but also have other important functions. For example, it performs a protective and trophic function for the tissues of the oral cavity. In addition, saliva is the main source of the buffer system of the oral cavity and protects the hard tissues of the teeth from demineralization during food intake. When taking xenobiotics (drugs, various food additives), the salivary glands can perform the excretory function. When kidney pathology develops, the salivary glands perform the excretory function.

Over the past twenty years, hypotheses about the incretin function of the salivary glands have been confirmed, and they perform not only an executive function among the organs, but also have a regulatory function. It is inevitable that the salivary glands, in most cases, are involved in the secretion and synthesis of biologically active substances, the general structure of which is similar to proinsulin, consisting of a long polypeptide chain. Eleven facts have already been found. In particular, its effect on nerve growth has been studied in detail. In 1986, the Italian R. Levi-Montalcini and the American Stanley Cohen fully covered this topic and were awarded the Nobel Prize in Physiology or Medicine.

At the same time, researchers (primarily clinicians) have identified and noted the functional connection of the salivary glands with other organs and systems. The salivary glands have a correlative relationship with the whole organism.

Therefore, the recommendations of a number of clinicians, in cases of unsuccessful conservative treatment of sialadenitis of the salivary glands, to remove them (R. Schultz, J. Wood; M. Arrigu, E. Myers) seem very contradictory. A number of surgeons, in addition to extirpation of pathologically changed salivary glands,

suggest denervation of the auriculotemporal nerve or irradiation of the salivary glands with X-rays. The same result is achieved by ligation of the salivary gland duct (S.G. Bezrukov) or introduction of a hardening glue into the duct (R. Zaskawi et al.).

As noted above, the compensatory response of the salivary glands to pathogenic influences contradicts the general biological logic. Many authors suggest the development of adequate models of salivary gland pathology, which would allow preclinical screening of new, pathogenetically based treatment methods.

The CRT test was used to assess the resistance of the enamel surface layer to acids (Morozova N.V.; Donat P.D.; Nauleman; Maiwald, Geiger).

The method was carried out by applying a circle of indicator paper with a diameter of 2 mm, moistened with 1.5 μl of 1 N hydrochloric acid, to the cleaned labial surface of the tooth. The time from the moment of acid application to the change in the color of the indicator to purple is a measure of acid resistance.

To date, many authors have proposed about 24 important risk factors for the development of caries in children, which allow us to estimate the level of caries resistance of permanent teeth and serve as the basis for dividing children into dispensary groups. It is also noted that in children with low caries resistance, the total calcium content in the oral fluid is 2 times lower, and the Ca/P ratio is 1.9 times lower. Moderate caries resistance ($P < 0.05$). In children with low caries resistance, the CRT test score was 1.12 times lower ($P < 0.05$) than in children with moderate caries resistance and 1.24 times lower ($P < 0.05$) than in children with high caries resistance. Thus, caries prevention in children in dispensary groups formed on the basis of the established level of caries resistance of permanent teeth, including local and general preventive measures, can reduce the incidence of caries by 1.6 times.

1.4.2. Qualitative and quantitative composition of oral fluid

It is known that the secretory function of the salivary glands is of great importance in processes such as salivation, endocrinology, and in regulating the activity of other glands of the digestive tract. Finally, saliva itself - oral fluid - always performs various functions.

The practical interest in the physiology of the salivary glands is explained by the fact that saliva separates many substances from the blood, the detection of which allows us to obtain information about the endogenous and exogenous components of the blood in saliva. As can be seen from the presented Figure 3, the oral fluid is a

polymorphic conglomerate consisting of various components of organic (protein) and inorganic nature.

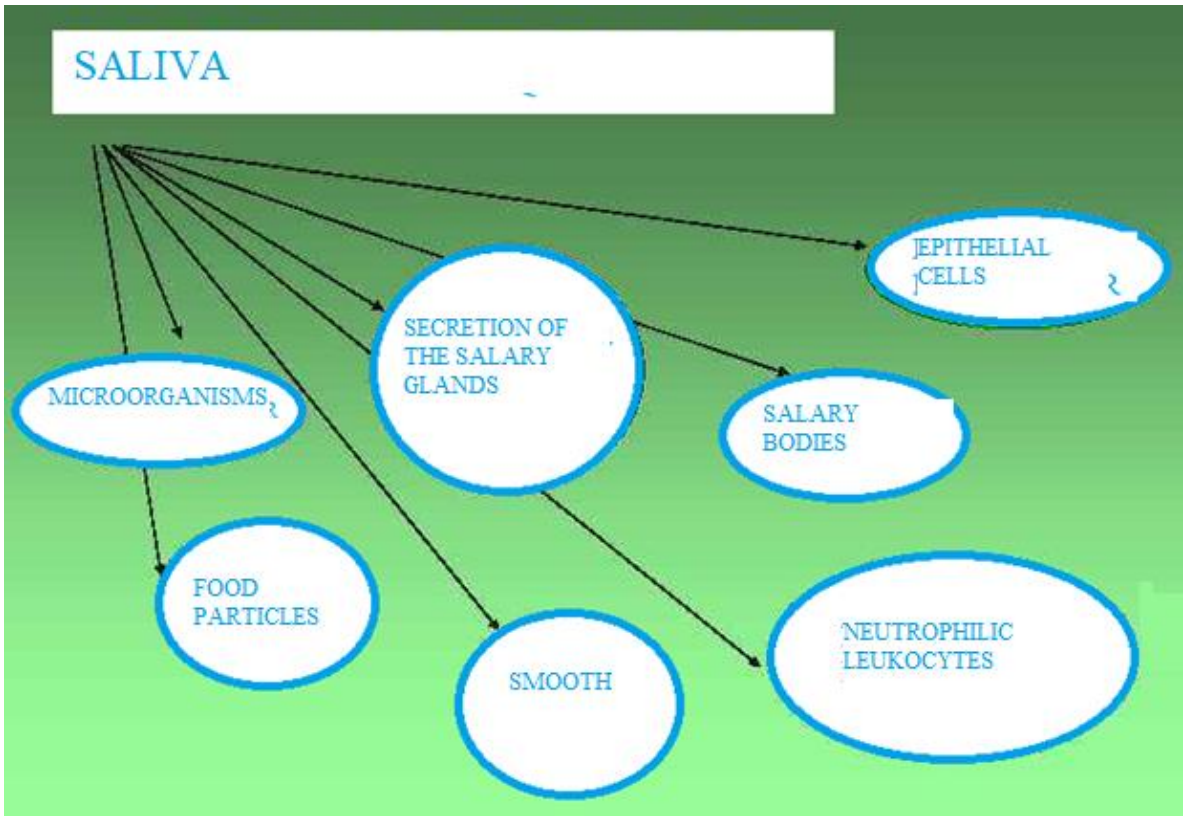


Figure 3. Qualitative composition of the oral fluid.

Quantitatively, during food intake, 0.3-0.4 ml of basal secretion is secreted per minute. The secretion process itself is considered constant, since the regularity of the secretory function of the salivary glands is a necessary phenomenon for the normal manifestation of all processes in the oral cavity. It is known that newborns experience a state of hypersalivation due to the presence of a large number of small glands in the oral cavity, which is very necessary for the baby's sucking movements. For research purposes, the level of secretory activity of the salivary glands under different conditions is of great interest. For example, stimulated secretion is 0.2 - 5.7 ml per minute.

Basal secretion and stimulated secretion indicators are of important diagnostic importance in modern medicine. It should be remembered that a decrease in the corresponding types of secretions below 0.15 and 0.5 ml per minute leads to a state

of hypofunction of the salivary glands, which leads to dysphagia, dysphonia, dysgeusia, the appearance of various cracks and ulcers.

Dysphagia is not a disease, but a medical term that includes clinical symptoms that cause difficulty or pain in the patient when swallowing food, liquid or even saliva. Pathology requires a comprehensive approach and careful diagnosis, since this condition can be observed temporarily or permanently. Dysphagia occurs due to various factors, including neurological diseases, damage to the esophagus by an object, benign and malignant tumors, mental disorders, neuroendocrine diseases, and disorders in the digestive system. Dysphagia can be clinically visualized by Figure 4 below.

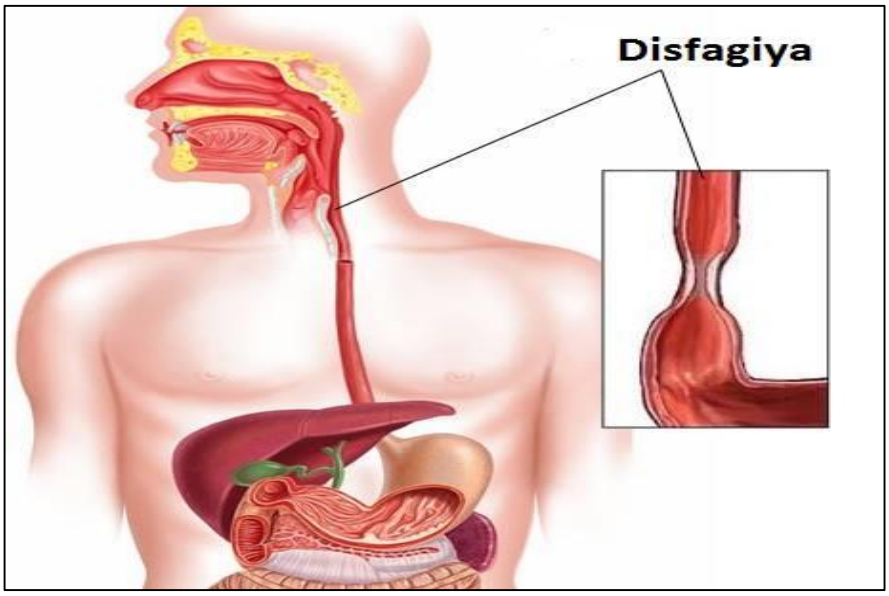


Figure 4. Clinical picture of the larynx in dysphagia.

Since the salivary glands and their secretions are located at the very beginning of the digestive system, it causes disruption of the functioning of all parts of the digestive system. The severity of swallowing disorders and the forms of swallowing or dysphagia can vary. If the complication is mild, it means that food takes longer to pass through the esophagus. It may be painless. Liquids may not be a problem. If the severity of the complication is severe, it may mean that solids and liquids do not pass through the esophagus at all, and this can cause you to regurgitate food and drink. If the complication is in the middle stage, it is something in between these two

intersection points. Swallowing disorders are always a symptom that needs to be properly explained and diagnosed. For example, the first sign of esophageal cancer is often a mild, painless difficulty swallowing that gets worse over time. Therefore, this complication should be investigated or confirmed as the cause of dysphagia as soon as possible. As a general rule, the sooner a serious problem is identified, the better the chance that treatment will improve (predict) the future of the disease.

There are 50 pairs of muscles and nerves that help a person swallow and eat. In other words, there are many things that can go wrong and cause swallowing problems. Acid reflux, heartburn, goiter, esophagitis or esophagitis, esophageal cancer, stomach cancer, esophageal herpes, recurrent herpes simplex, and epiglottitis are some of these complications. Epiglottitis is characterized by inflamed tissue in the patient's epiglottis. This is a potentially life-threatening complication. This complication is considered a medical emergency and may require immediate medical attention.

If a person thinks they may have a swallowing disorder and are having trouble swallowing, there are some symptoms that may be associated with a swallowing disorder. Symptoms include a runny nose, hoarse voice, a lump in the throat, vomiting, sudden weight loss, palpitations, coughing or choking when swallowing, pain when swallowing, and difficulty chewing solid foods. These feelings can make the person feel uneasy about eating and lose their appetite.

Children who have difficulty swallowing may avoid certain foods while eating. They may spit food or liquids out of their mouths, vomit during meals, have difficulty breathing, and lose weight. If swallowing disorders persist, they can lead to malnutrition and dehydration, especially in the young and elderly. These complications are serious and life-threatening and must be treated aggressively. Treatment depends on what is causing the swallowing disorder and the patterns of swallowing. There are several ways to treat swallowing disorders and swallowing problems. If a patient has a brain, nerve, or muscle problem, they may need to do exercises to train their muscles to work together to swallow. The doctor may also

prescribe certain foods and liquids to make swallowing easier. In another treatment, a device is inserted into the patient's esophagus to carefully widen any narrowed part of the esophagus. The patient may need multiple treatments. In some cases, a long, thin scope may be used to remove objects that are stuck in the patient's esophagus.

Reduced salivary gland secretion is called xerostomia, and people with it complain of heartburn, constipation, etc. This condition can cause discomfort, interfere with speech and swallowing, make it difficult to wear dentures, and impair oral hygiene, which leads to a decrease in the pH of the oral cavity and the growth of bacteria. Long-term xerostomia can lead to serious dental caries and oral candidiasis. Xerostomia is a common complaint among the elderly, affecting approximately 20% of them. Dysphonia is a disorder of voice formation in which the quality of the voice (loudness, strength, timbre) is impaired, as a result of which it becomes defective - weak, poorly modulated, hoarse, etc. It occurs as a result of organic or functional disorders of central or peripheral origin. The complete absence of voice, in which only whispered speech can be preserved, is called aphonia. Increased or decreased tone in the vocal folds, incomplete closure of the glottis, tonic spasm of the larynx muscles and convulsive approach of tense vocal folds, discoordination in the work of the external and internal muscles of the larynx, vibrating voice, confusion. speech causes breathing, discomfort in the throat.

The differences between the clinical manifestations of voice disorders depend, first of all, on the nature of the disorder (organic or functional, congenital or acquired). The specific features of voice dysfunction in each form of dysphonia (hypotonic, hypertonic, hypo-hypertonic, mutational, spastic) can also be traced, as well as the duration of the disorder (short-term or permanent changes), the degree of progression of the disease (severe, moderate, mild), the stage of the disease (early or late recovery), pathogenetic mechanisms (nature of the disorder).

The inorganic composition of the oral fluid is represented by the presence of bicarbonates and ions such as potassium, sodium, calcium, magnesium, chlorine, fluorine, etc. The concentration of these substances directly depends on the rate of

secretion and significantly differs from their concentration in the blood. The inorganic composition of the oral fluid plays an important role in the trophism of the oral cavity, the regeneration of oral tissues and teeth. For example, calcium and its hydroxyapatite ions play an important role in the maturation of enamel and its subsequent mineralization during tooth eruption. Today, it is known that saliva and gingival fluid contain physiologically active substances such as epidermal growth factor, parotid, kallikrein, and specific acidic proline-positive proteins, which prevent the crystallization of saliva and its nucleation.

Saliva proteins and their combinations form its proteome. To date, the protein composition of saliva has been fully studied, with recent proteomic studies showing the presence of more than 2000 different proteins and peptides in human saliva [13, 14].

Cataloging salivary proteins and peptides has revealed a large number of proteins with multifunctional properties: immunoglobulins - immune response; antimicrobial activity - lysozyme, lactoferrin, sialoperoxidase, histatin, defensins; mucins - provide hydration and protection of oral tissues; proline-rich proteins precipitate potentially harmful substances from the diet; other proteins (α-amylase) carry out the initial stage of the digestive process [15]. The work of many authors has proven that the optimal activity of salivary amylase is at a pH of 6.5 - 7.0, but in the oral cavity, amylase is resistant to low pH values, bound to the substrate for a short time. This explains its detection in the intestinal chyme.

The work of physiologists from Andijan has proven the low lipolytic activity of saliva, which, in turn, increases the sensitivity of proteins to pepsin and trypsin, which have a low proteolytic activity of saliva.

According to Zheng-Zhi Wu et al. [16], 309 different salivary proteins are associated with their functions: 21% are related to immunity, 1.6% to protein replication, 4.8% to cell motility and secretion, 2.3% to transcription and ribosomes,

4.2% to cell division. cell cycle, 9.7% to signaling, 5.2% to metabolism, 7.1% to cytoskeleton, and 28.7% are proteins of unknown function.

More than 90% of salivary proteins and peptides by weight (200 proteins and peptides) originate from the secretion of three pairs of salivary glands (parotid, submandibular, and sublingual). These include proline-rich peptides, α-amylase, cystatins, histatin, mucins, secretory IgA and carbonic anhydrases [17]. All other components found in saliva account for the remaining 10% by weight [18]. Some of them are secreted by minor salivary glands, epithelial cells, gingival crevice fluid and oral microflora, the sources of some proteins are unknown [18, 19, 20, 21]. As an example of the wide range of protein concentrations in saliva, the concentration of α-amylase in it is measured in mg/ml, and interleukins in it are measured in 6 and 8 pg/ml [22]. It is worth noting that salivary proteins and peptides are characterized by a large variability associated with the presence of complex post-translational modifications such as glycosylation, phosphorylation, acetylation, ubiquitination, methylation, deamidation, sulfation and proteolytic processing [13, 23]. Among these modifications, glycosylation is particularly important, as it adds great complexity to the study of the salivary proteome. Glycans are perhaps the most abundant and structurally diverse of all molecules in nature, and are therefore allocated to the so-called "glycome" of saliva. Their functional significance and impact on human diseases are better understood as a result of modern glycosylation studies [24]. Despite the great difficulties in understanding the role of salivary proteins in the post-translational modification of proteins, M. Castagnola et al. showed that many post-translational modifications occurring during secretion are mediated by enzymes specific to other exocrine and endocrine glands, and the presence of these modifications opens up great prospects, since the concentration of some proteins may reflect their concentration in the blood. Saliva is used as a biological fluid for the diagnosis and prognosis of diseases [18]. Some salivary peptides and proteins are secreted by all major glands, while others are secreted only by specific glands. For example, basic proline-rich proteins are secreted only by the parotid glands, while type C cystatin is secreted mainly by the submandibular and

sublingual glands; acidic proline-rich proteins and statherin are secreted by all glands, although in different relative amounts [25]. The composition of saliva has been shown to vary depending on different physiological conditions: the peak of basal saliva occurs in the middle of the day, and stimulated salivation is also variable and is determined by food stimuli, as well as mucosal moistening and lip and tongue movements. The parotid glands are dominant, stimulating the production of saliva 2 times more than the submandibular glands. The protein concentration in saliva corresponds to this [18]. Age is another important parameter affecting the salivary proteome: recent studies have shown that the secretion of specific peptides differs significantly between children and adults [26, 27].

Saliva protein markers allow the use of saliva in diagnostics. Analysis and identification of salivary proteins is essential for the identification of biomarkers of disease and a better understanding of salivary physiology. Currently, proteomic analysis of saliva is important for the diagnosis and monitoring, as well as the prevention of various pathological conditions [15]. Currently, saliva is used to detect a number of viral diseases (parenteral hepatitis and HIV), and to determine the levels of hormones and drugs [28, 29]. Some progress has been made in the search for salivary markers of a number of diseases, including systemic diseases. The greatest hopes are placed on proteomic methods in the search for early signs of cancer, and indeed with their help, markers of several types of cancer have been found. Head and neck cancer is a very dangerous tumor disease. Mass spectrometry has identified protein markers of this disease: annexin A1, β- and γ-actin, cytokeratins 4 and 13, zinc-containing proteins (zinc finger proteins), and tumor antigen P53 [1]. Proteomic methods have identified 26 markers of oral squamous cell carcinoma, including a number of proteins and peptides, such as carcinoembryonic antigen, interleukin-1, α-defensin 1, TNF α CD 44, fibronectin, and thioredoxin, which were detected at high levels in patients examined. Salivary transferrin has been shown to be a highly specific, sensitive, and accurate marker for the early detection of oral cancer [8]. Using a combination of these markers, the sensitivity was 90%, the specificity was 83% [1], and a specific salivary peptide, c-erbB-2, was found to be relatively high

in patients with breast cancer. Compared with healthy women and women with breast tumors [17, 30]. Zheng-Zhi Wu and co-authors [16] found four proteins (1472.78; 2936.49; 6556.81 and 7081.17) in the saliva of patients with gastric cancer that were absent in healthy people and could be used as a basis for screening studies.

P. Rao et al. [31] A study of the salivary proteome of patients with type 2 diabetes and healthy individuals revealed differences in the concentration of 487 proteins and peptides (33% of which were not previously found in saliva), with 65 proteins having concentrations more than 2-fold higher than in healthy individuals. Most of these proteins regulate metabolism and immunity. Salivary α-amylase levels have been reported to be reduced in type 1 diabetes [17]. Sjögren's syndrome (SSS) is an inherited autoimmune rheumatic disease, the second most common of its kind. The salivary glands are the main target organs of Sjögren's syndrome (SSS), making saliva an ideal biological fluid for diagnosis [32]. In the saliva of patients with Sjögren's syndrome (SSS), eight mass spectrometric peaks with a twofold increase in intensity, β2-microglobulin, lactoferrin, immunoglobulin light chain, polyimmunoglobulin, were detected in the range of 10–200 kDa compared with healthy individuals. Lysozyme C receptors were recorded and cystatin C in all stages of Sjögren's syndrome (SSS); conversely, α-amylase and carbonic anhydrase VI were found in lower concentrations in Sjögren's syndrome (SSS) [33, 34]. Increased levels of β2-microglobulin, γ-glutamyltransferase, soluble interleukin 2 receptor, neopterin, and γ-interferon have been reported in the saliva of patients with Sjögren's syndrome (SSS) [10]. It should be noted that the diversity of salivary composition does not always indicate that these substances are present in the oral fluid. These substances can enter saliva as a result of secretion and excretion from many other sources.

CONCLUSION

The problem of overweight is not only a deviation in the somatic state, but also in the psychological perception of oneself and one's self-esteem. Obesity, especially among young people, has become a worldwide epidemic with a steady increase in prevalence over the past three decades, which raises some concerns, since

metabolic, cardiovascular complications associated with obesity, as well as metabolic syndrome, occur in patients, especially young, able-bodied, long before clinical manifestations.

Of course, the diet is determined not by a malfunction in the metabolism of some biologically active substance, even a very important one, such as serotonin, but by a whole complex of regulators. The role of norepinephrine (increased energy expenditure for thermoregulation) has also been known for a long time, this phenomenon is used in the mechanisms of action of many drugs against alimentary obesity;

Thus, the material presented in Chapter 1, first of all, studies modern views on the current issues of lipid metabolism disorders and related changes not only in adipose tissue itself, but also in glandular tissues, for example, the salivary gland.

CHAPTER II

2.1. Research materials

The study of the specific features of enzymatic homeostasis of blood and oral fluid in people with alimentary obesity required studies aimed at comparing the enzymatic activity of blood and oral fluid in people with different degrees of obesity. These studies were conducted in the ADTI clinic, 78 people participated in the study. Of these, 20 people were in the control group and 58 people were in the experimental group, which consisted of patients with different degrees of obesity.

The gender ratio of the control group was 1:1, and the experimental group consisted of 30 women and 28 men, which were 52% and 48%, respectively. All patients were divided into groups according to their body mass index (BMI) (Table 1).

Table 1

Distribution of patients by BMI

Age of patients Overweight	Age of patients Overweight	Age of patients Overweight	Age of patients Overweight	Age of patients Overweight	Age of patients Overweight
20-29	n=8	n=9	n=7	n=2	26
30-39	n=2	n=4	n=8	n=4	18
40-49	n=1	n=3	n=4	n=3	11

50-60	-	n=1	n=2	-	3
jami	11	17	21	9	58

Note: n – number of patients

According to Table 1, we can conclude that the problem of overweight to varying degrees exists at any age. However, we found that it is most common in people aged 20 to 50 years. As age indicators increase, the total number of patients with increased body weight decreases. However, if we take into account the degree of complexity of obesity in the age category, then it increases quantitatively to the TMI indicators of group 2 and decreases quantitatively to the TMI indicators of group 3.

Table 2. Absolute and percentage proportion of obese patients by age

Patient's age Absolute number Percentage	**Patient's age Absolute number Percentage**	**Patient's age Absolute number Percentage**
20-29 yosh	26	45
30-39 yosh	18	31
40-49 yosh	11	19
50-60 yosh	3	5
Total number of patients	58	100

According to Table 2, it can be seen that metabolic diseases manifested by obesity affect the group of people aged 20 to 50 years in percentage terms. The decrease in performance in this age period due to various degrees of complications is not only medically significant, but also socially significant.

As mentioned earlier, the experimental group consisted of 30 women and 28 men, which in percentage terms were 52% and 48%, respectively. When analyzing the gender and age characteristics of the patients, attention was paid to the prevalence of obesity of varying degrees of severity, the results of which are presented in Table 3.

Table 3. Absolute prevalence rates of different levels of obesity by age and gender characteristics

20 – 29 yosh								**Total**
Men				**Women**				
Overweight	**1 group**	**2 group**	**3 group**	**Overweight**	**1 group**	**2 group**	**3 group**	
3	6	3	1	***5***	***3***	***4***	***1***	26
30 – 39 years old								
1	1	3	5	***1***	***2***	***4***	***1***	18
40 – 49 years old								
-	1	2	1	***1***	***2***	***2***	***2***	11
50 – 60 years old								
-	-	1	-	-	***1***	***1***	-	3
Total								
4	8	9	7	***7***	***8***	***11***	***4***	**58**

Note: OV – overweight

The results of the distribution by gender and age criteria show that in our case, dietary obesity is more common in women than in men. In addition, as can be seen from the indicators in Table 3, the etiological conditions for the development of alimentary obesity increase with age. This is facilitated by metabolic disorders and other hormonal changes in the body, especially in women.

All patients underwent anthropometric examination with measurements of height, weight, waist and hip circumference. Electronic floor scales, stadiometer, measuring tape and caliper were used to carry out these procedures. All measurements were carried out in standard conditions in the control group and in the experimental groups. The control group consisted of representatives of age categories corresponding to the age categories of representatives of the experimental groups.

2.2 Biochemical methods of studying the material

We determined the activity of amylase, lipase in the collected biological material, namely blood and oral fluid, and in some samples we determined the level of total protein.

Amylase is an enzyme produced by the salivary glands and pancreas when starch (glycogen) is obtained from food. Amylase catalyzes the hydrolysis of glycoside compounds to maltose. In acute pancreatitis, a very high level of amylase is observed (more than 10 times the upper limit of normal). The activity of blood amylase also increases with parotitis - inflammation of the salivary glands. With inflammation of the salivary glands, amylase activity also increases in saliva, which is not observed with pancreatitis. A 5-fold increase in amylase activity can be observed in other types of acute abdomen - perforation of a stomach ulcer, intestinal obstruction. The diagnostic specificity of the method is increased by determining the pancreatic amylase isoform. Blood amylase activity decreases with pancreatic necrosis, arsenic and barbiturate poisoning. Considering that alimentary obesity can lead to changes in metabolic mechanisms, which can lead to structural and functional disorders of the salivary and other glands that produce the corresponding enzyme, we focused on determining amylase activity in the blood and oral fluid. Determination of α-amylase activity. The activity of α-amylase in blood plasma and oral fluid was determined by the amylolytic method of A.M. Ugolev et al., based on the photometric method for determining amylase activity according to Smith and Roy. The principle of this method is based on photometric measurement of the decrease in starch concentration as a result of enzymatic hydrolysis of starch by a change in the color of iodine-starch components. The substrate used was phosphate buffer, pH-7.2, 0.1% buffer solution prepared with soluble starch. Amylolytic activity is expressed in milligrams of digested substrate per unit of time.

Lipase (EC 3.1.1.3) is an enzyme that catalyzes the breakdown of glycerides into glycerol and higher fatty acids. The normal level of lipase activity is 0-190 IU / l (Nazarenko G.I. et al., 2002).

This enzyme is produced by a number of organs and tissues of the human body, including the stomach, pancreas, lungs, intestinal juice, allows it to separate leukocytes, etc. From a clinical point of view, the most important is pancreatic lipase. Pancreatic lipase plays a major role in the digestion of fats. Since the main source of lipase is the pancreas, there is a significant release of the enzyme into the circulating blood during pancreatic diseases. Determination of lipase activity in the blood is the most informative criterion for diagnosing acute pancreatitis. There is a misconception that in acute pancreatitis, the level of lipase in the blood increases later than amylase, but remains elevated for a long time. In fact, the content of lipase increases and decreases in parallel with the increase and decrease in amylase activity, but its normalization occurs later than the normalization of amylase. Sometimes the level of lipase in the blood increases before the increase in amylase activity and remains elevated for a long time. In acute pancreatitis, the activity of lipase in the blood increases within a few hours after an acute attack, reaches a maximum after 12-24 hours (up to 200 times) and remains elevated for 10-12 days. If the level of lipase in the blood increases by 10 times or more and does not decrease by 3 times the norm over the next few days, the prognosis of the disease is poor. The sensitivity of serum lipase for diagnosing acute pancreatitis is 86%, and the specificity is 99%. Simultaneous determination of alpha-amylase (blood and urine) and lipase levels is the basis for the diagnosis of acute pancreatitis. Elevation of one or both enzymes is detected in 98% of cases.

Lung cancer differs from ectopic pregnancy, parotitis in that lipase activity is lower than amylase. The edematous form of acute pancreatitis, as a rule, is not accompanied by an increase in lipase activity; fatty pancreatic necrosis is characterized by a significant increase in lipase activity lasting up to 2 weeks; with hemorrhagic necrosis of the pancreas, only a short-term increase in lipase activity compared to normal levels is observed on the 3-5th day of the disease by 3.5 times. With purulent pancreatitis, an increase in lipase activity in the blood is usually not detected. Sometimes an increase in lipase activity is observed in patients with pancreatic cancer, chronic pancreatitis, or in the presence of a cyst in the pancreas.

Lipase activity in the blood increases with necrotic processes in the intestines, peritonitis, biliary colic, with a decrease in fatty tissue - after bone fractures, soft tissue injuries, and operations for breast cancer. Hyperlipasemia in uremia and acute renal failure is a consequence of pancreatic congestion. A decrease in total lipase is also observed in uremia, tumor lesions of various organs, alimentary dystrophy, various vitamin deficiencies, cachexia.

Determination of lipolytic activity. Quantitative analysis of the lipolytic activity of digestive glands and blood secretions is one of the widely used tests for functional assessment of the pancreas and determination of the participation of lipases in interstitial metabolism. In our work, lipolytic activity was determined by the Tits method, which is based on the calculation of fatty acids formed during the lipolysis of tributyrin titrated with an alkaline solution (caustic sodium 0.05 N). The difference in the volume of sodium hydroxide consumed for titration of experimental and control samples was taken as a unit of lipase activity. Lipase activity determined by this method is expressed in Tits units.

Determination of total protein content. The total protein content in some oral fluid samples was determined by the Lowry method. The method is based on the ability of copper protein derivatives to reduce Folin's reagent with the formation of colored reaction products.

2.3 Statistical processing of the material.

The obtained numerical data were subjected to statistical analysis. Data analysis was carried out using the Statistica 10 software package from StatSoft, Inc (USA). The arithmetic mean (M), arithmetic mean error (m) and standard deviation (σ) were calculated. The significance of differences in the variation series in unrelated samples was assessed using the Mann-Whitney test, in paired related samples - the Wilcoxon test. Data are presented in the form M±m, where M is the mean, m is the standard error, or M± σ, where M is the mean, σ is the standard

deviation. The difference between the compared series was considered significant at a 95% confidence level ($p<0.05$).

Correlation analysis was conducted. The correlation of the indicators was calculated using the Spearman method. The correlation coefficient (r) has two properties: it is evaluated by statistical significance and reliability. It indicates the presence of weak (r=0.3), moderate (r=0.3-0.6) and strong (r=0.65 and more) connections, which indicate the contribution of each of these characteristics to the change in the other.

CHAPTER III.

THE SIGNIFICANCE OF ORAL FLUID AND BLOOD AMYLOLITIC ACTIVITY IN OVERWEIGHT PEOPLE

3.1. Amylolytic activity of blood in people with various manifestations of overweight.

Modern medical terminology defines socially significant diseases as the most common diseases that change the quality and duration of life. In our time, the relevance of the problem of obesity among young people is undeniable. Researchers around the world associate this, first of all, with the almost sedentary lifestyle of most adolescents who are not accustomed to a healthy eating culture. The problem of overweight has a negative impact not only on deviations in the somatic state, but also on the psychological perception of oneself and self-esteem of a person. Obesity among young people is becoming an epidemic worldwide, which is associated with a constant increase in prevalence over the past three decades and raises some concerns, since metabolic, cardiovascular complications associated with obesity, as well as metabolic syndrome, occur long before clinical manifestations in young patients. [2]. Obesity in both adults and children and adolescents is a metabolic disorder, the accumulation of excess body fat and weight gain.

Some modern studies on the problem of obesity show that the intestinal microflora also affects the overall energy balance in the body [9, 10]. Today, it is proposed to consider the proposed scheme of metabolic shifts resulting from

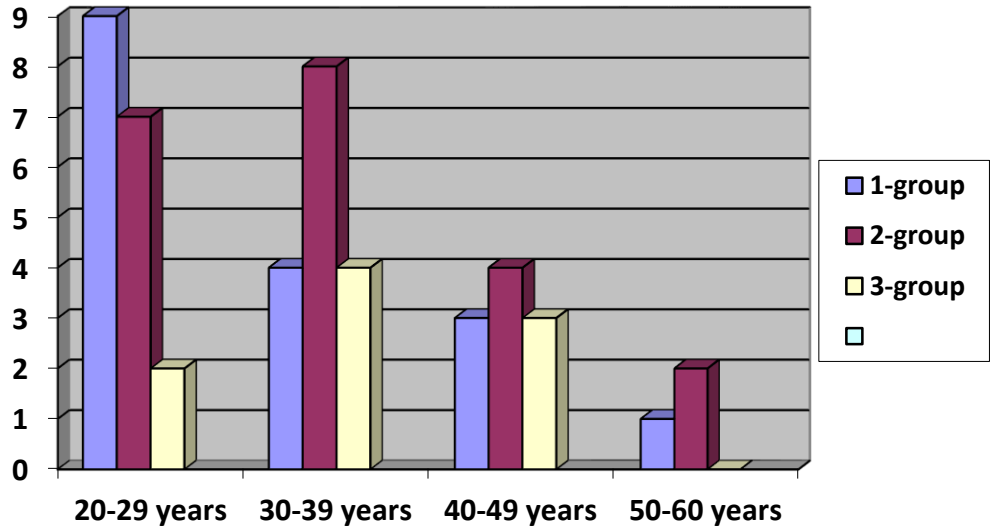
dysbiotic shifts as a consequence of a specific microbial signal that suppresses the human post-induced fat factor (FIAF). The result is an increase in the synthesis and accumulation of fat mass [6]. The combination of certain types of microflora can contribute to subsequent obesity by forming new complexes of triglycerides obtained as a result of fermentation of plant products in the intestine [11]. Experimental studies show that changes in the intestinal microflora lead to energy accumulation and, as a result, obesity. The problems of obesity in young patients, considered at the present stage, have shown that the oral microflora is a very sensitive system of indicators that responds with qualitative and quantitative shifts to changes in the state of various organs and systems of the body. More than 300 obligate and facultative (transient) microorganisms are found in the human oral cavity and throat. Its main function is to ensure the colonization resistance of the macroorganism (Borovsky E.V., Leontyev V.K.; Latyshev O.Yu.). Western Swedish scientists studied the relationship between the level of influence of comorbidities, lifestyle, and socio-economic factors with indicators of obesity and healthy oral cavity. The researchers recommended studying such indicators in healthy oral cavity in further experiments, the data obtained led to the conclusion that there is a connection between poor oral health and obesity [12].

Currently, many researchers have studied the changes in the content of various markers (bicarbonate alkalinity and enzymes) in the saliva of patients with various acute and chronic pathological changes in internal organs and systems. The state of the salivary microbiota has been studied by a number of scientists: in 2005, A.A. Zhigin and A.P. Levits determined the activity of lysozyme, in 1996, the ratio of Nessler urease activity, in 2007, A.P. Levits determined the enzymatic method [14, 15]. According to the conducted studies, in young obese patients, the activity of the unstimulated salivary lysozyme enzyme decreases to 51.0 ± 6.0 units/l (normal 89.0 ± 14.0 units/l) ($r < 0.05$), and the urease content sharply increases to 0.660 ± 0.032 μkat / l (normal 0.090 ± 0.009 μkat / l) ($r < 0.001$). Since it is confirmed that the normal microbiota of the gastrointestinal tract in young patients is indirectly altered

in the body against the background of obesity, urease activity is determined inversely to lysozyme activity (r = 0.78).

Thus, in young obese patients, in accordance with dysbiosis, urease activity sharply increases with a decrease in lysozyme activity. The level of dysbiosis in obese patients increases rapidly (approximately 8 times) (7.97 ± 0.76) ed. compared to healthy people with normal body mass, which is equal to (1.0 ± 0.10) p <0.001. This direction can be the basis for research in order to correct changes in the oral microbiocenosis in young patients with alimentary obesity, to develop therapeutic and prophylactic agents, including these data indicate that the development of local nonspecific immune disorders is accompanied by a change in the relationship between the normal microbiota in the body.

Our goal was to analyze the literature data on the importance of enzymatic homeostasis of amylase activity in obesity of various degrees of severity. To achieve this goal, we first divided patients into appropriate groups. Patients in each group were divided by age and gender (Fig. 1). Data on the absence of overweight in elderly and senile people were discussed. According to all the data, it is possible to understand the central mechanism of metabolic control in this age group, both hormonal and endocrine.



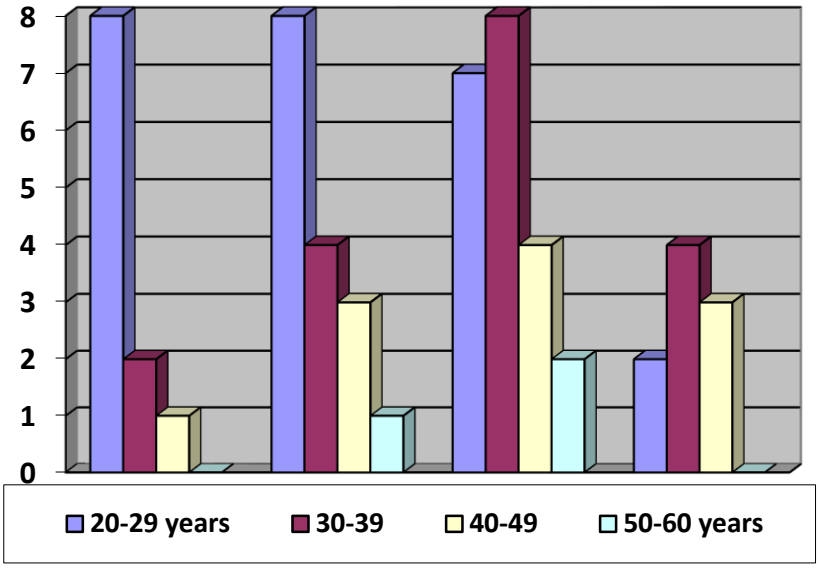


Figure 1. Expression of different levels of alimentary obesity by age

As can be seen from the presented diagram, obesity was more common in people aged 20 to 40. In the group of patients over 50 years old, the TMI index was up to 29 and more than 40.

In all patients, venous blood was taken on an empty stomach in the morning, and amylolytic activity of the blood was determined. As we know, amylase catalyzes the hydrolysis of glycosides to maltose. A very high level of amylase in the blood serum is observed in acute pancreatitis (10 times higher than the highest level of the norm).

The amount of amylase in the blood also increases in inflammation of the salivary glands - parotitis. In inflammation of the salivary glands, amylase activity also increases in saliva. According to our results, in people with nutritional obesity of IV and various degrees, the amylolytic activity of the blood tended to increase its activity. However, it also decreased with age, i.e. In patients aged 50-60 and older, the amylolytic activity of the blood is changed, not always to an adequate level (diagram 1).

3.2. Amylolytic activity of the oral fluid in people with varying degrees of excess body weight

We have already emphasized the information about saliva in our study. The homeostasis of enzymes in saliva and changes in their functional activity depend not only on this gland itself, but also on the whole organism. When comparing the amylolytic activity of the blood with the amylolytic activity of saliva, a similar trend of changes can be seen in Table 1.

Table 1.

Years	Normal value Enzyme Overweight	Normal value Enzyme Overweight	Normal value Enzyme Overweight	Normal value Enzyme Overweight	Normal value Enzyme Overweight	Normal value Enzyme Overweight	**bioma terial**
20-29	30 me/l	**α-** amilaza	↑ →	↑	↑ ↑	↑ ↑ ↑	blood
	28 me/l	**α-** amilaza	→	→	↑ →	↑ ↑	saliva
30-39	30 me/l	**α-** amilaza	↑	↑ ↑	↑ ↑ ↑	↑ ↑ ↑	blood
	28 me/l	**α-** amilaza	→	→	↑ ↑	↑ ↑ ↑	saliva
40-49	30 me/l	**α-** amilaza	↑	↑ ↑	↑ ↑ ↑	↑ ↑ ↑	blood
	28 me/l	**α-** amilaza	→	↑ →	↑ ↑	↑ ↑ ↑	saliva
50-60	30 me/l	**α-** amilaza	↔	↑ ↑	↑ ↑	↔	blood
	28 me/l	**α-** amilaza	↔	↑ →	↑ ↑	↔	saliva

Note: Unreliable change ↑→

increase in the indicator ↑

decrease in the indicator ↓

indicator unchanged ↔

However, these changes are not always clear and reliable (Fig. 2), which, apparently, depends on the age criterion, in which, first of all, involutional processes in the salivary glands and pancreas affect the synthesis of amylase, and in addition, as we know, adipose tissue synthesizes and secretes a large number of biologically active peptides, called adipokines, which act in a local (autocrine and paracrine) framework. Among adipokines, the most studied are leptin, adiponectin, visfatin, which are synthesized by adipose tissue, affecting the development of metabolic disorders and insulin resistance (IR). In addition, adipose tissue expresses a number of receptors that allow it to respond to afferent signals from internal organs and the central nervous system. Leptin (from the ancient Greek λετσος - thin) is a peptide hormone that regulates energy metabolism, which is produced mainly by fat cells and enterocytes of the small intestine. The hormone suppresses hunger, which in turn reduces fat storage in adipocytes [1]. It is encoded by the LEP gene located on chromosome 7 in humans [2]. Human leptin is a 16 kDa protein of 167 amino acids. Leptin is a peptide hormone that regulates energy metabolism and is produced primarily by fat cells and enterocytes in the small intestine. The hormone suppresses hunger, which in turn reduces fat storage in adipocytes. It is encoded by the LEP gene located on chromosome 7 in humans. Human leptin is a 16 kDa protein of 167 amino acids. The hormone acts on cellular receptors in the arcuate and ventromedial nuclei, as well as on other parts of the hypothalamus and dopaminergic neurons of the ventral tegmental area, thereby mediating feeding. Although the regulation of fat storage is considered the main function of leptin, it also plays a role in other physiological processes, as evidenced by the presence of multiple sites of its synthesis and leptin receptors in many cells, in addition to fat cells. Most of these additional functions have not yet been fully elucidated. In obesity, there is a decrease in leptin sensitivity (similar to insulin resistance in type 2 diabetes), as a result of

which it is impossible to detect satiety despite large energy reserves and high leptin levels.

Adiponectin is a hormone synthesized and secreted by white adipose tissue, mainly by visceral adipocytes, and is present in sufficient quantities in the blood - approximately 0.01% of total plasma protein. Its secretion is stimulated by insulin.

The concentration of adiponectin in blood plasma has a clear negative correlation with the atherogenic index, TG and Apo-B levels, as well as a positive correlation with HDL and Apo-A-1. This protein regulates energy homeostasis and has anti-inflammatory and antiatherogenic effects, inhibiting monocyte adhesion to vascular endothelial cells and inhibiting growth factor-induced proliferation of vascular smooth muscle cells. Adiponectin levels are decreased in obesity, in contrast to other adipokines such as leptin, resistin, and TNF-α, which are increased. The development of type 2 diabetes may be associated with dysregulation of the secretion of this hormone. Decreased adiponectin expression has been shown to be associated with insulin resistance. Adiponectin has protective functions against hyperglycemia, insulin resistance, and atherosclerosis (AS), and modulates insulin sensitivity and glucose homeostasis.

Low serum adiponectin levels are an independent predictor of type 2 diabetes. The higher the blood adiponectin level, the lower the risk of developing type 2 diabetes, regardless of body mass index (BMI), race, and sex.

Serum adiponectin concentrations have been shown to be inversely correlated with bone density and visceral fat mass. It has been suggested that adiponectin may play a role in the protective effect of visceral fat on bone density. Adiponectin also inhibits the inflammatory processes associated with AS by suppressing cytokines and adhesion molecules in vascular endothelial cells and macrophages, respectively. The higher the level of the hormone secreted by fat cells, the lower the risk of developing myocardial infarction. Adiponectin counteracts the accumulation of fat

in the arterial walls, which reduces the likelihood of thrombus formation that can lead to myocardial infarction.

Adiponectin is currently considered one of the most reliable biochemical predictors of type 2 diabetes.

Visfatin is a newly discovered adipocyte hormone, and there is a direct relationship between plasma visfatin levels and type 2 diabetes. Visfatin binds to the insulin receptor at a site different from insulin and causes hypoglycemia by reducing glucose release from liver cells and stimulating glucose utilization in adipocytes and myocytes. Visfatin is elevated by hypoxia, inflammation, and hyperglycemia and is downregulated by insulin, somatostatin, and statins. This hormone is located in the cytoplasm as well as in the nucleus of cells and has been detected in many tissues and organs, including the brain, kidney, lung, spleen, and testis, but is predominantly found in visceral adipose tissue. Visceral adipose tissue is considered more harmful than subcutaneous adipose tissue. Visfatin is an endocrine, autocrine, and paracrine peptide with multiple functions, including promoting cell proliferation, biosynthesis of nicotinamide mono- and dinucleotides, and hypoglycemic effects. Visfatin, also known as B-cell colony-stimulating factor, consists of 491 amino acids (aa) in humans, chimpanzees, cattle, pigs, rats, and mice, 490 aa in rhesus monkeys, 285 aa in sheep, 587 in opossums, and 588 aa in dogs. The visfatin gene is highly conserved throughout evolution. For example, the canine visfatin protein sequence is 96% and 94% identical to human and rodent visfatin, respectively. Since the evidence for a direct association between the visfatin genotype and human type 2 diabetes is still weak, more molecular, physiological, and clinical studies are needed to determine the role of visfatin in the etiology and pathogenesis of type 2 diabetes. Thus, adipose tissue is involved in the coordination of many biological processes, including energy metabolism, neuroendocrine, and immune processes.

A number of studies confirm the existence of a relationship between the level of gene expression in adipose tissue, the content of adipokines in the blood serum, as well as between these indicators, age, and basic anthropometric characteristics.

Many authors have reported on changes in the content of adipokines in the blood during obesity in children and the degree of its severity. A relationship between the content of serum adipokines and the presence of metabolic disorders associated with obesity has been established.

The data in Table 1 show the characteristic trends in changes in salivary amylase and blood amylase. It is clear that with the development of complications of obesity, the activity of blood amylase increases significantly. Almost in parallel, the activity and secretion rate of salivary amylase increase. Changes in this direction were characteristically manifested in the age group from 20 to 50 years. In the age group from 30 to 50 years, the amylolytic activity of blood increased to high limits, starting from patients in group 1. It should be noted that we noticed a characteristic trend in salivary amylase, which was manifested in a slightly slower increase in amylolytic activity.

3.3. Lipolytic activity in saliva of overweight people.

Lipolytic activity of blood and saliva has long attracted researchers due to its informative properties. However, lipolytic activity depends on the source and the current functional state of the gland. Thus, lingual lipase is a digestive enzyme produced by glands located in the mouth. The function of lingual lipase in infants is to break down milk fats, mainly triacylglycerols.

The glands that produce lingual lipase are located in the mucous membrane of the root of the tongue and in the baby's pharynx. Their stimulation occurs during natural breastfeeding when sucking and swallowing movements have the property of stimulating mechanoreceptors. Milk is quickly digested, and lingual lipase mixed with milk begins to act only in the stomach. The optimal acidity for lingual lipase is pH 4-5, equal to the acidity of the gastric juice of infants.

The discovery in 1973 of lingual lipase, which is secreted by the serous glands of the tongue and hydrolyzes medium- and long-chain triglycerides in the stomach, renewed interest in the role of the stomach in fat digestion. In humans, lipase is present in the serous (von Ebner) glands of the tongue, where it is localized in

zymogen granules. The highest lipase activity in the body occurs in the stomach. According to immunocytochemistry, gastric lipase is restricted to the chief cells of the fundic mucosa and colocalizes with pepsin. Human lipase purified from the serous glands of the tongue or gastric juice has a MW of 45K to 51K, but is prone to aggregation (MW 270-300K and 500K) and is highly hydrophobic. The secretion of gastric lipase appears to be triggered by at least two receptor mechanisms. The products of gastric lipolysis maintain the sterility of the gastrointestinal tract. These enzymes are essential for the digestion of milk fat in newborns because, unlike other digestive lipases (pancreatic or lactase), lingual and gastric lipases can enter the milk fat globule and initiate the digestion process. In patients with cystic fibrosis, lingual and gastric lipase activity has been found to be reduced and may persist in the upper small intestine in these patients, possibly replacing some of the pancreatic lipase. In these patients, lingual and gastric lipase supplementation may be more effective than current pancreatic enzyme supplementation in preventing steatorrhea. The same therapeutic benefit may be obtained in patients with alcoholic pancreatic insufficiency. The need for lingual lipase decreases with changes in the nature of nutrition, reducing the amount of lingual lipase produced by the oral glands and its importance in fat digestion. In adults, lingual lipase secretion is small, but with a decrease in pancreatic lipase secretion, oral fluid lipase secretion may increase. In diseases of the pancreas, lipase activity increases relatively and begins to be released into the blood in large quantities. In inflammation of the pancreas, its content in the blood increases significantly. After an acute attack of pancreatitis, the level of lipase in the blood serum increases 200 times within 4-8 hours, reaches a peak after 24 hours, and decreases after 8-14 days. The detection of lipase in pancreatitis should have high clinical sensitivity and specificity. At the same time, the determination of lipase and amylase gives 98% accuracy in diagnosing pancreatic damage. The norm of lipase is as follows: in adults - up to 190 units / l, in children under 18 years old - up to 130 units / l (turbidimetric method).

The results of our studies showed that lipase in the oral cavity fluid during caries is not very informative for tooth damage and requires a lot of work to use.

When conducting a correlation analysis between lipolytic activity and the degree of obesity, a multidirectional tendency of the correlation was noted. Thus, the correlation coefficients for obesity in groups 4 and 1 were weakly significant and had low values ($r = 0.42 \pm 0.3$). However, in the 30-39 age group, in obesity groups 2 and 3, these indicators already had high values ($r = 0.6 \pm 0.4$). However, this indicator cannot be considered a true indicator of the oral cavity, since liver (fatty hepatosis) and pancreatic damage were noted in these obese groups. It is possible that it was pancreatic lipase that corrected the study indicators in this way.

Thus, it should be noted that the determination of the lipolytic activity of oral fluid is a very laborious procedure and does not always have to be performed in the study of amylolytic activity.

CONCLUSION

Thus, the study of several correlations of physiological parameters with weight indicates the systemic nature of obesity, affecting more than 40 different physiological functions. These changes are combined into 3 groups that are correlated and physiologically related: associated with increased external respiration and oxygen exchange; associated with age and blood triglycerides; associated with eating disorders. Changes in age and lipid metabolism, although they are predisposing to obesity, are not mandatory.

When conducting correlation analysis, no indicators with a very high correlation were identified ($r > 0.8$); Average correlation values ($0.6 > r > 0.4$) were observed for weight and 4 parameters: pulmonary ventilation (l/min) $r > 0.410$*, vital capacity (cubic cm) $r > 0.477$*, hemoglobin $r > 0.467$ *, amylase (g/l × h) $r > 0.402$*; the remaining parameters, although their relationship with weight was statistically significant, had a low correlation ($0.4 > r > 0.18$). Body weight with age showed a low, but significant, correlation ($r = 0.22$, $p < 0.05$).

To date, a large number of data have been published demonstrating the unusually high potential of saliva for diagnostic purposes, and a review of published

works devoted to this problem allows us to draw the main conclusion that the study of the salivary proteome is at the stage of data accumulation. The lack of standardization in the collection of materials, methods of analysis, as well as the requirements for the representativeness of samples from which conclusions are drawn, lead to "discord" in the data obtained by different researchers and create obstacles to their practical use. In addition, to date, the physiology and biochemistry of saliva and salivary glands, as well as the specifics of the interaction of salivary proteins with oral microorganisms, have not yet been sufficiently studied. Solving these problems and, first of all, unifying the methods of material collection makes saliva an ideal biological tool both for diagnosing diseases and for predicting the development of the disease.

CHAPTER IV

The relationship between amylolytic activity of blood and oral fluid in people with excess body weight.

4.1. Dynamics of the relationship between laboratory parameters of amylolytic activity in different degrees of alimentary obesity.

In groups with different degrees of alimentary obesity, the pH of the oral fluid, the buffer volume of saliva, the total calcium and phosphorus index showed a relationship between them ($R < 0.05$).

In the group with grade 1 alimentary obesity, the pH of the oral fluid, the buffer volume of saliva, the total calcium and phosphorus index were correlated with each other. In the study of enzyme homeostasis for amylase in representatives of group 1 with TMI from 30 to 34, a relationship was established between the activity index and the TMI index and the rate of blood amylase secretion. The amylolytic activity of the saliva of the oral cavity fluid and the parotid gland showed a slight tendency to lag. In group II, there was also a correlation between the pH level and total calcium and the buffer capacity of the oral cavity fluid ($P <0.05$). In all groups, a strong relationship was established between the pH level of the oral cavity fluid and the total calcium index. Thus, in groups of different severity of alimentary obesity, the total calcium index was associated with all laboratory parameters, but this relationship was not observed throughout the entire observation period, that is, they were the same in some groups of patients ($P <0.05$).

In each group, the relationship was observed at different later periods. In the main groups treated with physical methods for alimentary obesity, a lower correlation was observed between total calcium and salivary indices, except for the group with overweight TMI from 25.5 to 29.5 ($P < 0.05$), in the groups in which patients received not only physical methods of treatment, but also drugs such as Dietress, the reliability of the correlation between amylase activity and its flow rate was lower. We considered this situation as a treatment effect. It is known from the work of T.V. Reshetova et al. that the appetite-regulating drug Dietress sensitizes type I cannabinoid receptors through allosteric modulation mechanisms, which is accompanied by an increase in their sensitivity to endogenous cannabinoid neuropeptides. As a result of these processes, the endocannabinoid regulation of the mesolimbic system is normalized. Experimentally, when the drug is administered to animals, it inhibits the lateral hypothalamus from self-stimulation, indicating the saturation of the positive emotional reinforcement system and a decrease in the euphoric value of food. Taking the drug is accompanied by a decrease in food intake and weight loss, without having an inhibitory or stimulating effect on higher nervous activity. Previous studies have studied and analyzed the effects of Dietress in different dosage formats on patients with different degrees of obesity [7]. The observed relationship between the pH of the oral fluid and other indicators of different degrees of alimentary obesity, which we divided into groups, showed a real relationship between them. Thus, in a correlation study conducted across all obesity groups, the correlation coefficient r ranges from 0.5 to 0.8 ($r = 0.5 \pm 0.1$; $r = 0.8 \pm 0.3$), indicating a direct and significant relationship between almost all indicators of different levels of TMI.

Table 1.

Percentage expression of the correlation between amylolytic activity of blood and oral fluid in different obesity groups.

Indicator	OV	Group 1	Group 2	Group 3
blood	0,4 ± 0,2	0,6 ± 0,3	0,8 ± 0,2	0,5 ± 0,3
%	40	60	80	50
saliva	0,35 ± 0,1	0,6 ± 0,2	0,75 ± 0,1	0,7 ± 0,2
%	35	60	75	70

The figures in the table show that the relationship between the degree of obesity and amylolytic homeostasis is indeed direct and very high.

In the group with grade III alimentary obesity, not only was a correlation established between the buffer capacity of saliva and amylase activity ($P < 0.05$), but also, despite the increase in amylase activity, the patient's age was slightly longer.

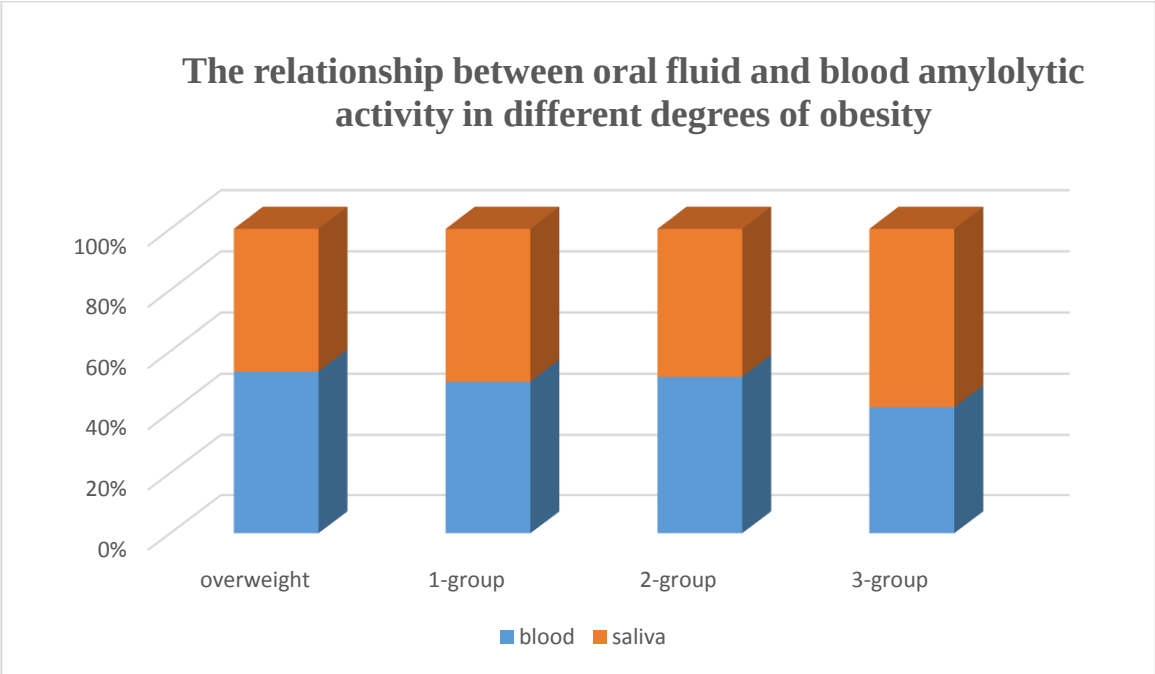
Thus, in all groups, evidence-based results were obtained on the existing relationship between amylase activity and the rate of amylase secretion with the degree of obesity in different age groups. In this regard, we believe that it is necessary to include in the registry of examination of people at risk of obesity not only the study of enzyme homeostasis of blood, but also of oral fluid. Our results show the promise of studying oral fluid not only in terms of determining its biological functions in the body and ensuring the dynamic stability of the internal environment, but also as an alternative to blood for diagnostic purposes.

4.2. Cluster analysis of clinical and laboratory indicators in different degrees of alimentary obesity.

Cluster analysis in combination with the multivariate scaling method made it possible to clearly see the internal connections between the variables under study. As it turned out, two clusters consisting of clinical and laboratory indicators are formed in all groups with different degrees of severity of alimentary obesity. During the study, indicators can move to one or another cluster. We found that the correlation of certain clinical and laboratory parameters of oral cavity and blood homeostasis in clusters can determine the success of initial obesity treatment. During the study, indicators may shift to one or another cluster, but nevertheless, the relationship between the indicators can be considered one-sided. The results of cluster analysis of amylase activity and amylase secretion rate confirm clinical patterns associated with the possibility of self-regulation of lipid metabolism. The use of lipolytic drugs and physical correction of obesity change the results of the correlation between TMI and amylase activity, but do not completely eliminate it.

During the entire observation period, two clusters were formed, consisting of clinical and laboratory indicators. The parameters changed chaotically with each other in the clusters throughout the entire observation period. Similar to the

comparison group, a lack of stability in the correlation of clinical and laboratory parameters was found during decompensation of lipid metabolism, which negatively affects the microbiota of the oral cavity.



The results of the cluster analysis of clinical and laboratory indicators show that the II degree of alimentary obesity (with the establishment of an optimal correlation between the indicators of enzymatic homeostasis of the oral cavity fluid and blood, when favorable conditions are created) can be eliminated by taking medications. The III degree of alimentary obesity cannot be eliminated by creating an optimal correlation without natural correction of body mass according to an individual scheme. The established facts confirmed the existence of a strong positive correlation between the results of the cluster analysis of enzymes in the blood and saliva, and the results of clinical observation in the patient group were explained.

Thus, based on the cluster analysis, a relationship was established between the results of treatment and changes in enzyme homeostasis in alimentary obesity, which once again confirmed the existing correlation.

CONCLUSION

Although a large amount of data has already been published indicating the unusually high potential of saliva for diagnostic purposes, a review of published works on this issue.

It is possible to draw the main conclusion that the study of the salivary proteome is still at the stage of data collection. The lack of standardization in the

collection of materials, methods of analysis, as well as the requirements for the representativeness of samples from which conclusions are drawn, create obstacles to the practical use of the data obtained by different researchers. In addition, to date, the physiology and biochemistry of saliva and salivary glands, as well as the specifics of the interaction of salivary proteins with oral microorganisms, have not yet been sufficiently studied. Solving these problems and, first of all, unifying the methods of material collection, makes saliva an ideal biological tool both for diagnosing diseases and for predicting the development of the disease.

When conducting correlation analysis, no indicators with a very high correlation were identified ($r > 0.8$); Average correlation values ($0.6 > r > 0.4$) were observed for weight and 4 indicators: pulmonary ventilation (l/min) $r > 0.410$*, vital capacity (cubic cm) $r > 0.477$*, hemoglobin $r > 0.467$ *, amylase (g/l × h) $r > 0.402$*; the remaining indicators, although their relationship with weight was statistically significant, had a low level of correlation ($0.4 > r > 0.18$). Body weight with age showed a low, but significant, correlation ($r = 0.22$, $p < 0.05$).

Thus, the study of several correlations of physiological parameters with weight indicates the systemic nature of obesity, affecting more than 40 different physiological functions. These changes are combined into 3 groups that are correlated and physiologically related: associated with increased external respiration and oxygen exchange; associated with age and blood triglycerides; associated with eating disorders. Age and changes in lipid metabolism, although they are predisposing to obesity, are not mandatory.

CONCLUSIONS

1. Clinical polymorphism in the manifestation of alimentary obesity is accompanied by characteristic changes in the enzyme homeostasis of blood and oral fluid.

2. The shift in the amylolytic activity of blood and oral fluid is significantly determined relative to the lipolytic activity of the corresponding fluids and is associated with the degree of obesity.

3. The existence of a relationship between changes in the enzyme homeostasis of blood and oral fluid and the manifestation of obesity.

4. Pathogenetic substantiation of the diagnosis of alimentary obesity and a comprehensive assessment of the effectiveness of treatment using non-invasive methods can be used in practical health care for optimal therapy and medical examination at primary medical examination.

PRACTICAL RECOMMENDATIONS

1. It is necessary to expand preventive measures related to the fight against alimentary obesity, educate the population about a healthy lifestyle, and include early diagnostic methods in the examination algorithm.

2. Changing the oral microflora in young people, together with an active lifestyle and high-quality energy expenditure, can create a new strategy for the prevention and treatment of this problem.

3. It is necessary to include in the examination registry of people at risk of morbid obesity the study of enzyme homeostasis not only of blood, but also of oral fluid.

4. Our results indicate that oral fluid should be studied not only from the point of view of determining its biological functions in the body and ensuring the dynamic constancy of the internal environment, but also for diagnostic purposes alternative to blood.

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