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E-Book

# Diabetes 2 Types for Fellow an Edition _ Part 3

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*"We cannot solve a problem, using the same mentality which we have created them"*

*-A. Einstein*

Competent treatment a diabetes of 2 type at Children and Adults - psychosomatic and an infectious disease (3 part).

Clinical a BOOK (clinical cases are approved in the practice).

(Own researches and the analysis of references).

## Role of kidneys in a glucose homeostasis

As glucose is not capable to get freely through a cellular membrane, in suction it in intestines and reabsorbtion in kidneys glucose carriers (SGLT), coded by gene SLC5A participate sodium-dependent. The family of genes SLC5A is revealed in various fabrics and in details investigated. By the present moment molecular structures two sodium-glucosic co-transporters glucose - SGLT1 and SGLT2 are allocated, cloned and deciphered. Both carriers of glucose are identical on amino acid to structure and consist of 672 amino acids.

SGLT1 - The conveyor with high affinity, but small ability to transport glucose through a cellular membrane, expressed mainly in cages of a thin gut, is less in cages of kidneys (in distal segments S2 and S3 the proximal tubule, where reabsorbtion approximately than 10% of glucose, not exposed to the return siction in segment S1), and also hearts, skeletal muscles, a trachea and lungs. Low levels of the given fiber are fixed in genitals (a uterus neck, ovary, prostate gland, VAS deferens channels). Mutations SGLT1 lead malabsorbtion glucose and galactoza's.

SGLT2 - The conveyor with low affinity, but high ability to transport glucose. SGLT2 in epithelial cages of initial department the proximal tubule of nephron's, in a S1-segment, where reabsorbtion the glucose most part almost always settles down. It is shown, that SGLT2 it is selective expressed in kidneys and not expressed in more than other 70 fabrics, including a liver, skeletal muscles, a fatty fabric, a mammary gland, a bladder and a brain. SGLT2 it is considered the basic transport fiber involved in reabsorbtion of glucose from glomerular of an ultrafiltrate back in a blood channel.

Reabsorbtion glucose epithilial cages nephritic tubules demands covalent reabsorbtion some sodium. Return capture of sodium is carried out with the help adenosine-trio-fosfat's the pump through basolateral a cage membrane. Reabsorbtion glucose and sodium cages occurs in the ratio 1:1. Glucose allocation in blood from cages nephritic tubules is carried out by means of glucosic conveyors of family GLUT.

As have shown results of genetic researches of persons with family nephritic glucosuria's, in 90% of cases the mutation of gene SCL5A2 coding SGLT2 is found out inactivation. Thereby it is proved, that at person SGLT2 is the basic mechanism reabsorbtion glucose in kidneys. Thus at patients with family nephritic glucosuria's are not observed hypoclycemia's or other clinical consequences lowered reabsorbtion glucose though they have expressed glucosuria's. It, and also that at patients with a diabetes 2 types are paradoxical increases reabsorbtion glucose in kidneys owing to increase of an expression and functional activity SGLT2, has served as a starting point for the further researches concerning inhibition SGLT2 as to a therapeutic target at a diabetes 2 types. Inhibition SGLT1 is unreasonable, as intestinal malabsorbtion glucose and galactoza's leads to a wearisome osmotic diarrhoeia.

## Competent treatment of the DIABETES 2 types. 2 part. Modern hypoglycemic preparations

Adequate it is considered glicemia on an empty stomach and before meal of 5, 1-6, 5 mmol/l, in 2 hours after meal - 7, 6-9 mmol/l, before a dream - 6-7, 5 mmol/l, and HbA1c - 6, 1-7, 5%.

The high-calorie and fat products forbidden for the use during a diet, can appear again in a diet if them to use during certain time of day.

Experts consider, that the fixed schedule of food intake can be more effective, than an exception of a food allowance of fat products. Opening will help much to struggle effectively with excess weight, not refusing completely from favourite products.

The general directions in medicamentous treatment of a diabetes of the second type

1. Secretogens (insulin stimulators)
2. Inhibitors an alpha-glukozidazy
3. Preparations Glitazons
4. Combined therapy

## Secretogens (insulin stimulators)

Very popular medicines, are made on a basis Sulfanylurea, differ various efficiency and in the speed suction. The strict dosage is required, overdose can put the reason hypoglicemia's. This pathological condition caused by sharp fall of concentration in blood of glucose, Easy stages are characterised by pallor of a skin, sweating, the raised palpitation. In heavy forms there is consciousnesses, speech infringements, a loss of movements and orientation. The patient can run in coma's.

Stimulation of beta cages of a pancreas by operating substance that leads to increase of secretion of insulin is made. Period of validity is limited to viability of cages.

Advantages. Have strongly pronounced medical effect, by 2% reduce HbA1C, stimulate early peak of secretion. Carry out blocking only calium channels. The patients accepting such medicines, it is possible not to translate in a stage of a coronary syndrome on insulin.

Lacks. During reception there is an aggravated feeling of the hunger, the accelerated rates the weight of the patient increases.

Pregnancy and chest feeding, obvious insufficiency of beta-cages, atrophy of functions of work of a thyroid gland concerns contraindications.

Maninil - the modern preparation, concerns the second generation, has expressed hypoglicemic effect. The metabolize liver cages, does not render negative influence on kidneys. The maximum daily dose cannot exceed 20 mg, to older persons the dose decreases to 10 mg. Tablets are accepted twice a day, the dose is corrected taking into account weight of disease. The effect is estimated after 4 weeks of constant reception if positive changes are insufficient it is necessary to pass to the combined treatment.

Diabeton with modified release (w MR) (Gliclazid) 60 mg - are on the second place on frequency of appointment, feigns an early maximum of secretion of insulin, can not only lower sugar level in blood, but also improve it reological indicators. Positive impact on blood supply makes, does not suppose development of pathologies of a retina of an eye, shows antioxsidant properties. Depending on a disease stage time or two times a day can be applied. The first effect is defined in a week after the reception beginning, increase of a daily dose is supposed only after the urine and blood analysis. The maximum reception cannot exceed 320 mg/days.

Glimepirid 4 mg - concerns preparations of the third generation, releases insulin throughout 24 hours, it can be appointed at a myocardium heart attack. After reception in an organism it does not collect, allocated with urine and excrements. Is accepted once a day, the step of degree and an initial dose makes 1 mg. The estimation of efficiency of action is made after a week of treatment, changes of quantity of the appointed preparation are supposed only after the urine and blood analysis. At transition to other preparation an exact parity between doses of various medicines to define it is impossible.

Inhibitors an alpha-gljukozidazy - in Russia from the big family of these effective preparations there has passed the state registration only one means – Acarboza. Acarboza carries out a role of the filter which is not giving to possibility to be absorbed in blood to difficult carbohydrates. It contacts enzyme of a thin gut and does not allow it to split difficult polysacharids. Thus, development hyperglicemia's is warned.

Advantages. Does not affect glucose level, does not stimulate its manufacture. Positively influences weight of a body, the patient starts to dump excess weight moderately. The effect is reached at the expense of that, the smaller quantity of high-calorific glucose gets to an organism much more. In practice it is proved, that as a result of long the use акарбозы is considerably slowed down progress of an atherosclerosis of vessels, they increase the passableness, function of smooth muscles of walls of capillaries improves. The preparation in blood is not soaked up, that excludes occurrence of pathologies of internal bodies.

Lacks. In intestines because of a considerable quantity raw fermentation that can become the reason of swellings and diarrheas begins enzymes of carbohydrates. Effectiveness of a preparation is much less, than Metformin and derivatives Sulfonilurea.

Reception of patients with a cirrhosis, various inflammations of intestines, nephritic insufficiency, to pregnant and feeding mothers is forbidden. By-effects do not meet almost.

The initial dose - three times on 50 mg is accepted to meal. After 4 weeks of reception of a preparation in treatment it is necessary to make a break.

Glucobay 100 – psevdotetrasacharid a microbic origin, influences quantity of soaked up glucose, stabilises its indicators in blood within days. The maximum concentration comes in 2 hours after reception, is deduced by intestines (50%) and kidneys (50%). Effectiveness is checked after 4 weeks of medicamentous therapy, on indicators the daily dose can be increased to 200 mg three times a day. Joint application with adsorbents is not recommended.

Miglitol (Mizobid) 25 - is Inhibitor's the alpha-glukozidazy, hypoclicemic a preparation. The initial dose to 25 mg three times a day, check efficiency is made approximately in 4-8 weeks. On the basis of laboratory analyses the dose is corrected and can increase to 100 mg at one time. As collateral action can arise a swelling, a diarrhoeia, meteorism and seldom skin rash. It is not recommended to accept at diseases of intestines, obstruction of a thin gut and ulcer pathologies. Reduces availability of Propranolol's and Ranitidin's.

Voxid 0,2 mg - competitive ингибитор the alpha glucose, splitting polysacharids. Oppresses formation and suction glucose, lowers its concentration in blood. Does not render negative influence on activity β-glukozidazy. The preparation is slowly soaked up in blood that minimises risks of occurrence of negative reactions, quickly deduced from an organism with cal's. It is forbidden to appoint to patients with a diabetic coma, after difficult operative intervention and pathological conditions of intestines.

## Preparations Glitazons

The medicine applies for today two medical means of this group: Pioglitazon and Rosiglitazon 8 mg (Roglid).

Operating substances stimulate receptors of cages of muscular and fatty fabrics that leads to increase in quantity of made insulin. Peripheral fabrics start to react better to presence endogen insulin.

Advantages. Are considered as the most effective medicines among peroral preparations. At the expense of blocking lipoliz in blood the quantity of free fat acids goes down, a fabric will be redistributed in the hypodermic. Operating substances increase percentage lipoproteids with high density, lower level trio-acylglicerids.

Lacks. Negatively influence functioning of cardiovascular system, monotherapy lowers physiological level HbA1C. Long reception can become the reason of increase in weight of a body.

Are used, as monopreparations or in a complex with other medical means. Sometimes there are the reason of a delay of a liquid in an organism, anemias and deviations of hepatic enzymes from norm.

Diab-norms - has effectively proved during monotherapy of patients with excess weight, stimulates gamma receptors. Raises speed of recycling of glucose, improves the control of plasma concentration. Long consumption in the maximum doses can cause infringement of sight and a sleeplessness. Sometimes promotes infectious diseases of respiratory system.

Pioglitazon 30 mg (Pioglar) - stimulate γ-receptors, participating in process of decrease in concentration in glucose blood, lowers quantity trio-acylglicerids. Possesses high absorption, it is deduced from an organism sick of bile, the maximum concentration in blood is reached in 24 hours. For equilibrium concentration it is required seven days. It is not recommended to reception to pregnant women and feeding mothers.

Avandia (Rosiglitazon) 8 mg - are Increased by sensitivity of receptors of fatty fabrics to insulin, keeps and restores physiological function of beta cages. Considerably lowers level of fat acids, improves the control glicemia's. It is forbidden to accept the patient with a hypersensibility on Rosiglitazon, to nursing mothers and pregnant women.

Attention to the doctor and the pharmacist! Bruises or wounds of diabetics are well treated freshly cut by slices of turnip ordinary!

Attention! The agency under the control over a foodstuff and medical products of the USA (FDA) informs, that it is going to limit considerably use of this preparation as a whole, first of all at patients with a diabetes of the second type which can supervise sugar level in blood by means of other preparations. This decision FDA is based on the received data according to which Avandia can raise risk of such cardiovascular events as a heart attack of a myocardium and a stroke.

According to the new program of an estimation of risks REMS, Avandia it will be accessible to new patients only in the event that they cannot successfully supervise glucose level other preparations and for any reasons cannot accept Pioglitazon (other preparation from this a class, as Avandia). Those patients who already receive Avandia, can at desire continue therapy.

## The combined therapy

If monotherapy has shown the not efficiency even at the maximum dose of reception treatment by several preparations should

be appointed. The concrete choice is made taking into account features of a current of illness and possibilities of an organism of the patient. The medicines influencing increase of secretion of insulin and sensitivity of a peripheral fabric more often steal up. The second preparation is added only after inspection, thus the dose of the first does not decrease.

### The purposes of Treatment of a diabetes 2 types

As at the heart of this disease lay both function infringements insulin-secreting pancreas islets, and decrease in sensitivity of peripheral fabrics to insulin or insulin resistance, as a result of it level of sugar of blood raises above normal indicators.

The basic therapeutic purpose for sick of a diabetes 2 of type is decrease glycolisad haemoglobin (HbA1c) to level below 6,5% for what it is necessary to support glucose level on an empty stomach at level 5, 5 mmol/l, and in 2 hours after meal - more low 7, 5 mmol/l.

Treatment of a diabetes 2 types includes a diet, the dosed out physical activity, training of patients to self-checking of a diabetes and medicamentous therapy.

2 types are applied to treatment of a diabetes following preparations:

1. The means influencing decrease suction of carbohydrates in a gastroenteric path (Acarboza, etc.);
2. Biguanids (Metformin);
3. The means stimulating secretion of insulin, preparations sulfanilurea (Glibenclamid, Gliclazid, Glicvidon and preparations of III generation - Glimepirid);
4. Preparations of short action (Glinizids).
5. Monoinsulin Therapy.
6. The combined therapy which consists in appointment peropal hypoglycemic preparations and carrying out insulin therapy.

### The qualitative control over disease is provided by special devices - дозаторов.

They are applied since 1980th years, but absolutely new devices which are intended for independent use as means for introduction of penicillin (syringes-handles) now are used. But now, especially at heavy patients, have started to apply constant introduction of insulin pomp a method. Pricks are replaced with constant introduction of insulin, and in those dosages which are necessary at present. Speed of its introduction can be regulated independently. It differ modern pompal devices which as much as possible authentically simulate pancreas work, and replaceable therapy becomes similar to natural secretion of insulin. In a pomp preparations of insulin of short action are used. It is the reliable assistant in indemnification of disease for children and teenagers with the heavy form of a diabetes. For transition on pompal therapy hospitalisation is not required, all medical manipulations are spent in a polyclinic. However installation of a pomp demands from the doctor of special skills and ability, and for its competent use special training is necessary.

With the help pomp insulin introductions 4 variants of introduction of insulin are made, there is a programming possibility at once 5 basic bazal programs, the minimum dosage of insulin makes 6, 1 units at o'clock, time increase and fall of giving of insulin.

To patients with a diabetes receiving insulin, it is necessary to count up quantity of carbohydrates in the food. For this purpose there is a system of grain units (GU). Such quantity of a product in which contains 10-12 r carbohydrates is accepted to 1 grain unit.

### A food at excess weight

### Water exchange.

Water is the major component of a live organism. As ideal “transport” means of organic and inorganic substances, and also optimum environment of dissolution and various reactions in exchange processes, it is impossible to overestimate its role and value. But also here, speaking about balance and harmony, it is necessary to underline, that both its surplus, and a lack are equally harmful to an organism. At a diabetes 2 types are possible infringements of processes of an exchange of water, both in one, and in other party: Dehydration comes as a result of long starvation and at the raised loss of the liquid caused by activity of kidneys at a diabetes. In other case when kidneys do not cope with the problems assigned to them, there is a superfluous accumulation of water in intercellular space (pasty and hypostases) and in body cavities (anasarca). This condition is called hyperosmolar hyperhydration. For restoration of acid-alkaline balance, stimulation of metabolic processes and restoration of the optimum water environment, doctors recommend to drink mineral water.

### The best water from natural mineral sources:

Bojomi; Essentuki; Mirgorod; Pyatigorsk; Istisy; Berezovskys mineralized waters.

It is possible to drink artesian water, any pure spring water. If those are not present, it is better to filter water from the water crane.

Important! At a diabetes 1 and 2 types the use of mineral water not only is authorised, but also it is extremely desirable, is well

influences an exchange of carbohydrates, motivates insulin receptors, strengthens reaction of the enzymes participating in process of delivery of glucose in a fabric of an organism.

The low-calorie diet which main principles are is applied:

- Limitation fats, sugar and alcohol;
- Moderate restriction of the food rich with fibers or carbohydrates;
- Free the use of food rich with vegetative fibres, poor nutrients.

In an organism 1 g the squirrel provides development of 4 kkal, 1 g carbohydrates - 4 kkal, 1 r fat - 9 kcal.

All products share on following groups:

1. Products which are used without restrictions: cabbage, cucumbers, salad, pepper, a vegetable marrow, eggplants, a beet, carrots, a siliculose string bean, a garden radish, a radish, turnip, green peas (young), spinach, sorrel, mushrooms, tea, coffee without sugar and cream, mineral water, drinks on sugar sweeteners. Vegetables can be used in the crude, boiled or baked kind. Use of fats (oil, mayonnaise, sour cream) in preparation of vegetable dishes should be minimum.
2. Products which should be used in moderate quantity: low-fat meat and fish, milk and sour-milk products (low-fat), cheeses less than 30% of th fat content, cottage cheese less than 5% of th fat content, a potato, corn, mature grains bean (peas, a string bean, lentil), groats, pasta, bread and bakery products (but not rich), fruit, eggs.
3. Products which are necessary for excluding or as much as possible to limit: creamy, vegetable oil, fat, sour cream, cream, cheeses more than 30% of th fat content, cottage cheese more than 5% of th fat content, mayonnaise, fat meat, smoked products, sausage products, fat fish, a skin of a bird, canned food meat, fish and vegetative in oil, nuts, sunflower seeds, sugar, honey, jam, jams, sweets, chocolate, cakes, pies and other confectionery products, cookies, products from fancy pastry, ice-cream, sweet and alcoholic drinks.

Each patient should keep a self-checking diary under the certain scheme.

And Free fatty acids (FFA) it is necessary to tell about fat food more (the note of the author).

Two hormones participate in distribution of fat acids in a human body mainly:

- Hormone growth which supervises mobilisation of fat acids from a fatty fabric,
- Leptin which supervises β-oxidation of fat acids in mito chondrions.

**Figure 1**

One of the important functions leptin is a deduction trio-acylglicerids in adiposities. Normal level leptin's protects other bodies from fat accumulation (vessels, a liver, muscles, etc.). Leptin activates karnitin-palmitoil-transferaza's¬ -1 which connects fat acid with karnitin's, and last transfers it through a membrane mitochondrions. This process is strictly regulated. Leptin also stimulates oxidation of fat acids and reduces quantity trio-acylglicerids in a muscular fabric. Also it is established, that leptin suppresses activity Acetyl-KoA-karboxilaz!

Chronic stresses, overeating, undereating, surplus of sugar and fat, hypodynamia lead to work infringement leptin systems. If there is a resistance to leptin's it leads to increase in quantity of free fat acids. Visceral the fatty fabric will be the most powerful source FFA. Visceral fat increases proportionally to an index of weight of a body and 2 types are independent predictor developments of a diabetes. Visceral the fatty fabric is a basic source of free fat acids (FFA).

At visceral adiposity in a liver through system gatepost veins arrives excessive (at 20-30 time exceeding norm) quantity of free fat acids that subjects a liver to serious overloads and, as a result, leads to development specified above metabolic infringements.

Visceral the fat which is present round internal bodies, mesentery's and an epiploon, differs from hypodermic on type adipocities, it's endocrine functions, lipolitic activity, sensitivity to insulin and other hormones. Unlike a hypodermic fatty fabric, the venous blood flowing from visceral of fat, through portal system directly

arrives in a liver. It causes direct receipt in a liver of a considerable quantity of free fat acids (FFA) and adipocines, synthesised in visceral a fatty fabric. Adipocines, in turn, activate the hepatic immune mechanisms conducting to formation proinflammatory mediators, such as C-jet fiber (CJF) and others. Free fat acids, in a considerable quantity arriving in a liver from visceral a fatty fabric, cause development hepatic insulin resistance.

Secreting monocytar chemoattractant a protein-1 (MCP-1), promoting macrofagal infiltration a fatty fabric, adipocyties cause a proinflammatory condition. Macrofagies, in turn, represent the important source proinflammatory cytocines, such as the factor necrozis tumours - α (FNT - α) and interleukin-6 (IL-6). Visceral the fatty fabric differs greater infiltration inflammatory cages, and consequently are secreted considerable quantities proinflammatory cytocines in comparison with hypodermic fat.

Ektopic fat - fat which is not in hypodermically-fatty cellulose. This is fat visceral, either hepatic, or intermuscular. But it is united by that it not hypodermic fat, and being with a "wrong" place. The further development of illness will depend on in what fabrics which have been not intended for their storage, will collect (FFA). If they collect in skeletal muscles is will lead insulin resistance, if in a liver - to dislipidemia's. At first, as a rule, develops - insulin resistance, then, with its weighting - ischemic illness of heart (IIH).

**Figure 2**

Last years mechanisms of regulation of a stream of fat acids in an organism are investigated. The family of nuclear receptors PPAR has been opened, they became known in connection with ability to induce proliferation peroxisoms and cancerogenez in a liver in reply to influence xenobiotics. Three isoforms PPAR - α, γ and δ are opened, and properties of receptors PPAR α and PPAR-γ are most studied¬. Ligands for receptors the sated, monosaturated and monounsaturated fat acids serve.

PPAR-γ expressing in adipocities also reduces secretion of fat acids in blood from a fatty fabric. PPAR-α are expressed in cages of a liver, skeletal and warm muscles also operates as "lipostat", regulating processes of endocellular synthesis and β-oxidations of fat acids in mitochondrions and peroxisomas. PPAR are stimulated leptin's, a hormone of growth and insulin, their expression submits ¬cyrcad to a rhythm, they are expressed in reply to food intake. These receptors carry out endocellular regulation of fat acids, supporting a stationary consumption level of energy a cage, but they do not participate in maintenance of a homeostasis of fat acids at organism level.

Raised level FFA leads to their accumulation in cages, reorganisation of cellular membranes and to decrease insulin resistance. Surplus trio-acylglicerids in cages causes increase in synthesis inflammatory cyticines. Fatty fabrics are considered at present, how a place of initial occurrence and development insulin resistance.

It occurs because of:

- Receipts in a blood-groove of raised levels FFA and,
- The raised secretion adipocytocines.

The big weight adipocytes synthesises the raised quantities proinflammatory cytocines, that leads to chronic inflammatory pro-

cess, which: breaks a transfer way insulin a signal and, damages functions mitochondtions, that breaks a glucose homeostasis. In particular, are secreted fatty cages IL-6 and the FNT-ALPHA make heavier insulin resistance, and secreting angiotensin-2, raises arterial pressure and promotes atherosclerosis development.

### Infringement of the adaptive mechanism

In a cage from the fat acids which have been not spent on β-oxidation, at first are synthesised phospholipids, and then trio-acylglicerids, which accumulate in cytoplasm. Endocellular trio-acylglicerids in not fatty fabrics contain mainly palmitic acid. From palmitic acids it is synthesised sfingomielin, which is the basic component membran refts, participating in activity regulation membran receptors.

Synthesis sfingomielin, depending on the maintenance in a cage palmitic acids, is carried out on a way "palmitic acid → ceramid → sfingomielin". The synthesis way ceramid from palmitic acids leads oxidant apoptoz's. Ceramid is inductor apoptoz's, as on an oxidising way (ceramid blocks a complex III Electron transport chain (ETC), causing the strengthened generation of oxidizers, and without involving mitochondrions Accumulation trio-acylglicerids in cardiomiocytes association with synthesis decrease cardiolipin's and change of respiratory function mitochondrions as cytochrome with oxidaza a complex IV Electron transport chain (ETC) it is connected with cardiolipin's.

### The molecular mechanism of work of a respiratory chain

- Respiratory chain: I will stop only on 3 and 4 stages of this process. They are most important for treatment of a diabetes 2 types.
- III complex: Component Electron transport chain (ETC) - consists from cytochrom's b556, b560 and c1, and also iron ore the squirrel Risk. Work of the third complex is interfaced to carrying over of two protons of hydrogen in intermembran space, and electrons from lipophil Ubiquinone on peculiar properties cytochrome of fiber Risk that it is dissolved in fat is. Other proteins of this group which met as a part of complexes of a respiratory chain, water-soluble. This feature influences position of albuminous molecules in thickness of an internal membrane mitochondrions. The third complex functions as ubihinon-cytochrome C-oksidoreduktaza. Fat-soluble antioxidants (Vitamins A, **E**, D (the note of the author), that is why help.
- IV complex: It cytochrome-oksidant a complex, is a terminal point in Electron transport chain (ETC). Its work consists in carrying over electron's from cytochrome-with on atoms of oxygen. Subsequently negatively charged atoms About will enter reaction with protons of hydrogen with water formation. The main enzyme - cytochrome C-oxygen-oksido-reduktaza. Into structure of the fourth complex enter cytochromes - a, a3 and two atoms of copper. The central role in carrying over electron's to oxygen has got to cytochrome a3. Interaction of these structures chokes cianid's nitrogen and carbonic oxide, that in global sense leads to the synthesis termination adenosinetriophospat (ATF) and destructions. It only proves, that it is necessary to be afraid some carbonic oxide, cianids's. And also that treatment by antioxidants effectively (the note of the author).

### Infringement of the adaptive mechanism (continuation).

Change of structure of a membrane mitochondrions leads to liberation of cytochrome C and to apoptoz's without participation of oxidizers. Thus, accumulation palmitic in cages of not fatty fabrics conducts acids to synthesis increase ceramid's and to synthesis decrease cardiolipin's, that induces apoptoz, and to change of activity of receptors.

Important! Application of antioxidants which steal individually to each patient, effectively reduces blood sugar in 2 times at the treatment initial stage, and further normalises sugar to norm (the note of the author).

In this connection accumulation in cages trio-acylglicerides (trio-acylglicerides do not induce apoptoz) consider, how attempt of an organism to avoid effect lipotoxicy.

Sfingomielen and palmetic acid show high affinity to cholesterol. Maintenance increase sfingomielen and palmetic acids in a membrane it is possible to explain associate with the years accumulation in cholesterol membranes, and also sensitivity change insulin a receptor.

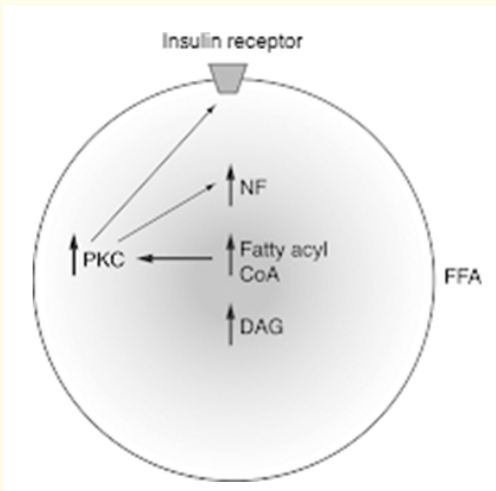


**Figure 3**

Insulin the receptor is connected with membran rafts, and structure change rafts influences its sensitivity.

Accumulation trio-acylglicerids in not fatty fabrics and the decrease in sensitivity interfaced to it insulin a receptor conducts to resistance occurrence to insulin and hyperglicemia's, - to the raised maintenance of glucose in blood. The receptor to insulin represents tirozinkinaza's.

The means autofosforilation activate various ways, in particular, way PI-3-K (fosfoinozitol-3-kenaza) for which account there is a transport of glucose in a cage as the conveyor of glucose GLUT4 comes to the active working condition. At the expense of active lipoliz's free fat acids (FFA) and proinflammatory cytocines, they influence substrata insulin a receptor, thereby, way PI-3-K therefore effects which are rendered by this way on a glucose exchange are blocked is blocked, and glucose cannot enter into a cage. In such a way develops insulin resistance, - the excessive quantity visceral a fatty fabric blocks insulin a signal and leads to that insulin receptors become tolerant to insulin, and its biological role is perverted.

Depending individual sensitivity and genetics, insulin resistance can develop in different fabrics. Surplus FFA mediates progressing insulin resistance many fabrics - muscular, including myocardial, hepatic, adipoz, and also endotelial cages, promotes progressing of ischemic changes in a myocardium, including the changes connected with infringement of beta oxidation FFA in a myocardium.

The liver becomes overloaded with fat acids. It because active fat acids in a liver are synthesised, oxidation of fat acids decreases, actively there are fat acids to a liver from visceral a fatty fabric and, besides, fat which in structure chilomicrones gets to a liver, also overloads a liver with free fat acids.

**Figure 4**

The given processes lead to that the liver not in a condition metabolic by β-oxidations FFA, joins peroxy oxidation lipids therefore in a considerable quantity active forms of oxygen are produced, arises oxidant stress, and these factors lead fosforiliration a substratum insulin a receptor, thereby, resistance to insulin is again started. There is an original vicious circle, and already to define at the patient, that initially, difficult enough. It is proved, that macrofags visceral a fatty fabric possess proinflammatory activity. Also CDs-8 are found in a fatty fabric + T-limfocyties which actively allocate proinflammatory cytocines also - in a liver in a condition of a fatty dystrophy can already pass and in the following stage with development in patients not alcoholic steatohepatitus (STADA) and other consequences to which conducts not alcoholic fatty illness of a liver (NAFIL), which has some kliniko-morphological forms and develops at the patients who are not abusing alcohol. The combination of a diabetes 2 of type and NAFIL is connected not only with high risk of development of a cirrhosis and hepatocellular carcinoma's at the given category of patients. That is why the author considers, that the diabetes and a cancer go nearby, therefore for diabetes and cancer preventive maintenance antioxidants, and for diabetes treatment only antioxidants are necessary, for a cancer antioxidants - are counter-indicative (the note of the author). It is checked up on clinical cases at patients.

Soon after a liver, fat starts to collect in muscles. Characteristic for insulin resistance a metabolic pathology - accumulation round muscular fibrillas trio-acylglicerids. However, accumulation trio-acylglicerids in skeletal muscles as it is necessary, is not a development immediate cause diabetes 2 types, but can be a marker intermediats lipids, such, as acetyl KoA, ceramids and diacylglicerin.

According to recent researches, infringement of a way of transfer insulin a signal is connected, basically, with pathological metabolism FFA in cages of the skeletal muscles which are "not consulting" with their recycling when FFA it is a lot of. Really, local accumulation in skeletal muscles such metabolits FFA as ceramids, diacylglicerol or acyl-KoA conducts to transfer infringement insulin a signal and - to infringement of transport of glucose.

**Figure 5**

### Vicious circle insulin resistance

Insulin resistance, caused by high level FFA, raises concentration FFA in plasma even more. As it was found out, insulin resistance fatty cages secreting raised levels FFA. It, actually, also allows to consider raised levels FFA as a marker insulin resistance (IR). Really, at insulin resistance level FFA in hepatocytes raises, as in it:

- Increase lipogenez de novo,
- Esterification FFA exceeds their oxidation,
- Esterified fatty acids are reserved in a kind trio-acylglicerids or go on synthesis lipoproteids very low Density CH (cholesterol)-LVLD (rich trio-acylglicerids),
- Decrease mobilisation regulated by insulin trio-acylglicerids.

Insulin resistance adipocytes intensively split containing in them trio-acylglicerids and liberate formed of them FFA in a blood-groove (both at adiposity, and without it). Stream FFA from fatty cages raises and, moreover, FFA also leave from lipoproteids very low density CH (cholesterol)-LVLD both from chilomicrons plasmas and on a blood-groove partially go to other bodies, and partially - back in a liver where again turn in trio-acylglicerids. There is "rating" of liver FFA and trio-acylglicerids. It has the heaviest consequences.

### Atherosclerosis acceleration

Raised levels FFA lead dislipidemia's and aterogenez's.

Insulin resistance conducts to dislipidemia's increase in a liver trio-acylglicerides stimulates formation Apo-B and CH (cholesterol)-LVLD.

### The molecular mechanism aterogeneses

- From a liver high levels CH (cholesterol)-LVLD secreting in plasma where because of lipoliz's from CH (cholesterol)-LVLD are formed FFA and highaterogenic remnant (residual) particles lipoproteins, rich trio-acylglicerides.
- From plasma FFA and remnant particles are again absorbed by a liver, that raises level FFA in hepatocytes even more and stimulates synthesis CH (cholesterol)-LVLD even more.
- In a liver, at high level CH (cholesterol)-LVLD and normal level of fiber CETP (cholesteryl ester transfer protein) - a carrier of an aether of cholesterol, trio-acylglicerides from CH (cholesterol)-LVLD pass in lipoproteids high density CH (cholesterol)-LHD, and cholesterol from CH-LHD passes in CH (cholesterol)-LVLD.

As a result are formed: rich with cholesterol very much aterogenic remnant and CH-LPVP, containing it is a lot of particle lipoproteids very low density CH (cholesterol)-LVLD trio-acylglicerides and not enough cholesterol.

- Such particles CH-LHD lose trio-acylglicerides (under the influence of hepatic **липазы**) and the basic apolipoprotein - APO **A**1. As a result level antiaterogenic CH-LHD goes down.
- At high level CH (cholesterol)-LVLD (rich trio-acylglicerides), fiber CETP transfers trio-acylglicerides from CH (cholesterol)-LVLD in CH-LPHD, and cholesterol - from CH-LPLD in CH (cholesterol)-LVLD.
- Rich trio-acylglicerides CH-LPLD because of activity hepatic or lipoprotein lipaza's lose trio-acylglicerides, decrease in sizes and become very much aterogenic small dense particles CH-LPLD.

Thus, raised levels FFA lead to level decrease "antiaterogenic" CH-LPHD, to formation extremely aterogenic small dense particles CH-LPLD and to increase of plasma levels trio-acylglicerides.

But there is one more way which high levels FFA cause aterogenez. This way more direct and short. Raised at insulin resistance level FFA causes in mitochondrions macrovascular endothelial cages supersynthesis of active forms of oxygen that conducts to oxidation CH-LPLD and updating CH-LPHD. It induces inflammatory process in walls of vessels, formation and accumulation of cholesteric plaques and, as a result - an ischemia, (but it is a theme of the separate book).

**Figure 6**

Insulin resistance, caused by high level FFA, raises level FFA even more. That is why it is impossible to accept fats at a diabetes 2 types though, they are available after all products for diabetics (the note of the author).

The note of the author:

- To eat, for example, a slice of grain bread or bread with bran without margarine in a basis, and on qualitative vegetable oil (olive, linen, mustard, corn) with a slice of house fat - it is useful for intestines.

But to eat, for example, the overroasted fat meat, fat sour cream with spoons, pies fried, a potato-fri harmfully. It is possible to eat fat sour cream a little. If to eat so it is long, stomach growth will be provided. And such stomachs are characteristic for diabetics 2 types. And, fat at men is distributed between muscles and to men to grow thin very difficult. At women usually fat is postponed hypodermically. The diet and special therapy is necessary to raise concentration testosteron's (S.J.Kalinchenko, 2012).

And, visceral fat at adiposity meets, both at men, and at women.
In all it is necessary observe a measure not to be ill.

**Figure 7**

## Oat a root

When speech comes about Oat a root, some think, that it is sowing campaign Oats. But it not so. Oat a root - a vegetable plant, it still names Salsity, a white root, a sweet root. Its root crops are rich with sugars, fibers, mineral salts and inulin's. It is recommended as a dietary product for sick of a diabetes, reduces level of the maintenance of sugar in blood (costs on the second place after stachis by efficiency of preventive maintenance and treatment of this disease). To taste oat the root reminds fish, not without reason it for spicy gentle taste still name a vegetable oyster.

## Amaranth (Graines)

Curative properties of an amaranth were known still to the American Indians, it in the Middle Ages monks treated. An Amaranth apply at hemorrhoids, an anaemia, an avitaminosis, a diabetes, adiposity and a neurosis. Medical preparations deduce from an Amaranth redionuclids, preventive growth of malignant tumours. Easier to use in food unlimited quantity of a plant.

## Diet at a diabetes 2 types

About 80% of patients with a diabetes 2 types have excess weight which weakens insulin action (own and entered from the outside), considerably reduces efficiency hypoglycemic medicines and leads to increase of level of sugar of blood, therefore the priority in this situation - weight reduction (not to full norm, but on 5-10% from initial) and its maintenance at this level at the expense of proceeding observance of a diet, therefore "the best diet is that which the patient can observe all life".

This diet should be tasty, various, not causing feeling of hunger, but to contain less calories, than the patient used earlier. It is absolutely real if to use a principle of replacement of products: for example, replacement of sausages (they more caloric) on equal quantity on weight of boiled meat (or oils on a sandwich - on a cucumber or a tomato slice) leads to that the feeling of hunger is satisfied with smaller quantity of calories.

## Food planning (a diabetes 2 types are a lot of weight)

### Group 1. These products should be excluded from a food

Strongly raise blood sugar:

Sugar, honey, dried fruits, fruit juice, confectionery products, sweets, jam, lemonades ("Forfeit", "Pepsi", etc.), natural kvass.

Cream of wheat, mashed potatoes, it is strong "tenderize" porridges.

Contain many calories:

Oil creamy, vegetative (especially in salads, Russian salads and at food warming up), sour cream, mayonnaise, oil substitutes (Rama, etc.),

Fat, sausages and sausages, sausages and pastes, smoked products, fat meat, fat fish, a meat offal (a liver, a liver), chicken leg quarter, a skin of birds,

Fat ("yellow" and fused) cheeses, cream, fat cottage cheese,

Nuts and sunflower seeds, pies and pies.

### Group 2. To cut consumption by half

Bread (black or white), groats (rice, buckwheat, овсяная, etc.),

Potato, pasta, corn and soya products,

Cracker, drying (unsweetened), etc.

Fruit: to distribute within day, but no more than 3 "equal to an apple" in day

"Diabetic" sweets, wafers, etc.: in a kind of "an infrequent delicacy" (once a week)

Are admissible in moderate quantities: low-fat meat, fish, cottage cheese.

### Group 3. To increase consumption

Vegetables (but without addition of fats) in the form of vegetable garnishes: cabbage, a cauliflower, carrots, a beet, turnip, a garden radish, cucumbers, tomatoes, greens

Drinks without sugar (mineral water, tea) or on sugar substitute ("Hand bell", "Diets-pepsi", "Coca-Cola Lite", etc.).

Sugar substitutes: more preferably modern (tablets or liquids)

Fructose is undesirable (raises blood sugar).

The author of the book considers, that it is better sugar substitutes not to use (the note of the author).

Principal causes of failures at weight reduction

- There is a set of the products rich with fats ("the latent fats). These are all sausages, sausages, sausages, nuts, sunflower seeds, cheeses with fat content> 15%, etc. With these products it is possible to receive imperceptibly for itself a considerable quantity of calories.
- Fats very much caloric, therefore even a small amount of "superfluous" fats (for example, the tea or table spoon of vegetable oil in salad) is capable to bring to nothing efforts on weight reduction for all the day.

The requirement for fats at the adult person is insignificant. It completely becomes covered at the expense of meat, fish, cottage cheese, soups, etc. But refuelling of salads by fats (vegetable oil, sour cream, mayonnaise) are already "superfluous" fats.

Principles of a food for patients without surplus of weight

1. An exception of the products sharply raising level of sugar (group 1**а** from the above-stated list)
2. Not to use in considerable quantities the products moderately raising sugar ("slow carbohydrates" - vegetative products from group 2 given lists)
3. Divisibility of a food: daily quantity of food to divide not into 2-3 big receptions, and on 5-6 small
4. Increase in physical activity

### Physical activity

1. Individual selection with the account of age of the patient, presence of complications and accompanying diseases.
2. It is necessary to recommend walks on foot instead of driving, lifting on a ladder instead of using the lift.
3. One of the basic conditions - a regularity of physical activities (for example, walking daily 30 mines, swimming on 1 **ч** 3 r/ned).
4. It is necessary to remember, that intensive physical activities can cause sharp or delayed hypoglycemic (sugar of blood below norm), therefore a mode of loadings it is necessary to "fulfil" a condition at self-checking glicemia's; if necessary it is necessary to correct doses hipoglicemic means before loading.
5. At concentration of glucose in blood> 13-15 mmol/l physical activities are not recommended.

### DIET HERBS AT the DIABETES 2 types

Diabetes - difficult and long illness. The balanced diet choice, application in food hipoglicemic plants in the form of simple medicinal forms (infusions, broths, tinctures, etc.), and also preparation of culinary dishes from similar action of plants is especially important for diabetics. The author the book is possible manage simple methods sugar and to hold it approximately in norm (the note of the author). It is better, than an exhaustion of own reserves and replacement of insulin from tablets and pricks.

Considering duration of treatment, it is necessary to know plants which can be used in a dietary food from among accessible, grown up on garden sites or wild-growing.

For example, bean vegetable plants (beans, peas, a string bean) are characterised by the high maintenance of albumens which on a chemical compound and biological value are closest to fibers of an animal origin (meat, fishes, milk, etc.). Their value - in easy comprehensibility and the considerable maintenance of irreplaceable amino acids which are not formed in a human body and replenish with food.

Carbohydrates are presented by various sugars (glucose, fructose, galactoza, sucrose, maltoza, etc.), starch and cellulose's. In shutters of fruits of bean plants – "pods" - prevail sugar, in the ripened grains - starch. In mature grains of peas of starch contains in 6-7 times more, than in the green.

Peas are vitamin-rich - B1, B2, PP, E, Biotin's and Cholin's. The string bean contains B2 and the folic acid playing the important role in processes of a metabolism. Peas and a string bean are sources of the valuable vitamin E regulating an exchange of fats, fibers and nucleinic acids.

Bean vegetable plants long since used in national medicine. In traditional medicine are used them hypoglicemic properties. As auxiliary medical means at a diabetes apply string bean shutters, they possess ability to lower concentration of sugar in blood. Use infusions, broths and extracts (liquid and dry). A liquid extract appoint on 15 drops, and dry - on 0, 5-0, 75 g 3 times a day (to meal). In house conditions prepare from dry shutters broths: 20-25 g the crushed shutters fill in 1 l of water, cook 3 hours, add the boiled away part water, filter and drink within day. Course of treatment - one and a half-two month under the control of the doctor. Broths from a mix of shutters of a string bean, leaves of a bilberry and oat the straw, taken in equal parts are effective. 5 table spoons of a mix fill in 1 l of water, boil no more than 10 minutes then insist before cooling, but no more than hour.

## As dietary and dietetic therapy it is possible to apply dishes from peas, a string bean and beans

Buckwheat a sowing campaign. Buckwheat groats, thanks to the maintenance in it of mineral salts, organic acids, vitamins and it is easy усвояемых fibers, use as a valuable dietary product at diseases of a liver, kidneys and a diabetes. Most full it is acquired with milk. In such combination there is about 100 various useful substances, including a full set of irreplaceable amino acids. On physiological norms of a food the person should use within a year of 7-8 kg buckwheat.

Vegetable marrows, bush pumpkins. Having low caloric content, the alkaline environment created at their mastering, rich mineral structure and vitamin value, vegetable marrows and bush pumpkins are irreplaceable in a food sick of a diabetes. Thanks to application of various ways of preparation and conservation of vegetable marrows and bush pumpkins the population can be provided by these dietary products all year long. From them prepare various dishes.

Cabbage. Most often apply cabbage white cabbage, red and colour.

Thanks to the maintenance of a significant amount of mineral salts, organic acids, enzymes, fitoncids and to small quantity of nitrogenous connections, the cabbage of all kinds is necessary in a food of patients with defeats of kidneys and a diabetes.

On presence of ascorbic acid red the cabbage in 2 times, and under the carotin maintenance in 4 times surpasses white cabbage. Cellulose red than cabbage is more rough, than at other kinds. Therefore at infringements of function of bodies of digestion it use in a small amount in the form of salads, garnishes, marinaded.

Nutritional value of a cauliflower much more above white cabbage. The big half of nitrogenous substances in it make easily усвояемые fibers. The cabbage is vitamin-rich, mineral salts, the enzymes promoting regulation of level of sugar and cholesterol. The maintenance in spirit cabbage mannit's and inozit's renders sugar descrease and contrasclerosis action.

The cauliflower is not recommended sick of a gout as in it the significant amount purins connections contains.

Cabbage of all kinds use in food in the crude, boiled, fried and fermented kind, pickle. The list of dishes from cabbage rather extensive (G.V.Krylov, N.F.Kozakova, 1990).

## The grapefruit - reduces blood sugar

Tangerines promote decrease in risk of occurrence of diseases of cardiovascular system and a diabetes.

In tangerines contains phlavonol Nobiletin - the substance reducing level of cholesterol and insulin in blood of the person. It allows to assume, that the use a tangerine is excellent way of prevention of illnesses of vessels, heart and a diabetes.

## Tangerines feed our organism with vitamins, improve appetite and accelerate digestion

The use of tangerines has appeared very useful not only because of the maintenance in them of vitamin C. As it has appeared, they promote reduction of adiposity of a liver and reduce quantity of fatty adjournment in a belly cavity.

30 schoolboys have taken part in experiment with excess weight which throughout two months regularly drank tangerine juice and carried out physical exercises. Participants of control group also did gymnastics, but tangerine juice did not use. As a result it was found out, that for this period participants of the first group have got rid of 1, 5% of excess weight.

Tangerine the concentrate gives loss of 60% of belly fatty accumulation and authentic growing thin on 45%. Tangerines promote liver restoration. Experts have started creation on the basis of a tangerine of the medical drink, helping to struggle with adiposity, and also with senile weak-mindedness.

## Hypoglicemic plants

The Banana (not mature), the Goat (grass), a Nettle (leaves), Corn stigmas, the Burdock, an Oats (seeds), a Dandelion (grass), a Walnut (leaves), Purslane (leaves, stalks), a string Bean (a peel of seeds), a Bilberry (leaves), Barley (malt) - in beer contains, "a gold Moustache" - at diet observance especially well helps (1 sheet 20 of sm - on 0,7 l of boiled water - to boil 3 - 5 minutes on weak fire to insist days to drink 3 - 4 times a day to meal. Doses accurately to observe! Doses are given for adults! And, they too are individual. Address to the expert for consultation. Acidum Lacticum 200 (homoe-

opathy), Stevia angustifolia (hypoglycemic a plant), Topinambur, a Blackberry (berries), an ash, a field Horsetail, Valeriana (a rhizome with roots) - broth (small doses), Stepnica medicinal, Galega medicinal, Broth of leaves cattail broad-leaved is useful at a diabetes. The Mongolian tea: The wintered leaves Bergenia's to wash out, dry, cut. To use 1 tea spoon. On a boiled water glass to insist 5 minutes, to drink with sugar, honey or ksilit's at a diabetes, Cuff the ordinary. The Cowberry (infusion of berries) - contains copper. Gathering: Strawberry leaves - 2 parts, flowers a red clover - 2 parts, leaves Lovage - 3 parts, tops of chicory with flowers - 6 parts, all to mix, take 2 items of l. Gathering and to fill in with a boiled water glass, to cool slightly and to drink. To prepare new infusion in the evening and drink it with milk. Infusions need to be drunk on 2 glasses 2 - 3 times a week. Chicory (Cichorium intybus L.). The cabbage brine + is a little lemon juice - in it dairy acid contains a lot of.

GLIKEMIC INDEX (GI) - concentration of glucose in blood of the healthy person before and after (in 2-3 hours) reception of a concrete carbohydrate product. The more low GI a product, the grows more slowly and glucose level in blood, the easier a pancreas decreases. For this reason, at a food allowance choice, it is necessary to choose products with average or low GI (50-70). Industrial and culinary processing promote increase GI. Bread has high GI, bread of their flour of a rough grinding - 50 GI, i.e. low glicemic an index. Size GI is influenced also by starch structure, quantity and quality food клетчатки, containing in a carbohydrate product.

To grow thin it is necessary to limit sharply products with high GI, these are such as: sugar, sweet, pasta from a white flour, a white loaf, a potato, the cleared rice, corn and corn-flakes, spirits, grapes, dates. Inclusion in a diet of fruit and vegetables in which there is not enough glucose and starch, but is a lot of cellulose, grain bread, bean - will provide requirement of an organism for carbohydrates for the account polyshacharids and will warn adiposity.

## Diet

1. To exclude fast carbohydrates, grapes, raisin, to limit animal protein.
2. It is useful to drink - cucumber, plam, garnet juice, juice of a baked pumpkin, string bean broth to eat on 2 - 3 eggs soaked in apple vinegar, for a breakfast - gruel from a buckwheat flour on kefir (1 item of l in the evening. On 1 glass of kefir, to insist on night) - to drink is long from 2 months and longer (improvement of the general state of health, thirst reduction, dryness elimination in a mouth).
3. Honey agarics - courses till 3 weeks for 200 It is possible to prepare tincture - hats to insist on 40% spirit (1:5) within 7-10 days in a dark place, to drink on 0, 5 - 1 tea spoon 3 - 5 times a day to meal.

## Dicvertin - operating substances - Flavonoids

1. Reliabry reduces concentration malon dialdegid's - (MDA).
2. Lowers the maintenance tromboxan's
3. Raises - NO
4. Reduction of the maintenance of calcium in trombocytes
5. Increase of activity succinate dehydrogenase (SDG), catalaza's, glutation-peroksidazy,
6. Raises activity microsomal hepatic 7-a-gidroksilazy on processing Cholesterol
7. Utilises LPVLD a liver
8. Raises LPHD

## Interaction

Dicvertin + hypoglicemic derivatives Sulfanilurea = positive action;

And now we will return to medicamentous therapy of a diabetes 2 types which was enriched recently with two new classes of the preparations influencing on Incretines: Analogues and Agonists glucagon-like peptide-1 (GLP-1) and inhibitors of dipeptidyl peptidase-4 (IDP-4).

Incretines are hormones of a gastroenteric path which are developed in reply to food intake and cause stimulation of development of insulin. To Incretines two hormones concern: glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GDIP). Receptors to glucose-dependent insulinotropic polypeptide (GDIP) are on special cages (beta cages) of a pancreas. Receptors to glucagon-like peptide-1 (GLP-1) are in different bodies, therefore except stimulation of development of insulin, activation of receptors to glucagon-like peptide-1 (GLP-1) leads to display of other effects of the given hormone.

Before trying to explain the action mechanism Incretines, it would be desirable to remind, that insulin is the hormone reducing the maintenance of glucose in blood and promoting its transition in a fabric. And glucagon is a hormone of a pancreas which raises level of glucose of blood.

- Exenatid (Baeta)
- Liraglutid (Victoza).

Incretines reduce pressure, that it is possible to use in some cases, but can cause pancreatitus.

## The action mechanism agonists

So, the first group of preparations is agonists (the substances stimulating chemical and biological processes) receptors (GLP-1).

The following group Incretines is Inhibitors ("suppressors") dipeptidilpeptidazy-4 (Gliptins).

### To Gliptins concern

- Saxagliptin (Ongliza)
- Linagliptin (Transcenta).
- Sitagliptin (Yanuvia).
- Vildagliptin (Galvus).

Considering existing differences in mechanisms of action short peptids - glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GDIP), it is necessary to notice, that group preparations inkretin-mimetikov influence only through effects glucagon-like peptide-1 (GLP-1), reaching its high pharmacological concentration in plasma. Inhibitors of dipeptidyl peptidase-4 (IDP-4), being Incretin-activators, influence on both Incretin - and glucagon-like peptide-1 (GLP-1), and glucose-dependent insulinotropic polypeptide (GDIP), supporting their "physiological" concentration within days, operating not only in postgrandiale the period, but also during the period on an empty stomach. Besides, group preparations inkretin-mimetikov are applied in the form of hypodermic injections, and Inhibitors of dipeptidyl peptidase-4 (IDP-4) - in a kind peroral preparations.

Inhibitors of dipeptidyl peptidase - 4 (IDP-4) there have successfully passed clinical tests in the USA and the countries of the European union for wide clinical application at treatment of a diabetes of type 2. The first preparation of this new class hypoglicemic medicines just became Sitagliptin (Yanuvia).

In November, 2007 in published updated consensus algorithm of treatment diabetes 2 of type, which is developed by the American diabetic association (ADA) and the European association on diabetes studying (EASD), IDP-4 - Sitagliptin it is included in the list of recommended preparations.

It is necessary to notice, that Incretines - glucagon-like peptide-1 (GLP-1), glucose-dependent insulinotropic polypeptide (GDIP) and, probably, other hormones participate in regulation of secretion of insulin and glucagon endocrine cages of islets of a pancreas, making the basic impact on maintenance of a homeostasis of glucose in an organism. The important feature of effects Incretines on secretion of hormones of islets of a pancreas is them glucose-dependent that considerably reduces risk of development hypoglicemia's in reply to their influence, making thus considerable impact on improvement of a condition of a carbohydrate exchange. Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GDIP) increase glucose-dependent insulin secretion, glucagon-like peptide-1 (GLP-1) also reduces s glucose-dependent ecretion glucagon's, improving the control glicemia's and, not raising risk hypoglicemia's.

Secretion infringement Incretines (decrease in their secretion in reply to food intake) at type 2 diabetes is interconnected with processes "disregulation" insulin secretions that is the important factor in patogenez's diseases and conducts to deterioration of an exchange of glucose in an organism.

Sitagliptin (Yanuvia) it is applied in the form of monotherapy (100 mg of 1 times a day) or in a combination to others peroral hypoglicemic by preparations (Metformin or Glitazones), reducing an indicator glicated haemoglobin on 0, 79-2% and as it was already marked, reducing thus frequency of development hypoglicemia's. Influence of the given preparation on decrease apoptoz's b-cages and them neogenez is accompanied by increase in quantity of b-cages of islets of a pancreas that can slow down or even to stop progressing of a diabetes of type 2 and its late complications.

It is important to ascertain, that reception Sitagliptin (Yanuvia) is well transferred by patients, and frequency of development hypoglicemia's is identical to that which meets at the patients receiving placebo. One more powerful advantage at use by patients with диебетом 2 types of a new preparation is an absence of an increase of weight of a body.

Long-term efficiency Sitagliptin (Yanuvia) at its appointment in the form of monotherapy in a dose of 100 mg a day or monotherapies Metformin's in doses of 1000 mg and 2000 mg, or therapies by a combination of these preparations was investigated in 54-week randomised, double blind research in parallel groups.

In total 748 patients participated in research by a diabetes 2 types with the inadequate control glicemia's (HbA1c from 7,5% to 11%) which preliminary received treatment in the form of a diet and physical activity.

In population of the patients who have finished research, following average values of decrease HbA1c have been reached: 1, 4% (SITA100);-1, 2% (MF1000); - 1, 6% (MF2000); - 1, 7% (SITA100 +MF1000); -1, 9% SITA100+MF2000). More significant decrease in level glicated haemoglobin has been revealed at persons with higher initial level of this indicator.

Target indicators of treatment (HbA1c <7%) have reached from the patients who have finished research: from 35 those% who was on monotherapy Metformin's of 1000 mg, to 77 those% who was on combined therapy Sitagliptin's of 100 mg and Metformin's 2000 mg.

It is necessary to specify, that Sitagliptin (Yanuvia) possesses more expressed efficiency of treatment at patients with initially high indicators glicated haemoglobin.

At persons with initial level HbA1c> 10% application Sitagliptin (Yanuvia) in the form of monotherapy reduced this indicator on 2%. Taking into account influence of preparation Sitagliptin (Yanuvia) on processes of the broken secretion of insulin and glucagon's its application is shown in the form of monotherapy or in addition to treatment Metformin's or Glitazones when against only therapy Metformin's it is not possible to reach the adequate control glicemia's.

Undoubtedly, that revealed possibilities as Sitagliptin (Yanuvia) open new prospects in increase of efficiency of treatment of a diabetes 2 types.

Fenofibrat raises sensitivity of fabrics to glucose and leads to normalisation of the broken metabolic processes connected with raised glicemia's on an empty stomach and dislipidemia's.

In influence research Fenofibrat on a metabolism of carbohydrates, lipids and the hemostasis at patients with impaired fasting glycemia (IFG), and mixed dislipidemia's, is drawn a conclusion, that Fenofibrat renders complex beneficial effect.

In the beginning and in 30 and 90 days of treatment defined a level profile lipids, glucose level on an empty stomach and through 2 hours after sugar loading, indicator HOMA and level glicated haemoglobin, and also level/activity fibrinogen's, the factor VII and PAI-1. At comparison with control group at patients with broken glicemia's on an empty stomach and mixed dislipidemia's level increase fibrinogen's and PAI-1 in blood plasma, and also increase of activity of the factor VIII was marked. At patients with mixed dislipidemia's level fibrinogen's, the factor VIII and PAI-1 was above, than at patients with isolated broken glicemia's on an empty stomach. Fenofibrat not only improved level indicators lipids in blood plasma, but also raised sensitivity to glucose, led to normalisation caused impaired fasting glycemia (IFG) and mixed dislipidemia's changes of coagulation and fibrinoliz's. In group of patients with impaired fasting glycemia (IFG), and mixed dislipidemia's Fenofibrat renders complex beneficial effect on a hemostasis.

Attention! At patients with a diabetes 2 types and mixed dislipidemia's the combined therapy Fenofibrat and Metformin's has appeared more effectively, than a combination Metformin's with actions for updating of a way of life concerning positive influence on a system inflammation, a hemostasis and secretor function monocytes.

The most expressed pleuotropic effects concerning levels of C-jet fiber, fibrinoliz's and Inhibitor's the activator plasminogen's - 1 observed in group of combination Fenofibrat's with Metformin's.

## Lixisenamid (AVE 0010).

Lixisenamid (Lixymia), agonist glucagon-like peptide-1 (GLP-1) 2 types are developed for treatment of patients with a diabetes. Within the limits of research II b of a phase it has been shown, that Lixisenamid once a day provided effective decrease in level of glucose of blood in a combination to good shipping of a preparation.

The program of researches of III phase, in which frameworks combination Lixisenatid/Lantus (insulin Glargin will be applied (r-DNA) in the form of injections), predictably, it will be started later.

## Secondary preventive maintenance of a diabetes 2 types

- Preventive virus infections (Rubella, a parotitis, Koksaki, a hepatitis);
- Important! At children more often a diabetes of 1 type, more often between 3 and 5 years of a life (the remote consequences of vaccines), between 11 and 13 years, behind the second jump of growth, but always till 25 years, more often in the autumn and in the winter, therefore aim survey for the purpose of preventive maintenance on this pathology. This condition is fraught with various kinds a clod: hyperglicemic, lactatsidoza, hypoglicemic, ketoacidotic and effect Somogy (insulin overdose).
- Glurenorm (Glicvidon);
- Maninil
- Adebit (at surplus of weight of a body) - the preparation can give lactatsidoz's (accumulation in an organism of dairy acid).
    - Help measures - introduction jet insulin from sodium chloride! At the normal maintenance of glucose - enter glucose **в/в**.
    - It is dangerous hyperosmolar a coma - often at elderly, help measures - half insulin doses, a solution of sodium of chloride **в/в**.
- The psychotherapy and a psychological relaxation, at this disease develops pathological uneasiness and depressive reactions.
- Researches Bender, 1999, have shown, that the biological role bioooze is connected not only with a condition of hair and nails, and first of all that vitamin is a part some the enzymes participating in a metabolism of glucose: piruvatdehidrogenaza's and transketolaza's. At a diabetes deficiency bioooze meets more often, than in the general population. At the proved deficiency Bioooze application of preparations with high doses of Vitamin (the note of the author) is admissible.
- New preparations – Secretagogues - Novonorm, Starlix, Pioglitazon and Actos.

- Metfogamma 500 (Metrormin's a hydrochloride - 500 mg), Metfogamma 850 (Metrormin's a hydrochloride - 850 mg) with a break line.

### Attention to the Doctor and the Pharmacist!

- Preparations Phenformin and Buformin - Biguanidines are laid off!
- Instead of them – Glucofop, Siofor (Metformin, Metfogamma), Diformin, Dianomet.
- Collateral action Biguanidines: increase lactat's in muscles (a pain in muscles).

Primary preventive maintenance of cardiovascular diseases Atorvastatin's is costly - effective intervention at patients with a diabetes 2 types.

The best and convenient decision of a problem of completion of available vitamin deficiency at a diabetes is the vitaminno-mineral complex "Vitamins for sick of a diabetes. This complex contains 11 vital vitamins, and also two important for each diabetic of a microcell - zinc and chrome which participate in a carbohydrate exchange, promote insulin development, protect from fatal action of free radicals, promote maintenance of normal functioning of immunity and fast healing of wounds. The complex consists of vitamins, whose functions are most important and necessary for people with a diabetes. The connections which are not playing the vital role at patients, suffering are thus excluded by the given disease, therefore the complex included not all known Vitamins, but only 2 fat-soluble (Vitamins A and) and 9 water-soluble (the basic Vitamins of group B – pantotenic acid, Nicotinamid, Piridoxin, Cyanocobalamin, Niacyn, Biooozes, Riboflamin and folic acid, and also Vitamin C). Such rigid restriction of components allows to provide the maximum safety of means. "Vitamins for sick of a diabetes" are very convenient in application - a recommended dosage only 1 tablet a day. It is enough one packing of a preparation for one month of daily reception. For achievement of optimum effect the tablet "Vitamins for sick of a diabetes" needs to be accepted after meal as fat-soluble Vitamins a part a Vitaminno-mineral complex in this case are better acquired. Thus a tablet small, therefore she is easy for swallowing. It is especially important at dryness of a mucous membrane of the mouth often meeting at a diabetes. The preparation "Vitamins for sick of a diabetes" has scientifically proved and well balanced structure, optimum for preventive maintenance and treatment hypovitaminosis, in particular at the patients, suffering a diabetes. The preparation "Vitamins for sick of a diabetes" has been specially developed taking into account average daily requirement of the patients, suffering a diabetes and does not contain some sugar or sugar substitute. A recommended course of reception of a complex - not less than 2 months. The preparation in packing from 30 tablets is issued, on the minimum course of treatment it is enough to get only two packings. The preparation has high level of safety: it practically has no any by-effects (except allergies on preparation components). Also it, behind an exception, individual intolerance, does not have also contra-indications.

Attention! At patients with diabetic nephropatia's Vitamin B reception has appeared is not effective.

Patients are included in research with a diabetes 1 both 2 types and the clinical diagnosis diabetic nephropatia's with excretion albumin's with urine not less than 300 mg a day. Patients (on 119 in group placebo and Vitamin B) observed within 31, 9 months. During this time speed glomerular filtrations in Vitamin B group has decreased in authentic большей degrees, than in group placebo (on 16, 5 ml/mines/1, 73 м2 and 10, 7 ml/mines/1, 73, accordingly). However in group of Vitamin B levels gomocistein's have decreased with creater degrees, than in group placebo.

Thus, in data research has not proved to be true the assumption that Vitamin B can improve function endotelium's and by that to slow down progressing of complications of a diabetes.

Biologically active addition (BAA) General of feature of a preparation from a diabetes "Diapil".

In Russia BAA Diapil is not popular. It is obvious, that natural phytotherapeutic feature works what to accept it is necessary those preparations which grow in the region (the note of the author).

Enzyme α-glukozidaza is responsible for process of splitting of glucose in intestines. When glucose inclusion is broken because of decrease or absence of action of insulin, result is increase of levels of glucose in blood - a condition known as a diabetes. In this case action α-glukozidazy can be warned such medicinal products as Glucobay (Acarboza) (known also as Glucor and Prandaz); as a result digestion of carbohydrates is slowed down also they only are gradually liberated in blood in the form of glucose, thereby warning is superfluous high levels of glucose in blood.

Acarboza, active component Glucobay, is a biotechnological product which detains a metabolism of carbohydrates in intestines. Glucose is allocated in a blood-groove gradually, that leads to decrease in levels of glucose in blood. Thus, Glucobay (Acarboza) use for treatment of a diabetes 2 types.

Preparations Chrome's - the glucosic tolerant factor - a potato welded in a peel, fresh vegetables, bread from a flour of a rough grinding.

Attention! In large population research it is shown, that the waist circle is a risk factor of death at elderly irrespective of IWB (Eric Jacobs, 2010) with colleagues have analysed association between a circle of a waist and death rate in research Cancer Prevention Study II. Middle age of men has made 69 years, women of 67 years. Within 9 years of supervision have died 9315 of 48 500 men and 5332 of 56 343 women. The considerable circle of a waist (more than 110 at women and 120 at men) associated with double increase in risk of death as at men (relative risk 2, 02), and at women (relative risk 2, 36) in comparison with the least categories. Thus the waist circle associated with risk of death in all categories IWB.

## Russia can go another by is a herbal medicine of a diabetes 2 types!

"Insilat" - completely the natural preparation intended for preventive maintenance and complex treatment of a diabetes, normalisation of a carbohydrate exchange. Is a preparation of a choice for patients with tolerance infringement to glucose and patients with a metabolic syndrome ("prediabetes"). The preparation not only normalises the glucose maintenance in blood, but also development of complications of a diabetes brakes, interferes with a pancreas exhaustion.

"Insilat" it is well compatible with synthetic hypoglicemic preparations, and also to insulin, it can be used for increase of efficiency of complex treatment of a diabetes.

Momordica contains insulin like a protein known as insulin-P or polipeptid-P which shows hypoglicemic properties. Besides, the plant contains complex steroid substance charantin, also possessing powerful glicoglicemic action.

Momordica promotes activization of synthesis of insulin, optimising its action at level of fabrics, stimulates development glicogen's in a liver, strengthens regeneration processes β pancreascages.

It is widely applied in traditional Indian and Chinese medicine as means to decrease in level of sugar in blood at patients with a diabetes of 2 type.

Also it is established, that the extract Momordica's reduces level of the general cholesterol, lipoproteids low density ("bad" cholesterol) and trio-acylglicerids in blood whey.

Nephritic tea (The Orthosiphon staminate) possesses expressed diuretic properties. The diuretic effect is accompanied by the strengthened allocation from an organism of urea, uric acid and chlorides. Raises glomerular a filtration (an effective nephritic blood-groove), improves function nephritic tubules.

"Insulat" possesses hypoglicemic action (lowers level of sugar of blood), but does not cause hypoglicemia's (sharp falling of level of sugar of blood), unlike the majority synthetic hypoglicemic preparations. Under the influence of components of a preparation glucose gradually, arrives small portions in a blood-groove that allows to smooth sharp fluctuations of level of glucose of blood.

The preparation is safe, is well transferred, does not put harm to a gastroenteric path. The optimum dose of a preparation steals up the attending physician and the Clinical Pharmacist individually for each patient.

Preparation Siofor it is expedient.

Now it is the first preparation of a choice for achievement of the good metabolic control of glucose at insufficient efficiency of a diet and expansion of physical activities. Siofor in itself possesses anorectic action concerning easily acquired carbohydrates, well reduces suction carbohydrates. Treatment Siofor's with superfluous weight of a body leads to moderate weight reduction, on the average on 5-7 kg for 3-4 months.

By the way, Siofor does not stimulate emission of insulin from pancreas b-cages, thus, does not lead hyperinsulinemia's, does not give hypoglicemic.

It raises sensitivity of peripheral fabrics to insulin that promotes stabilisation and-or decrease in weight of a body. At long application it leads to alignment daily glicemic to a curve, decrease in daily average level glicemia's, to level reduction glicemia's on an empty stomach, and also to decrease and level normalisation glicated haemoglobin (НвА1с).

## So as a whole, Siofor operates patogenetic

- Gently reduces blood sugar, not leading hypoglicemia's;
- Difference from preparations Sulfanilurea's, does not stimulate secretion of insulin and does not reduce sugar of blood at persons with a metabolic syndrome without infringements of a carbohydrate exchange;
- Increase sensitivity of peripheral fabrics to insulin also strengthens absorption of glucose by cages, that is reduces insulin resistance;
- Brake neoglucogenez (superfluous formation of glucose) in a liver that promotes decrease glicemia's on an empty stomach;
- Delay suction carbohydrates in intestines, reduces appetite that leads to reduction postprandiale glicemia's;
- contribute to reduction of weight of a body at patients with adiposity;
- Render favorable effect on a metabolism lipids, reducing:
- Common cholesterol;

- Cholesterol of lipoproteids low and very low density;
- Level trio-acylglicerids therefore atherosclerosis progressing decreases.

Begin treatment usually with 1 tablet on 500 mg 1-3 times a day during meal.

In 10-15 days the dose Siofor's can be increased gradually under the control glicemia's, however it is impossible to accept more than 3000 mg Metformin's (Siofor's) a day.

The supporting dose usually makes 1500-2000 mg/days.

### The maximum dose - 3000 mg/sut - danger lactatacidoz's can be high!

Contra-indications: Siofor (Metformin) it is impossible to appoint to persons is more senior 60 years! Besides because of danger of collateral action – lactatacidoz's!

Usually at insulin resistance the pressure raises and there is a hypertension (own researches of the author).

Changes on an electrocardiogram (ECG) – own Researches (note of author's).

The first 10 minutes of record ECG of intervals in the second assignment, showing low variability still about what do not speak. Here, if all record has such character yes, is about what to become thoughtful. Day high variability, it is good. Rigid the rhythm is dangerous transition in variabelny or pendulum-shaped, that in turn gives very high risk of development various menacing arithmias (against health), sudden coronary death and other complications. Here not so it is a lot of sympathetic activity, not looking at a hypertensia. Here there is a transition of warm regulation from reflex vegetative level on gumoralno-metabolic, to increase cerebral ergotrop influences on rythmogenezis, therefore beta-blokatory and antagonists calcium - are not shown. Will be in that case favorable. And is I-APF. Indapamid it is necessary to leave, under indications, certainly. To well such patients to select a complex not difficult moderate exercises (moves, turns, inclinations) for 20 minutes daily. Also results - thyroid stimulating hormone (TSH), indicators of carbohydrate and fatty exchanges in dynamics are necessarily necessary. Thus it is necessary to drink pure water - artesian (the note of the author).

The dose Metformin's needs to be adjusted, at its overestimate it can be observed ricochet hyperglicemia and a hypertensia. It is better to divide doses hypoglicemic preparations into 2 receptions - in the morning (1/2 tablets) and for the night (1/2 tablets). It helps is better. Enalapril 5 mg not for the night, and in the evening till 19-00 - very much will approach. It we "will outwit" regulative mechanisms, especially, if there is a tendency to a night hypertensia. It is known reception. To accept a preparation it is necessary - only daily, the pressure 130/95 is not the indication of cancellation of a preparation. Or instead of Enalapril's to accept Lisinopril - it softer on action a preparation (the note of the author). It is necessary to consider concentration renin's in plasma of blood and presence of an initial bradycardia (for example, at were sportsmenes). At low renin's and a bradycardia to apply preparations to pressure decrease it is impossible! Otherwise, you risk aggravating a condition of the patient (the dream is broken to pant, heart stops). It is often noticed at night (the note of the author).

Important! On application antihypertensive therapies too happen ricochets (instead of pressure decrease, pressure liftings), that is dangerous! It needs to be considered at treatment of patients (the note of the author).

### Medicamentous therapy

Molecular mechanisms of action of pharmacological preparations.

Medicamentous therapy of a diabetes includes 2 types:

1. Application of the various medical products influencing decrease of absorption of carbohydrates in a gastroenteric path (Acarboza, etc.);
2. Biguanidins (Metformin);
3. Glitazones or Sensitizers insulin (Pioglitazon);
4. Application of the preparations stimulating secretion of insulin: Sulfanilurea preparations of II generation: Glibenclamid, Glipizid, Gliclazid, Glicvidon and Sulfanilurea preparations of III generation (Glimepirid).
5. The preparations, derivative amino acids, - Repaglinid and Nateglinid, which are regulators postprandiale hyperglicemia's or stimulators of secretion of insulin of short action.

When it is not possible to reach indemnification diabetes with the help peroral hypoglicemic preparations (at patients diabetes 2 of type with the expressed defect of b-cages of islets of a pancreas) application of the combined therapy (peroral hypoglicemic therapy + insulinotherapy, more often preparations of average duration of action for the night or 2 times in day) is recommended.

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