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CLINICAL PRACTICE GUIDELINE ON SCREENING, PREVENTION AND TREATMENT OF IRON-DEFICIENCY ANEMIA

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CLINICAL PRACTICE GUIDELINE ON SCREENING, PREVENTION AND TREATMENT OF IRON-DEFICIENCY ANEMIA

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2. LIST OF ABBREVIATIONS

IDA	-	Iron deficiency anemia
Hb	-	Hemoglobin
Ht	-	Hematocrit
g/l	-	Grams per liter
mg	-	Milligram
WHO	-	World Health Organization
TIAME	-	Tashkent Institute of Advanced Medical Education

3. BACKGROUND

Iron-deficiency anemia (IDA) is a condition characterized by a decrease of hemoglobin concentration, along with a moderate decrease in the erythrocyte count and hematocrit. Although bleeding, chronic enteritis, some helminthic infections and chronic diseases are the main etiological factors, the most prevalent cause of most IDA cases is lack of biologically available iron in nutrition.

IDA is one of the most serious problems worldwide and has negative medical, social and economic consequences.

Approximately one third of the world's population has anemia. People of different age groups suffer from anemia and the prevalence among different population groups varies a lot. Women of reproductive age, pregnant and breast-feeding women, children from six months to two years, teenagers and old people are all at risk of developing IDA[1,2].

According to WHO data, IDA prevalence fluctuates between 55% and 60% in developing countries and stands at 18% in Western countries. The highest IDA prevalence is recorded in South-Eastern Asia (India, Thailand, Vietnam, Cambodia) where up to 75% of pregnant women are anemic. Annually, 20-40% of maternal mortality cases worldwide are associated with IDA [3, 4].

Isolated mild and moderate forms of IDA in children rarely lead to a fatal outcome. However, severe IDA increases the risk of mortality, especially in the perinatal period [5,6]. A pregnant woman with IDA is subject to high risk of delivering an infant with hidden iron deficiency or an immature infant. IDA in children leads to impairment of psychomotor development and ataxia and to overall arrest of development. In addition, people with IDA often experience fatigue, weakness, have low work efficiency and are more subject to various infectious diseases due to weakened immunity [7,8,9,10,11,12].

Many countries in the world conduct various programs on prevention and treatment of IDA in pregnant and non-pregnant women of reproductive age. Some countries conduct similar activities for pre-school age children.

IDA is one of the major healthcare problems in Uzbekistan [13,14]. According to data from the Information-Analytical Center of the Ministry of Health of the Republic of Uzbekistan, only in 2002 was IDA diagnosed, for the first time, in 648,820 people (296,678 children, 57,560 teenagers and 321,582 adults). The Demographic Health Survey

of 1996 found IDA in 61% of children under 3 years old, and 60% in women of reproductive age. Moderate anemia (45%) or severe anemia (14%) was found in most women [15]. A similar survey in 2002 indicates that IDA prevalence among children under 3 years old reaches 58% in some regions of Uzbekistan [16].

With a view to implementing the State Healthcare Reform Program, approved by Decree # УП 2107 of the President of Uzbekistan on November 10, 1998, and to improving the quality of health care, the Ministry of Health of the Republic of Uzbekistan issued Order № 129 of February 25, 2003 on establishing a working group on quality management and development of clinical practice guidelines for the primary health care level, including a CPG on IDA.

This clinical practice guideline covers issues of screening, prevention and treatment of IDA at the primary health care level.

The guideline was developed by the Evidence-Based Medicine Center of Tashkent Institute of Advanced Medical Education with technical assistance from the ZdravPlus Project/USAID. It is the first clinical practice guideline developed according to international requirements with support of international experts.

This clinical practice guideline is designed for general practitioners, pediatricians, obstetrician-gynecologists and therapists.

4. DEFINITIONS

Anemia is a decrease in the level of hemoglobin, sometimes of erythrocytes, compared with age level norms as a result of pathological condition(s). The following can also cause anemia: chronic infection, malaria, hereditary membrane defect, enzyme defect of erythrocytes and hemoglobinopathy, micronutrient and vitamin deficiency, chronic diseases, bleedings, digestive diseases, etc. Besides, various factors, when combined, can become a complex cause of anemia both in one person and in the whole population, influencing prevalence and severity of anemia. IDA is one of the most common forms of anemia. See Annex 1 for definition of levels of severity of IDA.

Iron deficiency is a functional deficiency of iron in tissues and lack of iron reserves with or without anemia. Insufficient content of iron in nutrition, high demand for iron during a rapid growth period (pregnancy and neonatal period), and/or large loss of blood (gastrointestinal bleeding, heavy menstruation, helminthic infections, etc.) usually lead to iron deficiency.

Iron-deficiency anemia (IDA) is the most common type of anemia. IDA develops as a result of depletion of iron reserves in the body. Decrease of mental and physical activity as well as weakening of immunity is often associated with IDA. In addition, it is noted that severe IDA decreases the ability of sustaining homeostasis.

Hemoglobin is a red protein of erythrocytes made up of heme and globin. Hemoglobin transports oxygen from lungs to tissues. Hemoglobin concentration is expressed in grams per liter of blood volume. In some countries the value of hemoglobin is expressed in grams per deciliter. There are several methods of quantitative measurement of hemoglobin. The most common method in Uzbekistan is the Sahli method which should be totally abandoned. The most preferred method of determining hemoglobin level is the use of a hemoglobin meter or the hemcyanmetgloboin method.

Hematocrit expresses the mass of erythrocytes as a percent of total blood volume. A decrease of hematocrit occurs only with a decrease of hemoglobin. A decrease of

hemoglobin and hematocrit concentration occurs only at an advanced stage of iron deficiency. Both tests, being indicators of advanced iron deficiency, are still the main methods of anemia identification.

Fortification/enrichment of food products with minerals and vitamins is an effective method of decreasing morbidity and its consequences, including IDA consequences.

Screening (preventive examination) is a large-scale examination of people who do not consider themselves sick in order to detect latent diseases or risk factors of future health problems. Screening makes it possible to make an early diagnosis of a number of diseases (cervical cancer, tuberculosis, fetus malformation, diabetes mellitus, etc.) and thus reduce the mortality rate. Screening is one of the most important methods of prevention in medicine; as a rule it is conducted with the use of simple and non-invasive diagnostic procedures. To detect IDA, it is recommended to conduct screening by determining hematocrit and hemoglobin among children, women of reproductive age and pregnant women.

Elemental iron – the main replacement therapy for iron deficiency is intake of oral or injectable iron drugs. Digestibility of iron from a drug (iron salt) depends on the content of elemental (active) iron in it. IDA treatment with iron drugs pursues two goals: correction of hemoglobin deficiency and replenishment of iron reserves in the body. Dosage calculation is based on elemental iron content in the drug (Annex 2).

5. INTRODUCTION

This clinical practice guideline is the result of a quality improvement project implemented at the primary health care level in Uzbekistan.

The objective of the clinical practice guideline is the establishment of a single system for prevention, diagnosis and treatment of IDA at the primary health care level. In addition, it can be used in the daily routine work of health facilities at other levels.

This guideline was developed to guide examination and follow-up, prevention and treatment of children, teenagers, non-pregnant women of reproductive age and pregnant women, as these population groups are especially prone to IDA development and its complications [17].

The main requirement for development of the clinical practice guideline was the use of evidence-based medicine data. Evidence-based medicine is a conscious and coherent use of interventions which are supported by scientifically proven evidence. Therefore, information used for its development was selected according to the level of evidence.

The search for good-quality clinical practice recommendations was conducted in national and international registers of clinical guidelines and in other clinical recommendation databases on the Internet. In addition, clinical recommendations, epidemiological data and evidence on the effectiveness of diagnostic, prevention and treatment procedures for IDA were searched in the electronic libraries "MEDLINE" and "EMBASE". The search for evidence for topics that were not mentioned or fully described in selected clinical guidelines was made through *The Cochrane Library 2003, Issue 4*.

As a result of searching and critical analysis of more than 1,000 related documents and full-text articles, there were selected 16 sources that became the basis for the development of this guideline. [4,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31].

6. PREVENTION AND TREATMENT OF IDA IN CHILDREN

Iron deficiency anemia is found quite often in infants. Anemia in children **under 5 years** is determined by a hemoglobin concentration **below 110 g/l**, or a hematocrit level below 33%.

For an infant under six months only breastfeeding is recommended. For children with IDA being breastfed, it is recommended to take iron beginning at six months old.

For most infants being fed with formulas it is recommended to use a formula enriched with iron before starting feeding with solid foods (until 12 months old). It is recommended to provide training and consultation on proper nutrition to parents in order to prevent IDA.

Mature infants should be examined for IDA (level of hemoglobin and hematocrit) at six months old, and immature infants not later than at three months old.

Infants diagnosed with IDA must take iron drugs or food enriched with iron (baby formula). To confirm the effectiveness of treatment, all infants with IDA must be tested again for hemoglobin and hematocrit four weeks after starting the treatment. If the prescribed treatment brings good results (increase of hemoglobin level higher or equal to 10 g/l, and increase of hematocrit by 3% or more) or these values fall within normal standards, then the treatment must be continued for another two months and after that iron treatment can be stopped. If the treatment has no good result, or the increase of hemoglobin level is less than 10 g/l, and increase of hematocrit is less than 3%, then the doctor must identify other possible causes of anemia by referring the patient to a hematologist. Infants with moderate or severe IDA (hemoglobin below 90 g/l or hematocrit below 27%) must receive consultation of a hematologist.

Children 6-12 years old who are subject to IDA risk factors (poor living conditions or nutrition) require repeated screening. Teenage girls must follow the recommendations for non-pregnant women of reproductive age.

6.1. RECOMMENDATIONS

6.1.1. Screening for IDA, determining hemoglobin and hematocrit

1. Examine all infants six months old for IDA.
2. Examine immature infants for IDA not later than at three months old.
3. Anemia in children between six months and five years is diagnosed if hemoglobin level is below 100 g/l or hematocrit is below 33% (Annex 1).

6.1.2. Mature infants, immature infants or infants with low birth-weight

1. Continue only breastfeeding until six months old.
2. Use iron-containing baby formula until 12 months old in case of early weaning.
3. Take iron-containing syrup (2 mg/kg per day – maximum 15 mg per day) starting not later than at one month old for immature infants or infants with low birth-weight.
4. Avoid taking whole cow milk until 12 months old.
5. Keep iron drugs away from children.

6.1.3. Age to start taking solid food

1. Start taking vegetables after turning six months old and by 8-9 months start taking meat.
2. Include in nutrition food products rich in ascorbic acid (fruits, vegetables or juice) and meat in order to ensure better digestion of iron.

6.1.4. Treatment of children with IDA

1. Infants with moderate or severe IDA (hemoglobin level below 90 g/l or hematocrit below 27%) must be examined by a hematologist. In case of moderate anemia, iron-containing baby formula or syrup (iron-

containing drops) of 3 mg/kg of elemental iron per day must be prescribed.

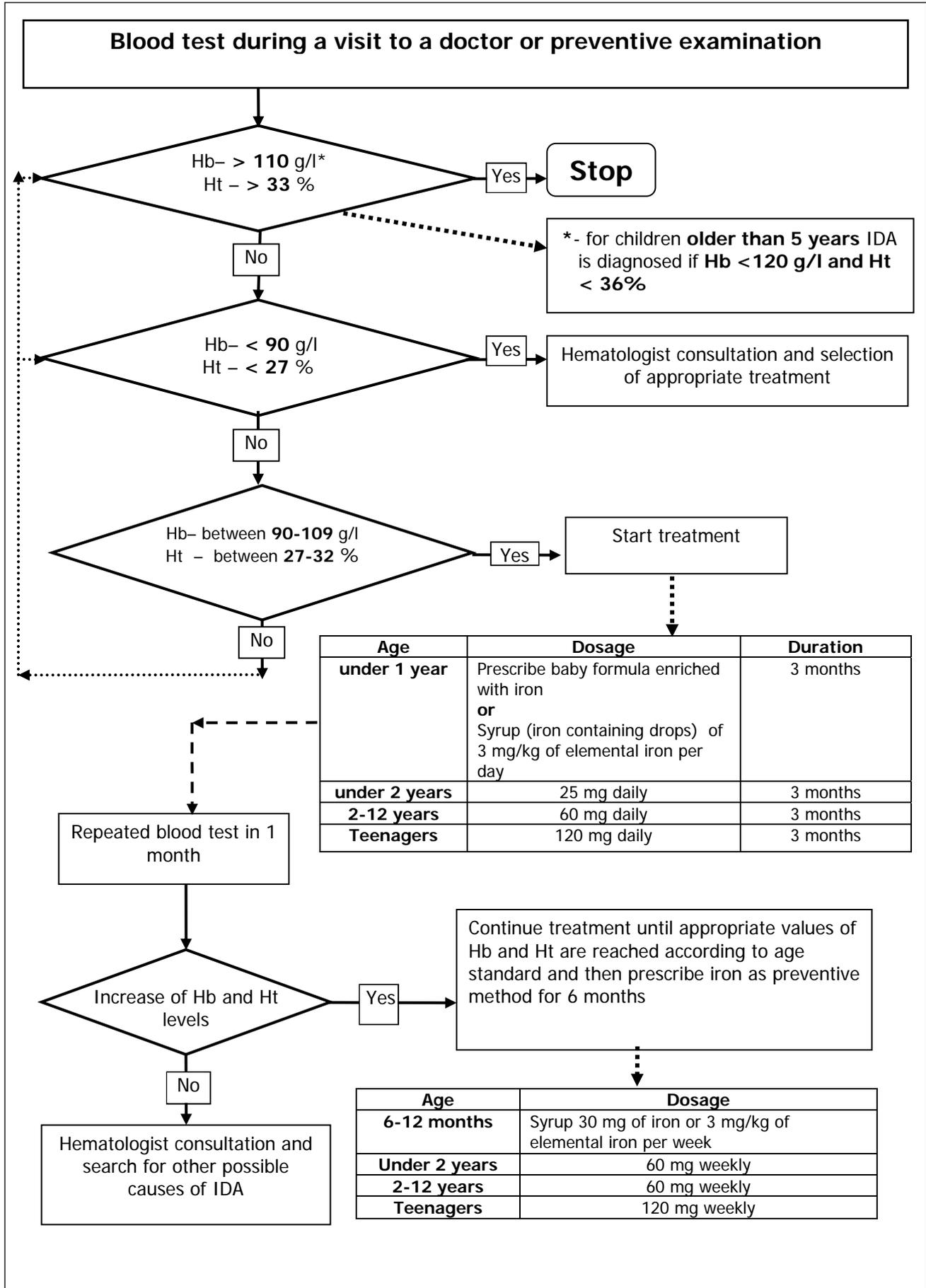
2. In four weeks, check the results of elemental iron treatment (increase in hemoglobin level by 10 g/l and increase in hematocrit by 3%, or to the normal standard limit). In case of positive results, continue taking iron syrup for another two months.
3. If the prescribed treatment brings no results, check to see if the child is taking iron drugs properly and refer him to a hematologist.
4. For children diagnosed with IDA at an early age it is required to conduct repeated testing of hemoglobin and hematocrit levels at 15 and 18 months old.
5. Keep iron drugs away from infants and children.

6.1.5. Post treatment Iron supplementation

1. After finishing the treatment course, it is recommended to take an elemental iron drug as a preventive method once a week for six months:

Age	Dosage of elemental iron drug (mg)
6-12 months	Syrup 30 mg or 3 mg/kg of elemental iron
12-18 months	60 mg
2-12 years	60 mg
Teenagers	120 mg

6.2. ALGORITHM OF SCREENING AND TREATMENT OF IDA IN CHILDREN



7. PREVENTION AND TREATMENT OF IDA IN NON-PREGNANT WOMEN OF REPRODUCTIVE AGE

All non-pregnant women of reproductive age must be examined for IDA at least once between 15 and 25 years old however it is recommended. Given the risk factors (malnutrition, heavy menstrual bleedings, blood donation, etc.) or record of IDA diagnosis in medical history, a more frequent screening (annual) is required.

If IDA is suspected based on analysis of peripheral blood sampled from a finger, then it is better to confirm IDA by blood sampled from a vein. For non-pregnant women of reproductive age anemia is diagnosed if the hemoglobin level is **below 120 g/l**, and the hematocrit level is **below 36%**.

The following treatment is recommended for women of reproductive age:

If the hemoglobin concentration is less than 100 g/l, a woman must take a therapeutic dose of elemental iron – 60 mg two times a day (total dose is 120 mg). In addition, it is necessary to educate her on proper nutrition. The doctor must check the effectiveness of the prescribed treatment after one month. If the result is very slight or there is no result at all (hemoglobin increased by less than 10 g/l; or hematocrit increased by less than 3%), the clinician must identify other possible causes of anemia by referring the patient to a hematologist. In case of inflammatory or infectious processes, low hemoglobin concentration or hematocrit volume may be caused by improper iron distribution in the body and requires additional treatment. If iron treatment brings positive results, then it must be continued until the hemoglobin level reaches 120 g/l. After that the iron dose can be reduced to 120 mg per week for six months.

Severe IDA is atypical for women of reproductive age and iron deficiency can rarely be a cause of such anemia. Detailed information about disease course, including nutrition, in-depth examination and additional laboratory analysis (complete blood count, serum iron, transferrin level, ferritin level, reticulocyte count, total protein, total bilirubin and its fractions) are recommended for final confirmation of IDA.

Balanced nutrition for preventing IDA may stop IDA development in women of reproductive age and eliminate the need for iron drugs. That is why it is necessary to pay special attention to eating meat and food products rich in ascorbic acid (to increase absorption of iron from food products) and to exclude tea and coffee during eating.

Multivitamin and mineral drugs containing about 30 mg of iron in each tablet can be prescribed for women with high risk of multiple microelement failure.

7.1. RECOMMENDATIONS

7.1.1. General screening of women of reproductive age

1. All non-pregnant women of reproductive age are recommended to go through IDA examination once annually.
2. In case of medical or social risk factors of anemia (regular blood donation, heavy menstrual blood loss, IUD, IDA diagnosis in medical history) more frequent screening for anemia is required.

7.1.2. Procedure of IDA screening

1. If anemia is suspected based on analysis of peripheral blood sampled from a finger, then it is recommended to confirm IDA by analysis of blood sampled from a vein.
2. Recommended hemoglobin and hematocrit levels:

Parameters	Units
Hemoglobin g/l	120
Hematocrit %	36.0

7.1.3. Preventive measures for women of reproductive age

1. Women having high risk of IDA and planning pregnancy should start prevention of anemia at least three months prior to getting pregnant. The following combination must be prescribed to prevent IDA: elemental iron (120 mg once a week) and folic acid (400 mg every day). Duration of the treatment is six months or until after the first trimester of pregnancy. Continue with 400 mg of folic acid per week.

2. For women at risk of multiple microelement failure a clinician can additionally prescribe drugs containing 30 mg of iron every day (of Totema type, etc.).
3. It's best to take iron-containing pills between meals with water or juice (but not with tea, coffee or milk).
4. Iron drugs must be stored in places inaccessible to children, as they can cause poisoning.

7.1.4. Treatment of women of reproductive age with IDA

1. **Mild and moderate IDA.**

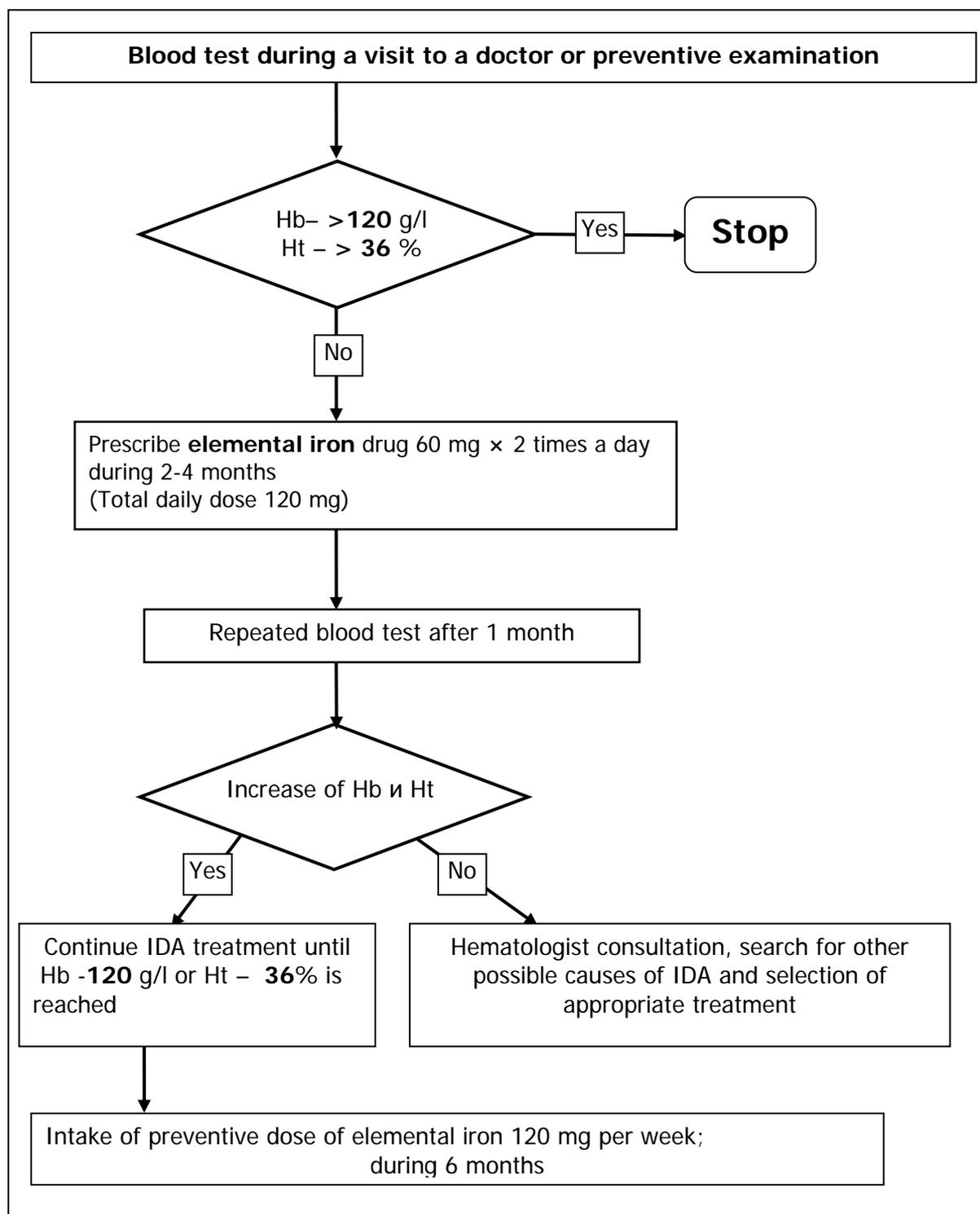
Prescribe therapeutic dose of elemental iron of 60 mg twice a day (total daily dose is 120 mg). Conduct consultation on proper nutrition. Check the effectiveness of prescribed treatment in 1-1.5 months. If the result is very slight or there is no result at all (hemoglobin level increased by less than 10 g/l or hematocrit increased by less than 3%), it is required to identify other possible causes of anemia and refer the patient to a hematologist. In the case of positive results of the treatment, it is required to continue taking the therapeutic dose for 2-4 months until 120 g/l is reached. Then the dose of elemental iron can be reduced to 120 mg per week for six months. Before the treatment is fully stopped, it is required to re-test the blood (hemoglobin and hematocrit must be within normal standards).

2. **Severe IDA** is atypical for women of reproductive age. In comparison to mild and moderate IDA, the severe form is diagnosed relatively rarely. To confirm the diagnosis of severe IDA, it is required to conduct an in-depth examination by a hematologist, including the following tests: complete blood count, reticulocyte count, transferrin level, serum iron, ferritin level, and total iron binding capacity, in order to differentiate IDA from other forms of hypochromic anemia.

7.1.5. Recommendations for nutrition

1. Eat products rich in iron and ascorbic acid (meat, fruits, fruit juice, etc.).
2. Avoid drinking tea or coffee during meals (Annex 4).

7.2. ALGORITHM OF SCREENING AND TREATMENT OF IDA IN NON-PREGNANT WOMEN OF REPRODUCTIVE AGE



8. PREVENTION AND TREATMENT OF IDA IN PREGNANT WOMEN

Pregnant women are more subject to IDA risk. IDA is found in almost 80% of pregnant women. Due to the increase in the volume of circulating blood during pregnancy (due to hemodilution) a moderate decrease in erythrocyte concentration and hemoglobin concentration is considered normal.

According to the standard, the level of hematocrit in non-pregnant women fluctuates from 36% to 44%, but in pregnant women the hematocrit level decreases due to “physiologic hemodilution” and does not mean IDA or a decrease in the oxygen carrying capacity. The volume of circulating blood by the end of pregnancy increases by 25 to 50%. At the same time the level of blood plasma increases by 50%, whereas the number of erythrocytes increases only by 20-30%. Such a disproportional increase results in hemodilution and reaches its maximum by the 32nd week of pregnancy. During pregnancy the volume of blood increases by 1-1.5 liters and the total volume of body fluid increases up to 6-8 liters, four liters of which is extracellular fluid. Such an increase in blood volume and extracellular fluid is necessary for optimal uteroplacental circulation. In spite of blood loss during delivery, usually the level of hematocrit increases immediately after delivery. Absence of hemodilution in late pregnancy indicates an inadequate increase in blood volume which can be associated with arrested fetal development, hypertension caused by pregnancy or antenatal fetal death.

All pregnant women must be examined for IDA during the first prenatal visit and at least once during each following trimester of pregnancy. During each visit the doctor must provide training in proper nutrition during pregnancy. Training should include recommendations on eating products rich in iron and products stimulating absorption of iron, refusing products which decrease the absorption of iron (which must be eaten separately from products rich in iron), and following other recommendations on proper nutrition.

Due to high IDA morbidity rates, all pregnant women exposed to risk of iron deficiency must take elemental iron drugs as a preventive method. Preventive prescription of elemental iron and folic acid during the whole period of pregnancy results in an increase of hemoglobin level during the pregnancy itself, during delivery, and during six weeks after delivery.

Hemoglobin and hematocrit levels must be checked during the first trimester of pregnancy. The doctor should prescribe medication if the hemoglobin level is below 110 g/l. If the hemoglobin concentration is below 90 g/l, then it is required to receive consultation of a hematologist and a gynecologist in order to clarify the diagnosis and to select appropriate treatment.

If the hemoglobin level is between 90 and 109 g/l, the doctor should prescribe 120 mg of elemental iron and 400 mg of folic acid per day for three months. If the hemoglobin level is between 110 and 120 g/l, the preventive treatment should be: 120 mg of elemental iron once a week and 400 mg of folic acid daily during the first trimester, followed by a decrease of the folic acid dose to 400 mg once a week for three months.

If the iron treatment brings no positive results, consultations of a hematologist and a gynecologist are required. The hemoglobin level should be checked during subsequent prenatal visits.

Iron intake can be stopped during delivery. If IDA was identified during pregnancy, during delivery, and in those who belong to a risk group (heavy blood loss during delivery or multiple births) the doctor must continue anemia treatment for 4-6 weeks after delivery.

Beyond 4-6 weeks postpartum, women must follow the recommendations for non-pregnant women of reproductive age.

8.1. RECOMMENDATIONS

8.1.1. Screening for IDA and selection of appropriate treatment

1. During the first trimester of pregnancy all pregnant women must have a complete blood count and a hemoglobin or hematocrit level test. If the hemoglobin concentration is below 90 g/l, consultation of a hematologist and a gynecologist is required.
2. Prescribe a combination of 120 mg of elemental iron and 400 mg of folic acid per day during three months if the hemoglobin is between 90 and 109 g/l, followed by a preventive combination of 120 mg of elemental iron and 400 mg of folic acid once a week.

3. Prescribe the following combination if the hemoglobin level is higher or equal to 110 g/l: 120 mg of elemental iron once a week and 400 mg of folic acid daily. After the first trimester reduce the dose of folic acid to 400 mg once a week.
4. Continue treatment of moderate IDA during pregnancy for three months, followed by prescription of a preventive dose of iron for six months.
5. Check the hemoglobin level during subsequent prenatal visits. If the treatment brings no positive results, additional examination by a hematologist and a gynecologist is required. If the hemoglobin level is normal for a certain phase of pregnancy, reduce the dose of elemental iron to 120 mg per week as a preventive method.
6. Stop intake of elemental iron during delivery. For women who were identified with moderate or severe IDA during or after pregnancy or who belong to a risk group (heavy blood loss during delivery or multiple births), the treatment must be continued for 4-6 weeks after delivery.

8.1.2. Screening of women at high risk of IDA during medical examination at 4-6 weeks after delivery

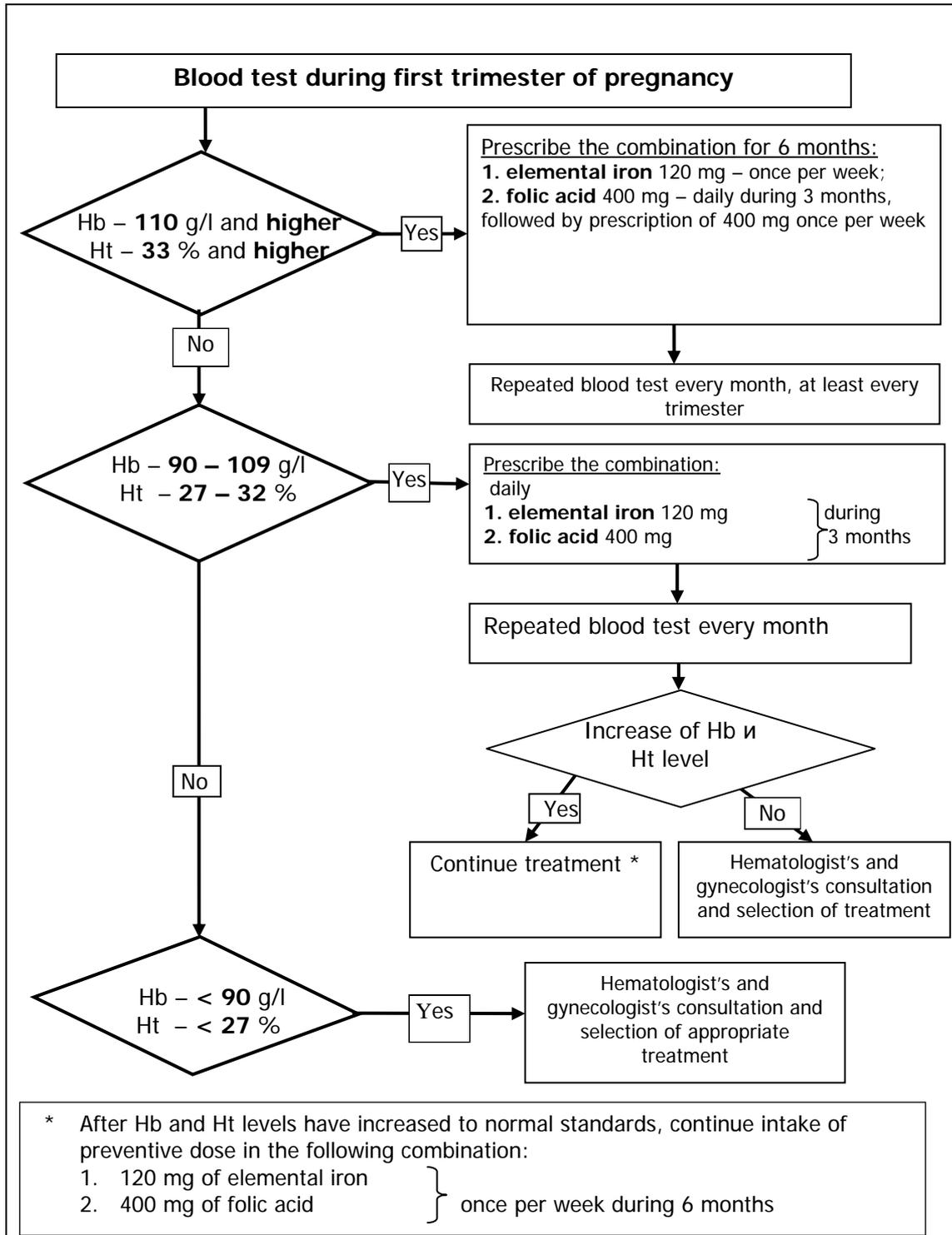
1. Screen for IDA women at high risk (risk factors including IDA that continued to exist during the third trimester of pregnancy, excess blood loss during delivery or multiple deliveries). Obtain a complete blood count (including hemoglobin or hematocrit). Interpret the results according to the same criteria as for non-pregnant women.

8.1.3. Recommendations on proper nutrition

1. Eat products rich in iron and products which increase the absorption of iron (meat, honey, fruits rich in ascorbic acid).

2. Products which obstruct the absorption of iron (tea, coffee, coarse-grained cereals, etc.) must be eaten separately from products rich in iron (Annex 4).
- * If 120 mg of elemental iron is prescribed, it is recommended to take one 60 mg pill two times a day.

8.2. ALGORITHM OF SCREENING AND TREATMENT OF IRON-DEFICIENCY ANEMIA IN PREGNANT WOMEN



ANNEX 1**Table 1. Normal standards of hemoglobin and hematocrit**

Age group	Hemoglobin	Hematocrit
Infants (mature)	105-195 gram/liter	32-60%
Children (1-9 years)	110-140 gram/liter	33-40%
Children (10-12 years)	115-150 gram/liter	35-45%
Men (adults)	130-180 gram/liter	40-50%
Women (adults)	120-160 gram/liter	36-44%
Pregnant women	110-140 gram/liter	33-42%
Women (post menopause)	130-180 gram/liter	40-50%

WHO/UNICEF, 1997

Table 2. Forms of anemia depending on hemoglobin value for children under 5 years and pregnant women

Mild anemia	90 – 110 gram/liter
Moderate anemia	70 – 90 gram/liter
Severe anemia	Less than 70 gram/liter

WHO/UNICEF, 1997

Table 3. Forms of anemia depending on hemoglobin value for children over 5 years and non-pregnant women

Mild anemia	90 – 120 gram/liter
Moderate anemia	70 – 90 gram/liter
Severe anemia	Less than 70 gram/liter

WHO/UNICEF, 1997

ANNEX 2

Table 1. Content of elemental (active) iron in different iron-containing drugs (WHO, 1989)

Chemical form of iron in drugs	Content of "active" iron in drugs (% of total iron content)
Ferrous fumarate	33
Ferrous sulphate	20
Ferrous gluconate	12

Table 2. Content of elemental iron in frequently used oral drugs

Drug	Form of iron compound in drug	Content of active iron in drug (mg)
Actiferrin	Ferrous sulphate	34,5 in 1 capsule
		34,5 in 5 ml syrup
		9,8 in 1 ml drops
Aktiferrin compositum	ferrous sulphate	34,5 in 1 capsule
Gemofer prolangatum	ferrous sulphate	105 in 1 pill
Gino-tardiferon	ferrous sulphate	80 in 1 pill
Sorbifer durules	ferrous sulphate	100 in 1 pill
Tardiferon	ferrous sulphate	80 in 1 pill
Totema	ferrous gluconate	50 в 10 мл
Feramid	ferrous chloride	15 in 1 pill
Ferro-gradumet	ferrous sulphate	105 in 1 pill
Felol	ferrous sulphate	47 in 1 pill
Fenyul's	ferrous sulphate	45 in 1 capsule
Gemofer	ferrous chloride	1,5 in 1 drop
Maltofer	Fe-hydroxide-polimaltosa	50 in 5 ml syrup
		50 in 1 ml drops
Maltofer FOL	Fe-hydroxide-polimaltosa	100 in 1 pill
Ferrum lek	Fe-hydroxide-polimaltosa	50 in 5 ml syrup
		100 in 1 pill

ANNEX 3

[32,33,34,35]

Side effects of iron drugs

The most frequently observed side effects caused by iron drug treatment:

- Constipation and diarrhea. These effects rarely become severe. However, elemental iron drugs can provoke aggravation of gastrointestinal diseases (ulcer or ulcerative colitis). In this case elemental iron pills can be replaced with intramuscular or intravenous injections.
- Nausea and vomiting frequently occur if high doses of elemental iron are taken. These can be eliminated by taking a lower dose or taking coated drugs (capsules). To eliminate the above side effects iron drugs may be taken after eating but this reduces the effectiveness of treatment by 60%. In case of severe nausea iron pills can be replaced with injections.
- Dark stool is usual during treatment with elemental iron drugs.
- Darkening of tooth enamel
- Acute poisoning caused by elemental iron drugs is very rare in adults

Poisoning caused by iron drugs

Most often, poisoning caused by iron drugs occurs in children under six years old due to overdose. There are several reasons for this:

- Parents are not aware that iron drugs can be dangerous for children
- Small children perceive some drugs, especially iron containing ones, as sweet candies
- Iron drugs are available in different forms and are sold over the counter. Multi-vitamin and mineral tablets, which doctors frequently prescribe to pregnant

women, contain elemental iron in high doses. In case of negligence, these drugs become easily accessible to children.

A poisonous dose of elemental iron depends on the child's weight. Poisonous action starts in the case of taking 10-20 mg of iron per one kg. Overdose of 50 mg per 1 kg leads to acute poisoning.

Symptoms and signs of iron poisoning:

The early stage of poisoning in children may have no symptoms. But it is deceptive, and in a few hours a child falls into shock/collapse due to severe chemical imbalance in the blood. Then, an excessive amount of elemental iron goes with bloodstream to all organs and can cause necrosis in stomach, liver, kidney and lungs, and can damage blood vessels and the brain.

Severe overdose of elemental iron has two stages. The following symptoms occur at an early stage within 30 minutes to 2 hours after taking the drug:

- Vomiting with blood
- Back pain
- Diarrhea
- Loss of consciousness
- Shock
- Electrolytic imbalance
- Clotting disorder

Afterwards, deceptive well-being and stabilization of the condition may occur. In case of severe poisoning, this period is very short. Life threatening symptoms develop in 12-48 hours:

- Heavy vomiting with blood
- Blood traces in stool
- Possible intestinal perforation
- Peripheral circulatory collapse with acute hypotension
- Low sugar content in blood (hypoglycemia)
- Low oxygen content in blood (hypoxia)
- Pulmonary edema
- Convulsions

- Coma
- Renal and hepatic failure is observed at the end of the second stage.

To diagnose elemental iron poisoning, it is required to:

- Gather a detailed history of disease development
- Have parents bring the drug package for the doctor to look at
- Have a blood test to determine the erythrocyte count, hematocrit, hemoglobin, serum iron and sugar.

Treatment of iron poisoning:

The following actions are effective during the first hour after poisoning:

- Have the patient drink milk and induce vomiting (artificial inducing of vomit must be conducted in the presence of health personnel because of possible aspiration of gastric contents).
- Have the patient eat a few raw or undercooked eggs (to create iron-protein complex).
- Stomach lavage with 1% solution of soda bicarbonate (to clean the stomach and reduce iron concentration). Stomach lavage is dangerous to conduct after the first hour of iron poisoning due to possible necrosis of the stomach.
- Prescription of a strong laxative and cleansing enema (to remove the iron drug).

Follow-up actions:

- Conduct symptomatic therapy in case of shock, dehydration, and bleeding and maintain appropriate breathing.
- Hospitalization of the patient in the department of intensive care and resuscitation and consultation of a hematologist (toxicologist).
- In case of severe poisoning it is required to administer intravenously a drop-by-drop solution of "despheral" (deferoxamine), which, when combined with iron, creates a complex compound that is excreted in the urine.

To prevent poisoning by iron-containing drugs it is required to:

- Tell patients with IDA and parents about the danger of iron poisoning, the methods of delivering first aid, and to keep all kinds of drugs away from children.

ANNEX 4

[36,37,38,39,40]

Rational nutrition to prevent IDA

Every patient must know which products are rich in iron and which products increase its absorption.

- The best products for increasing and maintaining iron reserves in body contain easy-to-digest heme iron. These are meat, fish, prawns, poultry, and organ meats (tongue, liver, kidneys).
- Eggs, milk products, vegetables, cereal products (bread, cereals and pasta), fruits, greens, seeds and dried fruits have only non-heme iron. Only 40% of iron in these foods is absorbed by the body as these products contain components and inhibitors that prevent absorption (the so-called non-heme iron).
- Eating products rich in vitamin C increases absorption of non-heme iron. These products include cabbage, sweet peppers, citrus fruits, sweet melons, honey, tomatoes, and sour-milk products. One orange or one glass of orange juice increases absorption of non-heme iron by 50%.
- Food products containing riboflavin (vitamin B2) also increase the level of hemoglobin. These products include liver, yogurt and other sour-milk products, and various dry cereals.
- Meals should include various products the combination of which increases iron absorption.
- Tea or coffee during eating significantly reduces absorption of iron due to compounding of insoluble complexes with tannins. Therefore, tea or coffee must be taken after some period of time after taking a main meal. During eating it's best to drink compote, juices, boiled water, and berry or fruit infusions.

Folic acid is necessary to prevent lack of folate in case of IDA in pregnant women:

- Products like citrus fruits, fruits, greens, green leafy vegetables, peas, and dried beans are highly rich in folate. In our conditions sufficient consumption of greens and vegetables quite satisfies the body's demand for folate.

- Usually, vitamins are prepared with folic acid which is two times more active than folate. The recommended daily dose of folic acid of 400 mg for adults significantly exceeds the standard recommendation of 400 mg of folate.

Lack of an additional supply of folic acid during pregnancy leads to folate deficiency in the body and increases the risk of neural tube defect. All women planning pregnancy and pregnant women must take folic acid. (Refer to section on prevention and treatment of IDA in women of reproductive age and pregnant women).

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