Cutaneous symptoms and syndromes in pathology of digestive organs

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It is worth admitting that modern doctors insufficiently use classical methods of clinical studies in the diagnosis of patients, due to having poor knowledge of them. In particular, little attention is paid to examining of skin, the diagnostics value of the skin characteristic changes and its appendages (hair, nails) in various internal diseases.

Meanwhile, the skin is a kind of screen or mirror, reflecting various pathological processes occurring in the human body, especially in the digestive system [9, 10, 17, 41, 43, 52, 57, 58]. Inspection of skin allows to diagnose certain diseases and pathological processes already at the first meeting with the patient, much earlier than the results of modern, highly labor-intensive and expensive instrumentation and laboratory research.

Moreover, on the basis of changes in the skin, identified during the examination, it is possible, suspecting a specific disease, to guide further diagnostic search in a certain way to purposefully seek confirmation of the existence of the disease assumed, using only methods and laboratory diagnosis, which will quickly and reliably establish a final diagnosis.

In this article, we give a brief review of the details, making it possible to summarize the known facts on the different changes of the skin, reflecting a greater or lesser degree of pathological processes in the gastro-intestinal tract, hepatobiliary system, and pancreas (pancreatic) .

Skin changes in various pathological processes of the internal organs are sometimes called dermadromas [9].

Changes on skin during various gastrointestinal tract diseases

During the diseases of the gastroduodenal nature (chronic gastritis and duodenitis, ulcers) there are usually no characteristic skin changes. We can only point at a

moderate weight loss in a phase of recurrent ulcer due to sitophobia (refusing food for fear of provoking pain), rash of the skin, especially in the area of hyperesthesia, hyperalgesia, or Zakharyin-Ged zone. With the intensive pain and frequent use of hot warming, there is focal brown pigmentation on the skin in the epigastric region, reminding of a tiger skin pattern.

Pallor in the blood and visible mucous membranes may indicate a complication of ulcer bleeding and development of posthemorrhagic anemia. As for specific localization of postoperative scars on the anterior abdominal wall, they denote surgery for ulcer and its complications (perforation, penetration into neighboring organs, etc.). Older authors pointed out that patients with ulcer had also premature graying of hair [15, 32].

Chronic diseases of the small intestine often lead to serious metabolic disorders in the body, to the development of maldigestion and malabsorption syndromes, to the small bowel dysbiosis (excessive microbial growth in the small intestine).

With malabsorption syndrome it is suggested to distinguish specific and non-specific skin changes (skin signs).

Specific cutaneous manifestations of malabsorption syndrome include enteropathic acrodermatitis, hypo- and avitaminosis, non-specific include acquired ichthyosis, hair and nails changes, eczematous and psoriasiform skin rashes [50, 51, 54].

Malabsorption syndrome skin changes are observed in the form of malnutrition, dry (due to dehydration of the body), scaling, elasticity of the skin reducing, which is going grayish.

In the corners of the mouth there appear linear surface cracks and damage (excoriation), erosions (angular canker or bridoe), focal elements of rash with sharp thickening of the skin and increasing of its figure (lichenification), inflammatory hyperemia and thickening of the vermilion border, with dry scales and erosions in the corners of the mouth (angular cheilitis).

In connection with atrophy of the papillae tongue becomes smooth (polished, coated tongue), it acquires a bright red ("cardinal" tongue), and on the mucous membrane of the mouth exanthema and aphthae (aphthous stomatitis) are formed [2, 11, 18, 46].

A significant role in these changes belongs to the developing during the malabsorption syndrome of hypo- and vitamin deficiency [56].

So, with a vitamin A (retinol) deficiency, skin becomes tough, scaly with hyperkeratosis symptoms, acquires a yellowish-gray color, papular rash appears. In the proximal parts of the limbs, and then on the corpus, back, buttocks, abdomen skin developing follicular keratosis (excessive thickening of the horny layer of the epidermis with the defeat of the mouths of the hair follicles) develops, the hair becomes dry, brittle, thinning and falling out, lose shine, dystrophic nail changes develop. The characterisic is the night blindness (hemeralopia).

Deficiency of vitamin B2 (riboflavin) proceeds with the development of angular stomatitis. In the corners of the mouth and on the lip fusion cracks occur coated with a yellow crust that falls off, forming ulcers, and with their healing scars appear.

The mucous membrane of the lips gets pale, scaly, and then begins soaking; epithelium becomes macerated and exfoliated, and on the lips vertical chinks appear. On the wings of the nose, on the nasolabial folds, the bridge of the nose and ears peeling and seborrheic crusts are observed. Tongue papillae become smoothed; it becomes purple with a bluish tinge.

Inside the mouth thrush is developing. Photophobia, tearing, burning sensation are observed, superficial vascular keratitis develops at times, visual acuity and light sensitivity reduce.

With a deficiency of vitamin PP (nicotinic acid) pellagrous syndrome is developing, for which the characteristics are (three D): dermatitis, diarrhea, dementia.

Around the neck pellagrous collar forms, or Casal's necklace (G. Casal), as clearly demarcated reddish-brown stripes. On the open areas of skin small round red spots appear, accompanied by pruritus and burning sensation.

Those spots get darker, swelling appears, inflammation and blisters that burst, and instead of them there are cracks and pitting. The skin becomes dry, rough, becoming brown with light strips from scratching. On the face and the hands, neck and feet erythema appears, while during the protracted course hyperkeratosis develops. The tongue is bright red, swollen, increased in size with the imprints of teeth on the edges.

Skin changes are combined with gastro-intestinal disorders (unpleasant sensations in the mouth, loss of appetite, epigastralgia, nausea, rarely – vomiting) [13, 45, 56].

Deficiency of vitamin K (phylloquinone) is manifested in the hemorrhagic syndrome (purpura); on the skin and in underskin tissue pinpoint petechial hemorrhagic rash, ecchymosis, and massive hemorrhage, bleeding gums is observed [45, 46, 56].

Cronkhite-Canada syndrome (L. Cronkhite, W. Canada) is a complex of congenital anomaly with autosomal dominant type of inheritance: it proceeds with diffuse cutaneous hyperpigmentation (hyperpigmentatio), atrophy of the nails, alopecia.

It is often combined with generalized intestinal polyposis, malabsorption syndrome and exudative enteropathy. A decrease of calcium, potassium and magnesium levels in blood often takes place [20, 26].

With the malabsorption of zinc imbibition, included in many enzymes, enteropathic acrodermatitis (acrodermatitis enteropathica), or Danbolt-Class (N. Danbolt, K. Class) syndrome develops. It's a systemic disease, which occurs mainly among babies. It's characterized by the appearance of erythematous lesions on the buttocks, in the perineum, inguinal areas, and around the mouth, nose and eyes, on the neck, hands and feet. In these erythematous foci bubbles appear, which are eventually transformed into the scaly plaques and erosion.

Periungual of nail-bone and nail bed with subsequent rejection of nails appears. Hair loss, onihopatii and photophobia are observed.

At the same time disrupts at the function of digestive tract appear. It is also characterized by a triad of clinical symptoms: mental disorder, growth retardation, anemia [34, 36].

Some authors have noted the connection between chronic diseases of the small intestine such as celiac disease (gluten enteropathy), occurring with maldigestion syndrome, and the syndrome of Duhring (L. Duhring), also called herpetiform dermatitis (dermatitis herpetiformis).

Duhring-Brock syndrome is characterized by the appearance of polymorphic itchy rash in the form of patchy erythema, papules, blisters, bubbles herpetiformis, grouped into rings, D-rings and garlands on the skin of the limbs and trunk (with the exception

of a face). There are also hereditary forms of Duhring syndrome with an autosomal dominant mode of inheritance and incomplete penetrance. In the blood eosinophilia is often defined.

In some cases of chronic diseases of small intestine with malabsorption syndrome acquired ichthyosis (ichthyosis acquisita) develops, the characteristic of which is dryness, stretching and scaling of the skin, widespread itching, especially after bathing. Patients' hair get thin, becoming dry. There happens atrophy and fragility of the nail plate, having diametric bands (Bo lines). Diffusive pigmentation appears on the skin, focal hyperemia and infiltration, flaking and itching that imitate chronic eczema and psoriasis.

Severe forms of malabsorption syndrome may be complicated by dystrophic (protein-free) edema and ascites [11, 18].

Crohn's disease (CD) can affect all parts of digestive tract, but most often terminal ileitis and granulomatous colitis develop.

Ulcerative colitis (UC) affects mainly the distal colon, but subtotal and even total loss of the entire colon happens.

The most typical skin lesions during CD and UC are erythema nodosum, gangrenous pyoderma, and Sweet's syndrome, veziculopustulezny exanthema, necrotizing cutaneous vasculitis, bullosa epidermolysis, etc.

Ganglionated erythema (erythema nodosum) is characterized by the appearance of the red color, slightly lifted up above the level of the skin, hot for the touch. During exacerbation of the process, the formation of adipositis (panniculitis) is possible. It's an inflammation of the fibrous subcutaneous tissue.

Under the gangrenous pyoderma (pyodermia gangraenosa) the appearance of purulent pustules on the skin of the lower limbs and other body parts is understood, which then transforms into neurotic festering ulcer with a red rim. At its core granulomatous vasculitis is believed to be.

Sweet's syndrome (R. Sweet) is a neutrophilic dermatosis with an appearance of painful erythematous plaques or assemblies on different parts of the body; it proceeds with fever and neutrophilic leukocytosis [40, 61, 62].

Nodular panarteriit (panarteriitis nodosa) is symmetrical and bilateral lesion of the skin of both lower extremities in the form of numerous undercutaneous nodules with a diameter of 2 cm with the obliteration of the skin vessels and a tendency to ulceration.

Blebby pidermolysis (epidermolysis bullosa) occurs with the formation of bubbles on the elbows, knees, hands and subepithelial deposition of immune globulin G.

Lower necrotizing vasculitis (vasculitis necrotica) is characterized by the appearance of peliosis (purpura), nodules, plaques and ulcers on the skin of the extremities (especially on fingers), prone to necrosis.

During the vesicles pustular exanthema (exanthema vesiculopustularis) pustular lesions and inflammatory infiltrates appear in different parts of the skin and around the vessels (perivascular).

Multicentric skin lesions proceeds with the formation of dense painless erythematous plaques up to 10 cm in diameter, with ulceration in the center. Histologically they are noncaseating granuloma localized in the folds of the skin, on the earflap and under the breasts.

Patients with CD and UC have erythematous plaques, aphthae and ulcers, as well as hyperplastic changes in the relief of the mucous membrane in the form of a cobblestone street, and histological studies reveal granulomas in places of skin changes on the face and in the mouth, the mucous membrane of the cheeks and gums. During the UC erythema nodosum is often revealed, vesicle pustulant exanthema, and during BC there appears gangrenous pyoderma, nodular panarteriit, bullous epidermal, changes in the oral cavity. The rest of the above described skin lesions occur both in UC and in CD [1, 48, 49].

The literature contains descriptions of skin changes, allowing suspecting neoplastic process in the stomach and intestine. In the late 50-ies of the twentieth century N. Kurt proposed criteria for determining the existence of the relationship between skin changes and malignant tumors, which are known as Kurt postulates: simultaneous beginning of skin changes and tumor development or skin changes soon after its beginning; parallel malignant and skin changes, the presence of a specific type and

location of the malignant process, combined with specific skin changes; statistically confirmed correlation between the incidence of malignant neoformation with certain skin changes, the presence of a genetic association between tumor process, and skin changes.

Acanthosis nigricans (AN) is characterized by the appearance on the neck, armpits, on the folds of the body, on the dorsum of the hands and in the groin, gray-black papillomatous, hyperkeratotic and warty formations, as if sprinkled with coal dust.

Benign (more often) and malignant (less) forms of AN are distinguished. The latest is characterized by an acute onset, severe disease with involvement of the palms skin and mucous membranes into the process. In these cases, the AN can be combined with cancer of the gastrointestinal tract, especially with gastric carcinoma (60% of cases). [59]

Peutz-Jeghers-Touraine syndrome (J. Peutz, H. Jeghers, F. Toraine) is a hereditary disease transmitted in an autosomal dominant manner. It appears in early childhood, with the presence of bluish-brown spots on the lips, dorsum of the hands, soles of the feet, face, and on the mucous membranes of the mouth and nose. During the life (typically 35 years), 90% of them develop polyps in the small intestine, and among 50% intussusception is observed.

An increased risk of cancers of the gastrointestinal tract is observed [24, 25, 47].

Gardner's syndrome (E. Gardner) is a hereditary mesenchymal dysplasia with an autosomal dominant mode of inheritance. It appears at 10 years of age. Proceeds with polyposis of the colon, osteoma of the skull bones and the skin lesions. On the skin numerous sebaceous cysts, fibroids and dermoid cysts are revealed. Affection of skull bones (maxillary, frontal, zygomatic, parietal) gives a person a special outline ("lion's head"). An increased risk of colon cancer is noted [26].

Torre syndrome (D. Torre) is characterized by the appearance of skin tumors such as adenomas fat, epithelium, as well as keratoacanthomas (keratoacanthoma); they are benign epidermal tumors of hair follicles in the form of spherical assemblies with crater-like depression filled with horny epithelium. It indicates at an increased risk of poorly differentiated colon cancer [21, 38, 39, 40, 47, 53].

The carcinoid syndrome (neuroendocrine tumor process) affects different areas of the gastrointestinal tract (30% of them are malignant), and is characterized by paroxysmal flushing with a sudden reddening of the face, the neck, the body, called flesh symptoms [16, 22, 27, 30].

Skin changes during the diseases of the hepatobiliary system

The most frequent change of skin diseases of the liver and extrahepatic biliary tract is jaundice (icterus).

There are liver (hepatocellular), obstructive (mechanical) and cholestatic (entri- and extrahepatic) jaundice. The icteric staining of the skin and visible mucous membranes start when bilirubinemia is more than 35 pmol/L, and severe jaundice, hyperbilirubinemia are observed at 120 mmol/l or more.

There is also a group of non-hepatic jaundice (hemolytic, functional, etc.) that need differential diagnosis with liver jaundice.

On the basis of hepatic jaundice lies a violation of the bilirubin exchange with the accumulation of the blood in the liver, organs and tissues, including skin, bile pigments (bilirubin, etc.) [3, 19, 29, 31].

Hepatic jaundice has usually olive-yellow color, mechanical has green and yellow, and hemolytic – lemon-yellow. The initial symptoms of jaundice (subictericness) usually reveal the sclera and the soft palate. Inspection of the skin and visible mucous membranes should be made mandatory in the daylight.

During the hepatic jaundice in the blood not only connected, but also unconjugated bilirubin appears, with mechanical – only associated, as in cholestatic jaundice, and hemolytic – only unconjugated bilirubin. During the liver and cholestatic jaundice the faeces are gipoholichen, during mechanical it is aholichen, and during the hemolytic – hyperholic. During the hyperbilirubinemia due to conjuncted bilirubin bilirubinuria is observed (urine becomes of a vivid yellow color) [3, 19].

Liver (hepatocellular) jaundice is observed during the acute and chronic hepatitis, cirrhosis of the liver of virus, alcohol, drug and autoimmun origin; with idiopathic hemochromatosis, with cholestatic liver disease (primary biliary cirrhosis, primary sclerosing cholangitis, cholestasis of pregnancy), and congenital cholestatic diseases

(progressive familial intrahepatic cholestasis or Bayler disease, benign recurrent intrahepatic familial cholestasis, Aaganes-Sammerskill syndrome) with an autosomal recessive mode of inheritance.

Jaundice occurs with hereditary and pigment gepatoz (functional hyperbilirubinemia), occurring with the accumulation of a conjugated bilirubin (Dubin-Johnson syndrome, Rotor) and unconjugated (Gilbert syndrome, Meylengraht, Nayarit Crigler I and II type and Lucy-Driscoll) in the blood [3, 19, 28, 29, 31].

Obstructive jaundice is caused by a mechanical barrier of bile flow occurs during the liver cancer, pancreatic head cancer, cancer of a large duodenal papilla, papillitis and papillostenoze, stricture of the common bile duct and the infringement of gall stones in it, as well as impacted gallstones in the ampul of large duodenal papilla.

Jaundice is often associated with skin itch (pruritus), the development of which has traditionally been associated with the accumulation of toxic bile acids in the blood. In the recent years, however, the leading role in the appearance of the skin itch has been assigned to abnormalities in neurotransmission system flowing with the changes in the central nervous structures in serotonin signaling system with the accumulation of endogenous pruritogennoy substances in the blood, the nature of which has not yet been established. Itchy skin may precede or accompany jaundice.

A painful itchy skin is the reason for the scratches (excoriationes), which have the form of linear defects on the skin, caused by damage to its integrity.

Characteristic hepatic signs are teangiectasis (teleangiectasia) – vascular "stars", "spiders", which are stellate angioma (vesicular/arterial spider) ranging in size from 1 mm to 1-2 cm in the central part of the pulse and the radial (arachnids) branching vessels. They are most of all localized on the face, neck, shoulders, chest, arms, and in the mouth. When pressed telangiectasia disappear, and after the cessation of pressure they appear again.

During the diffuse chronic liver diseases that occur with cholestasis palmar (palm) erythema (erythema palmaris) appears on the palmar surface of the hands. It's a symmetrical spotty redness of the palms, mainly in the thenar and hypothenar.

Often during chronic cholestatic liver diseases xanthomas (xanthoma) and xanthelasmas (xannthelasma) are detected on the skin in the form of flat or slightly raised above the skin yellowish patches with clear boundaries, which contain deposits of cholesterol and triglycerides, and are usually localized on the skin of eyelids, ear shells, elbows, buttocks.

A frequent companion of chronic hepatitis and liver cirrhosis are manifestations of high angiostaxis (hemorrhagia, purpura) in the form of petechial purpura, ecchymosis and extensive underskin hemorrhages.

For their appearance deficiency of clotting factor synthesized in the liver (prothrombin, proaktselerin, kappa factor, etc.) are to blame, as well as thrombocytopenia due to hypersplenism [3, 19].

In end-stage cirrhosis of the liver (viral, alcohol, etc.) male patients have signs of appearing feminism (feminismus): breast enlargement (gynecomastia), female type of pilosis (disappearance of "hair Tracks" on the belly, female type of hair growth in the pubic area), atrophy of the testes. These changes are associated with an excess of estrogen and serotoiin. Simultaneously with cirrhosis of the liver (especially biliary) clubbing of the fingers (drumsticks) and deformation of nail plates (hour glass) appear, and the nails become almost white.

Patients with decompensated cirrhosis of the liver have free liquid in the abdominal cavity: ascites (ascites) and subcutaneous edema (oedema) are formed due to portal hypertension, hypoproteinemia and increased vascular permeability.

At this time first belly takes the shape of a frog's one with flattening of the sides of its sections (on the spine), and then becomes rounded, tense with a protruding belly button (at the expense of increased intra-abdominal pressure and umbilical hernia). On the skin of the abdomen there appears an expanded network of subcutaneous veins in the form of Medusa's head (caput Medusae) with a branched-venous network around the navel, like rays diverging into the sides (Medusa is a mythical monster, on whose head snakes twist instead of hair). The cause of the appearance of saphenous veins network on the abdominal wall is portal hypertension, developed due to the

blockade of the intrahepatic branches of portal vein and venous collaterals formation [3, 4, 19].

Sometimes, during liver cirrhosis with ascites development in the skin of the abdomen and the strip tension as whitish lines on the sides of the abdominal wall. In addition, during chronic hepatitis and cirrhosis of the liver we can observe trophic changes in the skin, looking like banknotes, and in the corners of the mouth cracks and sores appear.

Idiopathic hemochromatosis skin gets bronzed due to the increased iron absorption in the intestine and depositing it into the liver and other internal organs, as well as into the skin. The disease is based on the hereditary enzyme defect, passed in an autosomal recessive manner.

Later the patients have cirrhosis of the liver and insulin-dependent diabetes mellitus. The skin is pigmented, especially on the legs, neck, face, in the genital area (melasma). Scant pilosis is noticed. Hemosiderosis and fibrosis appear in the liver, and deposition of hemosiderin is revealed on the skin [3, 19].

Chronic hepatic porphyria (porphiria hepatica), or late cutaneous porphyria (porphiria cutanea tarda), occurs in two forms: family and acquired (both with autosomal dominant inheritance). Proceeds with erythematous and bullous rash on exposed areas of the body (face, neck, upper chest, etc.). The color of the rash varies from earthy-gray to reddish-bluish and bronze.

It is typical to have blisters on the face and on the dorsum of the hands the size from a millet seed to a pea, which leave atrophic pigmentation and dark red spots. Hypertrichosis is observed on the face, temples, cheeks, nose and ears, as well as increased sensitivity to light, due to the accumulation of porphyrin in the skin. At the basis of hepatic porphyria lies a violation of porphyrin synthesis of bone marrow erythroblasts. The liver is enlarged. The urine has an increased uroporphyrin content [19].

Skin changes during pancreatic diseases

At various times induring acute and chronic pancreatitis (CP) there have been various changes of skin described, considered informative in recognition of these diseases.

During the acute pancreatitis limited areas of cyanosis can sometimes appear on the sides of the abdominal wall (a symptom of Grey-Turner, H. Grey, G. Turner); some areas of cyanosis appear on facial skin (symptom Lagerlof, N. Lagerlöf). In some cases in the subcutaneous pacefollower snow-white or yellowish foci of necrosis in the epigastric region appear due to infiltration of pancreatic lipase beyond the pancreas and enzyme digestion of adipose tissue (Balser's symptom; W. Balser). The appearance of ecchymosis in the circle navel due to local toxic damage of blood vessels has been described (a symptom of Grunwald, M. Grünwald), or the appearance of bluish-pinkish blotchy rash morbilliform, called reticulate livedo (livedo reticulosa), localized on the skin of the abdomen and upper thighs, and sometimes it is combined with urticaria [4, 5, 14, 23, 28, 33, 37, 44]

During an acute pancreatitis and/or exacerbation of CP some patients have knotty cellulitis on the skin (panniculitis nodularis) – an inflammation of the fibrous fatty tissue, occurring with the formation of restricted sites on the front legs and (rarely) on the trunk. These are small, superficially located knots of bluish-pink color. After their discussion skin produces small recess with light pigmentation.

In some cases cyanotic areas of skin appear on the anterior abdominal wall (a symptom of Holsted; W. Holsted), as well as hemorrhagic petechial rash and ecchymosis in the circumference of the navel and on the buttocks (Devis' symptom; N. Devis) [44].

Our native therapist S. A. Tuzhilin has found bright red, roundish clearly delimited spots on the abdominal wall, chest, back among patients with CP, calling them a symptom of red droplets or cranberry stains. The author saw them as small vascular aneurysms, but for some reason they do not disappear under pressure [5, 7, 23]. Their specificity for CP is questionable.

In addition, light brownish pigmentation (symptom Bartelheimer; N. Bartelheimer) has been described and atrophy of the subcutaneous fat in the projection to the anterior abdominal wall (Grott symptom; J. Grott) [6, 7].

During a severe CP Edelman syndrome (A. Edelmann) appears, including apart from skin lesions, neurological and mental disorders.

Patients have thinning and atrophic changes in the skin, which is going gray, pigmented with the development of a follicular hyperkeratosis (hyperkeratosis follicularis), localized in the hair follicles funnels. In addition, cachexia, polyneuritis, vestibular and mental disorders are marked [6, 33].

Tropical CP, or kwashiorkor, develops among the children in the tropical Africa during the chronic protein deficiency.

The disease occurs with an atrophy of muscle tissue, increasing diffuse depigmentation of the skin (African children), erythema with pale dusky purple spots and papules (kwashiorkor in the African language of Ghana means "Red Boy"). The skin is dry with mosaic patterns and signs of epithelial desquamation, cracks and erosion. There is an alternation of pigmented and depigmented areas (a symptom of the flag) in the hair [5, 14, 23, 28, 33, 55].

During the cancer of the pancreas migratory thrombophlebitis (trombophlebitis migrans) develops due to hypercoagulable state and thrombosis of superficial veins of the extremities (Trousseau's sign; A. Trousseau). In this case, the trunk and the limbs have painful linear bands along the surfactant veins. Anticoagulants are ineffective.

Glucagonomas syndrome develops in a form of neuroendocrine tumors of the pancreas, consisting of α-cells of the islets of Langerhans that produce the glucagon hormone. 68% of patients have necrotic migrating erythema (erythema necrolyticum migrans). In the 70-80% of the cases it's a malignant tumor, giving metastases to the liver, bones and lymph nodes. Pink spots, papules, swollen red plaques of a ring form with enlightenment in the center and a red rim; sometimes blisters and peels are formed, after which the skin has brown pigmentation. Their favourite localization is places of friction, pressure, skin folds, perineum, anus circumference and so on. The skin rash is accompanied by painful itching. Histologically skin lesions show a mononuclear infiltration and edema in the small circle of skin blood vessels with subsequent appearance of polypuklears.

Its characteristics are nekrolitic skin lesions with vacuolation and pyknosis, and in the appearance of crusts – parakeratosis. The whole cycle of skin changes lasts 7-10 days.

In addition, patients show glossitis, angular cheilitis, stomatitis, dystrophic nail changes (onycholysis). Cutaneous changes during glucagonomas, as believed, are due to a hypothetical tumor of dermatotoxic substances [6, 7, 8, 12, 30, 42, 60].

It should also be mentioned of such symptoms as black jaundice (melas icterus), developing along with cancer of the pancreas as a result of long-term progressive mechanical jaundice, skin gradually becomes dark green, almost black color and is combined with cachexia.

In connection with this symptom it is appropriate to recall the historical fact described in the medical literature. In the middle of the XIX century a famous Moscow professor A.I. Over (a russified French, a disciple of M. Y. Mudrov) was invited to Kharkiv for advice. When visiting the University Hospital, he stopped at the bedside of a dying patient with an unknown diagnosis, carefully looked at him and said (in Latin): «Hic pancreas laborat!» ("It's pancreas!"), And then left the room. During an autopsy, the patient had a pancreatic head cancer diagnosed. The diagnosis was made during the inspection on the basis of "black" jaundice and cachexia symptom [4].

These are the brief diagnostics of various diseases of the gastrointestinal tract, hepatobiliary system, and pancreas, based on the skin inspection.