Volgograd state medical university

Department of pathological anatomy

Lecture

Stress. Shock. Crush syndrome. Collapse. Coma. Hypervitaminosis. Hypovitaminosis.

Stress

- it is a non-specific complex of psycho-physiological reactions of organism as a response to the life-threatening factors

Stress

- In process of research of stress on the animals (white rats) Selye came to the conclusion that stress passed through three stages.

- **The first stage** was called him as **alarm reaction**, and it usually lasted for 24 - 48 hours.

- At this stage all reserved defensive possibilities of an organism usually become mobilized to struggle against a pathogen

Stress

- **The second step** named **the phase of resistance** when due to the long-standing compensatory mechanisms, very steady, an organism becomes adapted to stress and copes with the pathogen for enough a long time.

- In this case we say about a favourable course of stress

Stress

- **The third stage** named **the exhausting and its name can explain everything**.

- The conversion of resistance stage into exhausting one is associated with an insufficiency of adaptive mechanisms to oppose a pathogen and destructive processes in the organism, provoked by stressor.
- The stage is very danger and may lead to a death.

Stress

The triad described by Selye consists of:

1) hypertrophy of the adrenal cortex
2) thymic gland and lymph nodes involution
3) in 30%-40% of cases there were the ulcerative processes in the gastrointestinal tract.

Stress: changes of the adrenal cortex

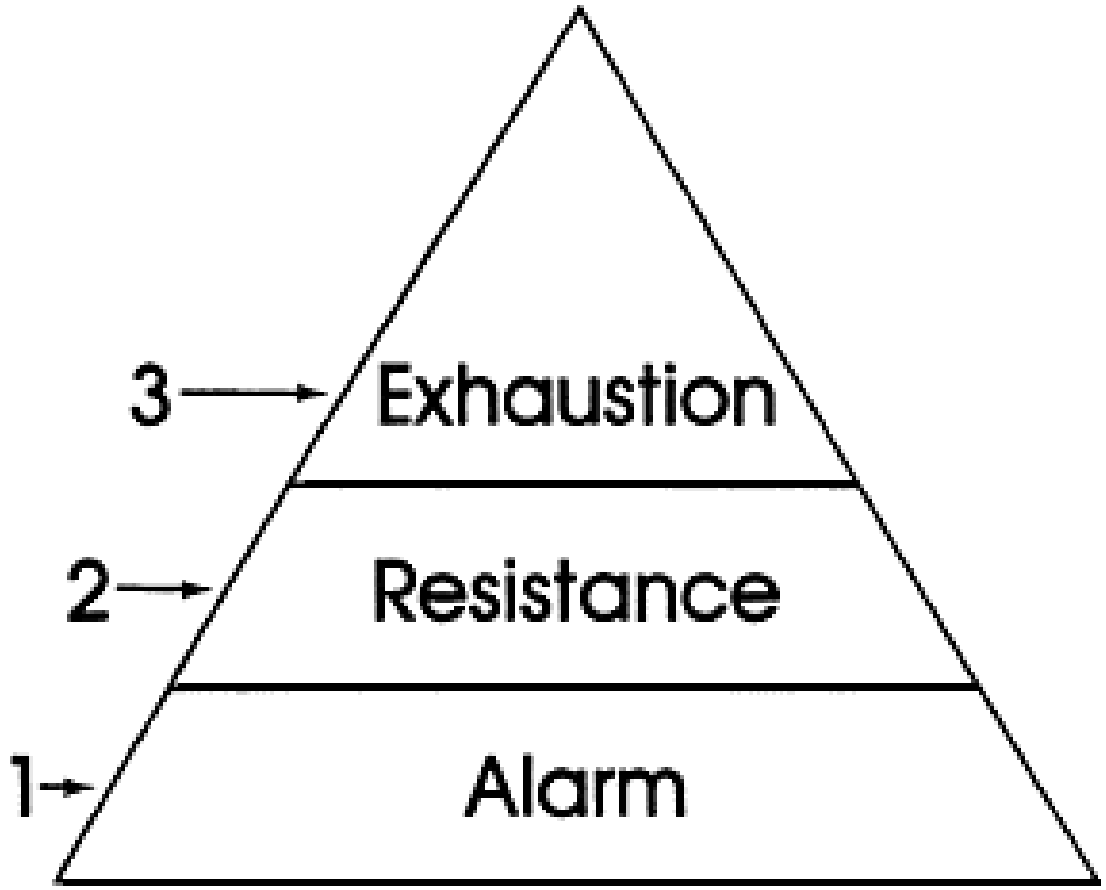
- **At the first stage** adrenal cortex was very rich of the secretion granules with their high activity, accompanied by an excessive cortisol production.

- **At the second stage** there was a very steady hypertrophy and hyperplasia of the adrenal cortex, those were provided by the lot of mitosis in this area, naturally, with increased cortisol secretion.

- **at the third stage** an adrenal cortex became very thin and exhausted of secretion granules.

- **Clinically** it sounds that stress seems to be is one of the reasons of an acute adrenal insufficiency.

STAGES OF STRESS



General adaptation syndrome (GAS)

- The term GAS introduced by Selye minds a non-specific reaction of whole organism to the stress situation.

- it as a part of an acute phase response, however, GAS seems to be the only the part of an acute phase response when hypothalamo-pituitary-adrenal glands system plays a pivotal role.

- There is no doubtful, that Selye didn’t study precisely the behavior of immune and hematopoietic systems during the GAS, but hypothalamo-pituitaty-adrenal axis activation precisely was in his field of view.

General adaptation syndrome (GAS)

1. Stressors activate different receptors of an organism: exteroreceptors – nociceptors which are found in the skin, mucosal lines, interoreceptors in the blood vessels wall, and sleeping nociceptors in the internal organs, moreover, analyzers, such as visual and hearing receptors

2. Next step is activation of monoaminergic neurons in CNS which control the peptidergic neurons of hypothalamus. It mast be added, that monoaminoergic mediators include such very important neurotransmitters as catecholamines, serotonin and GABA. They are responsible for a balance between releasing and statin- factors secreting by the hypothalamus

3. CRF, in turn, stimulates elaboration and secretion of ACTH by basophil cells of the pituitary gland The last event in described above chain is synthesizing and release of glucocorticoids by the adrenal cortex

Stress

Hypothalamo-pituitary-adrenal gland axis activation as a base of stress-reaction

Stressor influence the different receptors including analyzers

Activation of monoaminergic synapses in CNS

Hypothalamus activation and CRF secretion

Secretion of ACTH by pituitary gland

Increase of synthesis and production of glucocorticoids by adrenal cortex

Extreme states

1. Shock
2. Collapse.
3. Coma

Shock

Shock

- Definition – Shock is characterised by systemic hypo tension due to either reduced cardiac output or reduced effective circulating blood volume

- This leads to impaired tissue perfusion and cellular hypoxia

Types of shock depending on etiology

1. Cardiogenic shock
2. Hypovolemic shock
3. Septic shock
4. Neurogenic shock
5. Anaphylactic shock

Cardiogenic shock

- **Mechanism – Results from low cardiac output due to myocardial pump failure**

- **Causes**
  - **Myocardial damage (M.I)**
  - **Ventricular rupture**
  - **Arrhythmias**
  - **Cardiac tamponade (External compression)**
  - **Pulmonary embolism (outflow obstruction)**

Hypovolemic shock

- **Mechanism** – loss of blood or plasma volume leads to decreased cardiac output and reduced tissue perfusion

- **Causes** – massive hemorrhage or fluid loss from severe burns

Neurogenic shock

- **Mechanism** – result due to anesthetic accident or spinal cord injury which leads to loss of vascular tone and peripheral pooling of blood

- This leads to decreased cardiac return and cardiac out put leading to tissue hypoxia

Anaphylactic shock

- **Mechanism –** in this there is systemic vasodilatation and increased vascular permeability caused by an Ig E- mediated hypersensitivity reaction

- Acute widespread vasodilatation results in tissue hypoperfusion and hypoxia

Septic shock

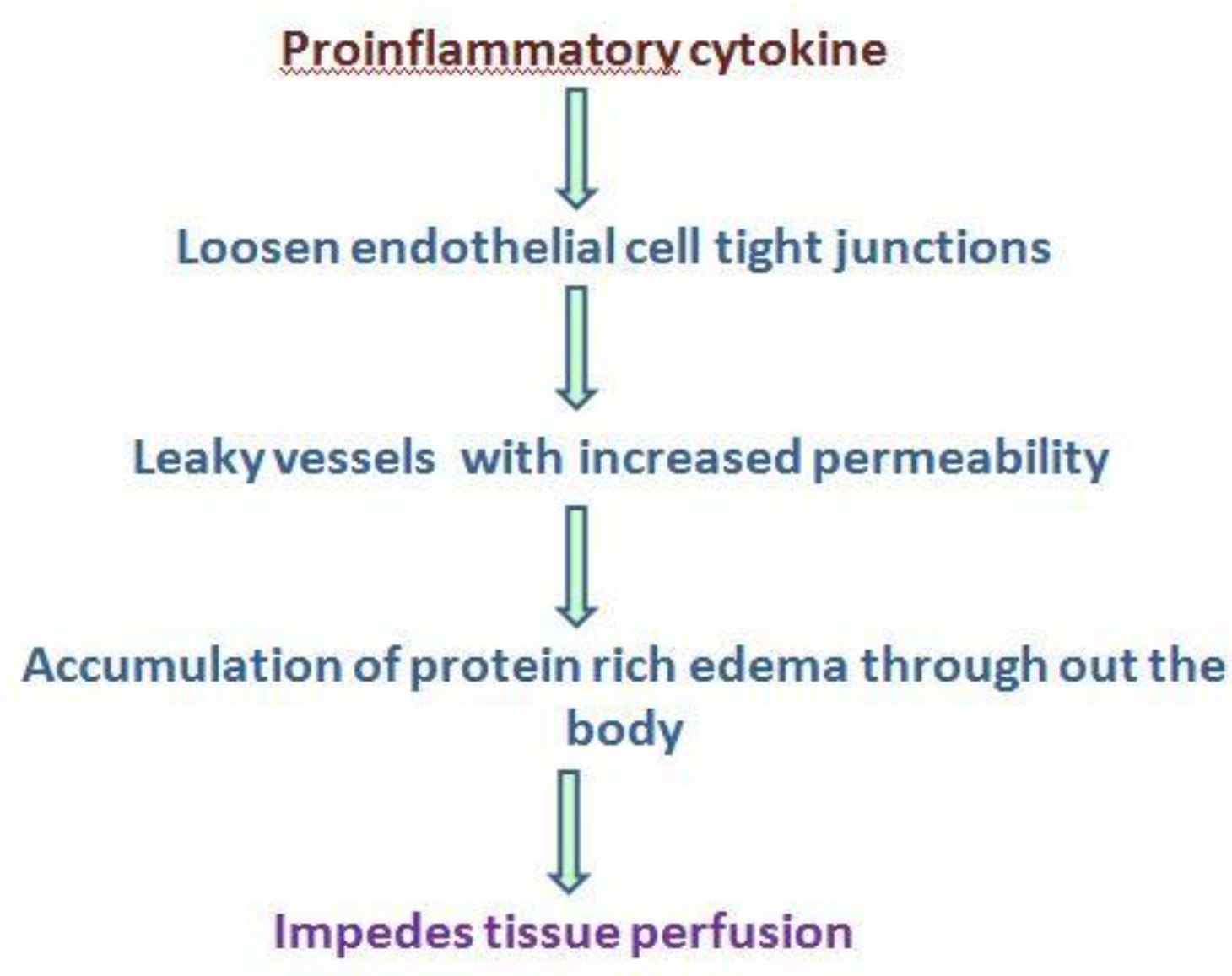
- **Definition –** Septic shock is defined as hypotension asoociated with severe sepsis and cannot be corrected by infusing fluids

- **Causes for Septic shock**
  - **Overwhelming microbial infections (bacteria and fungi)**
  - **Gram positive septicemia**
  - **Gram negative bacteria**
  - **Fungal sepsis**
  - **Rarely protozoa or Rickettsiae**

PATHOGENESIS OF SHOCK

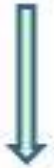
1. Inflammatory mediators
2. Endothelial activation and injury
3. Induction of procoagulant state
4. Metabolic abnormalities
5. Organ dysfunction
6. Immune suppression

PATHOGENESIS OF SEPTIC SHOCK

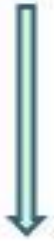


PATHOGENESIS OF SHOCK

Activated endothelial cells



Upregulate NO production and other vasoactive inflammatory mediators (C5a, C3a and PAF)



Vasomotor smooth muscle relaxation and systemic hypotension

PATHOGENESIS OF SEPTIC SHOCK

Vascular leak and tissue edema

↓

Decreased blood flow in small vessels

↓

Stasis of circulation and diminished washout of activated coagulation factors

↓

Deposition of fibrin rich thrombi in small vessel

↓

Hypoperfusion of tissue

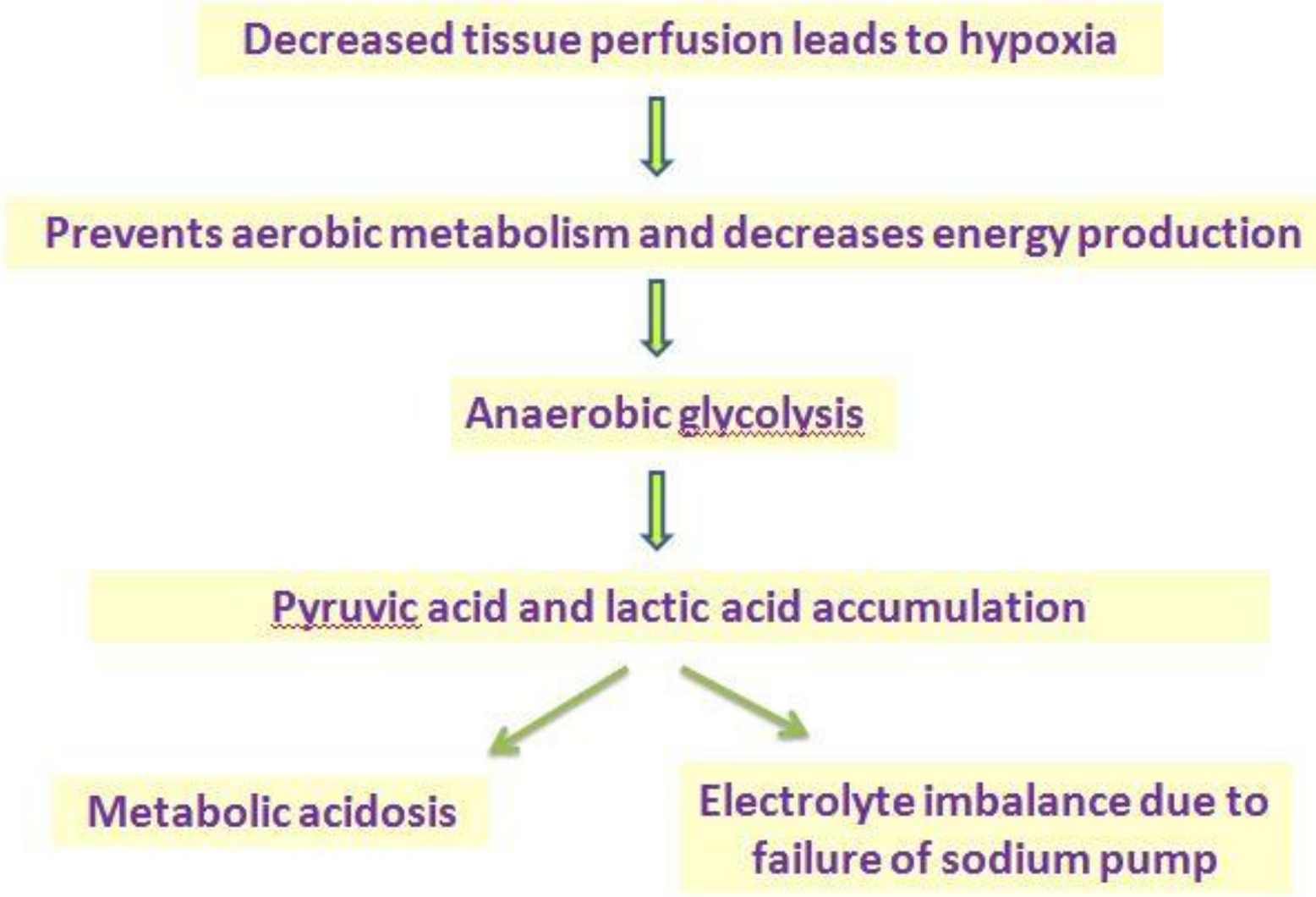
In DIC coagulation factors and platelets are consumed leading to concomitant bleeding and hemorrhage

PATHOGENESIS OF SHOCK

- All these factors leads to formation of thrombi leading to Disseminated intravascular coagulation (DIC) which causes ischemic damage in various organs.

- Later patient develops hemorrhage and bleeding due to the deficiency of platelets and coagulation factors

PATHOGENESIS OF SHOCK

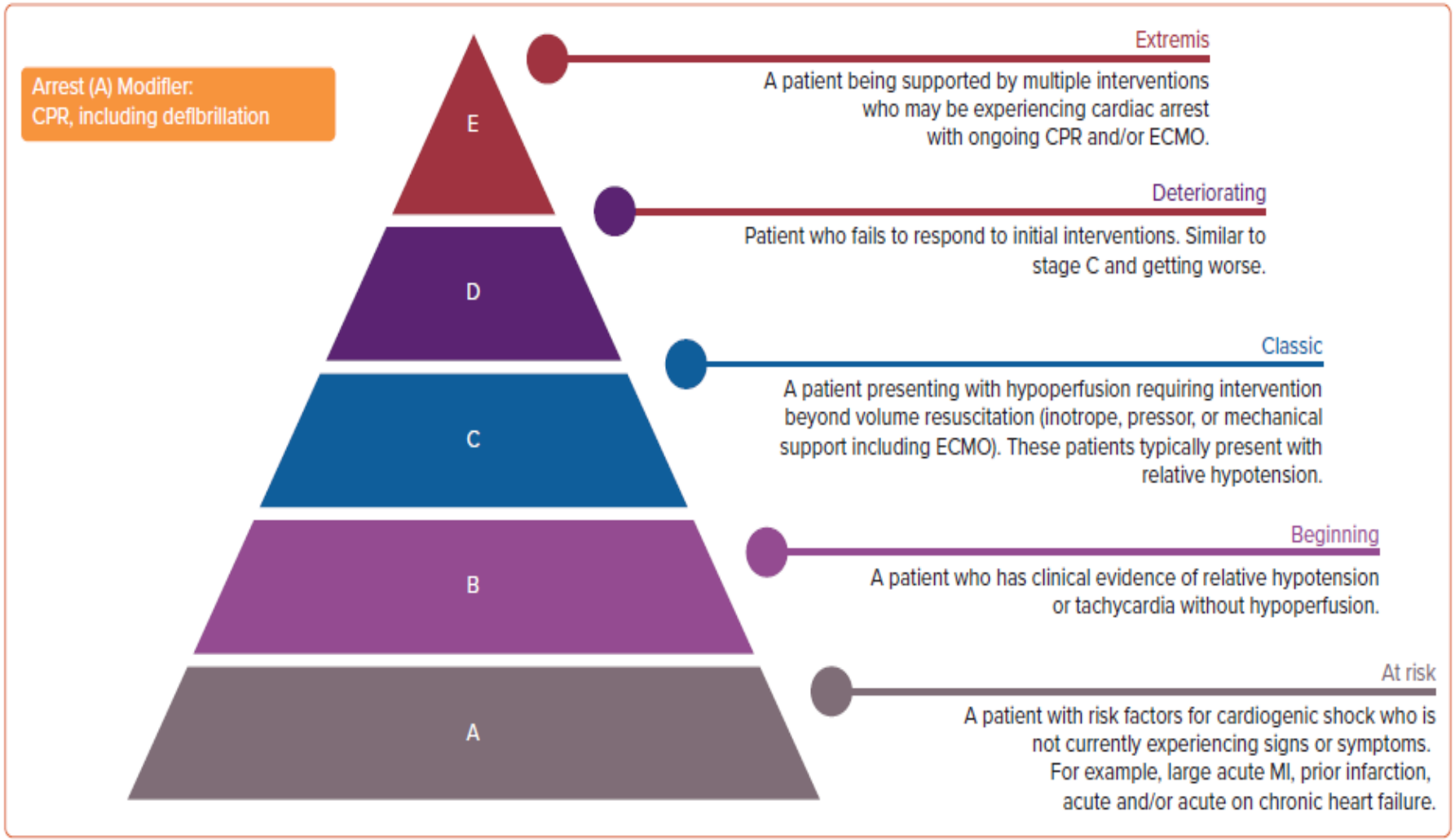


Stages of Shock

- **Initial stage -** tissues are under perfused, decreased CO, increased anaerobic metabolism, lactic acid is building
- **Compensatory stage -** Reversible. SNS activated by low CO, attempting to compensate for the decrease tissue perfusion.
- **Progressive stage -** Failing compensatory mechanisms: profound vasoconstriction from the SNS → ISCHEMIA
  Lactic acid production is high → metabolic acidosis
- **Irreversible or refractory stage -** Cellular necrosis and Multiple Organ Dysfunction Syndrome may occur →

DEATH IS IMMINENT!!!!

Figure 1: The SCAI Shock Pyramid and the Stages of Shock



CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; SCAI = Society for Cardiovascular Angiography and Interventions. Source: Baran et al.[19] Reproduced with permission from the Society for Cardiovascular Angiography and Interventions.

Organ dysfunction in shock

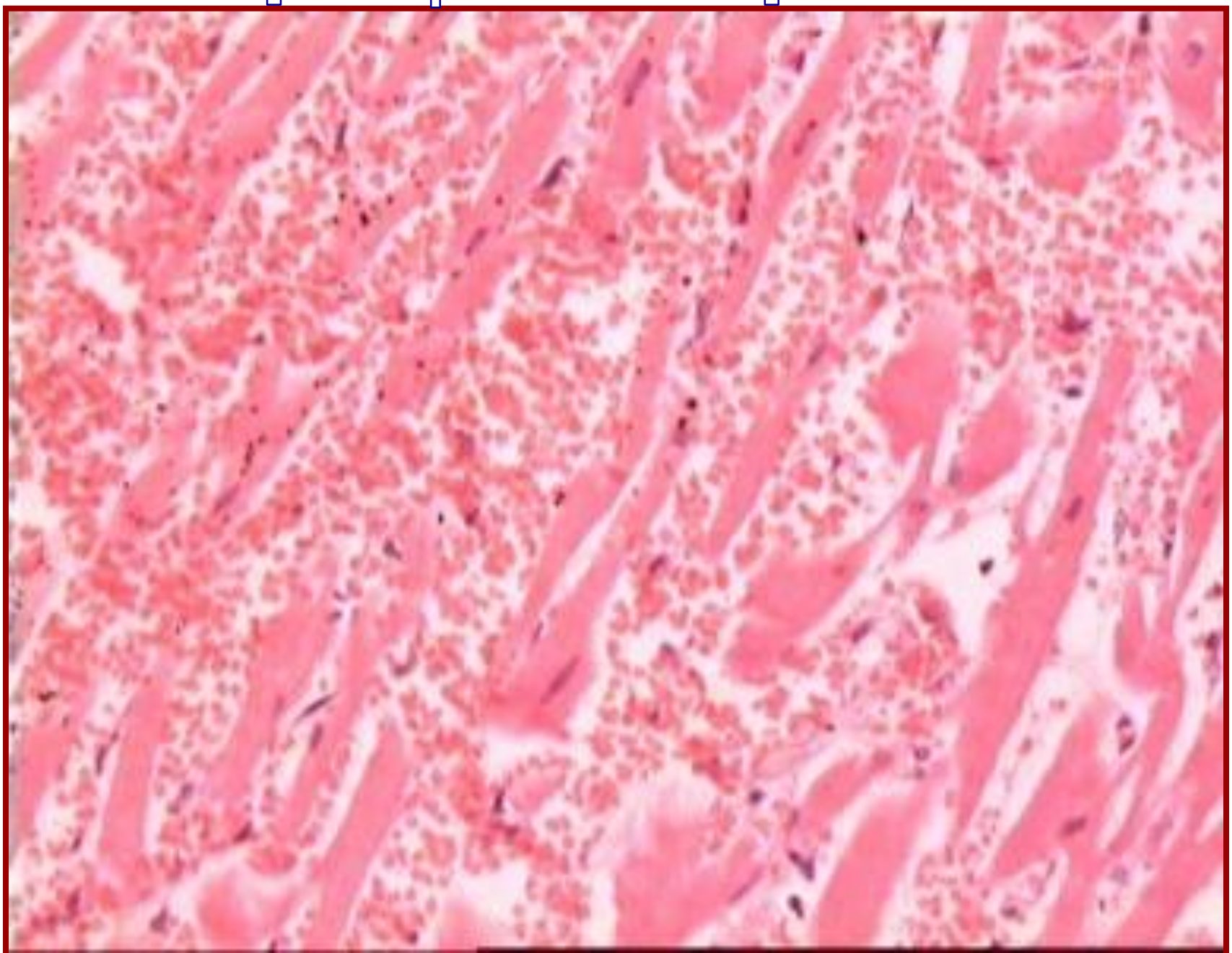
- Systemic hypotension, interstitial edema and small vessel thrombosis leads to decreased delivery of oxygen and nutrients to the tissues which produces alterations in cellular metabolism

- High levels of cytokines and secondary mediators diminish myocardial contractility, cardiac output, endothelial injury and increased vascular permeability

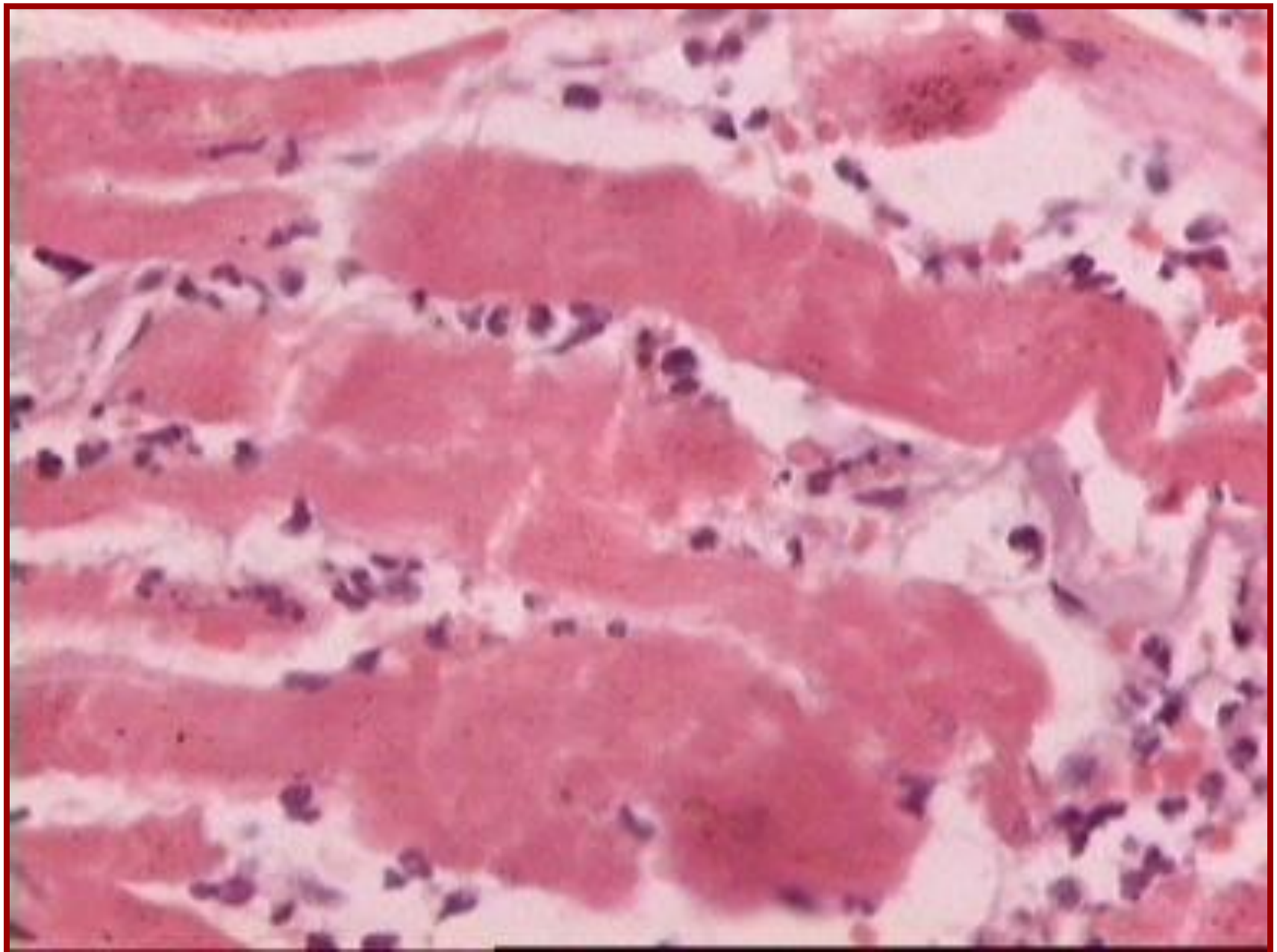
Morphology of shock

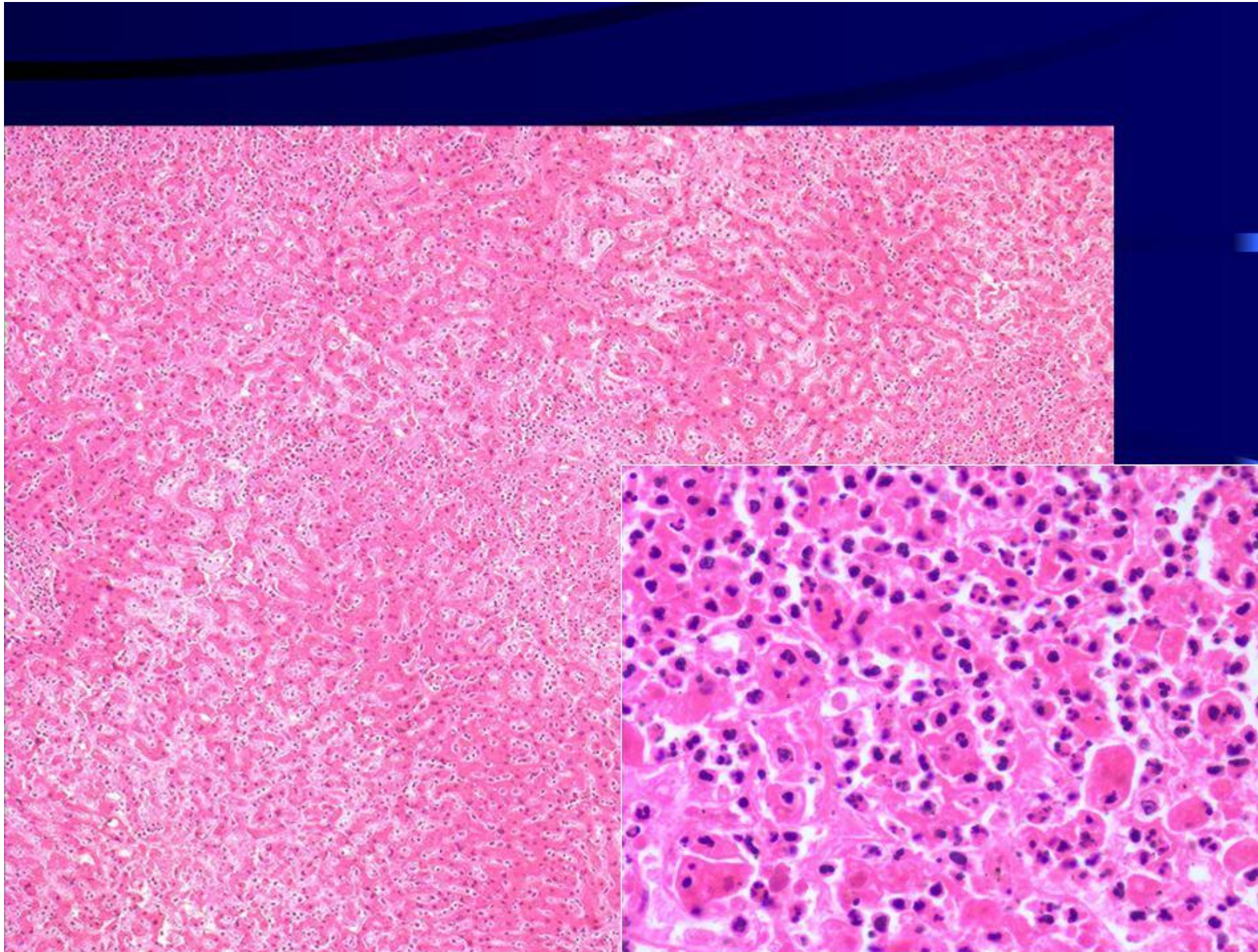
- **Changes manifest mainly in brain, heart, lungs, kidney, adrenals and GIT**
- **Adrenals – there is cortical cell lipid depletion reflecting relatively inactive vacuolated cells to metabolically active cells that utilize stored lipids for the synthesis of steroids**
- **Heart – due to hypoxia and fall in cardiac output – myocardial infarction**
- **Brain – cerebral ischemia develops leading to altered state of consciousness**
- **Liver – congestion and centrilobular necrosis**
- **GIT –erosions of gastric mucosa and Diffuse ischemic necrosis of intestine**

Интерстициальные кровоизлияния

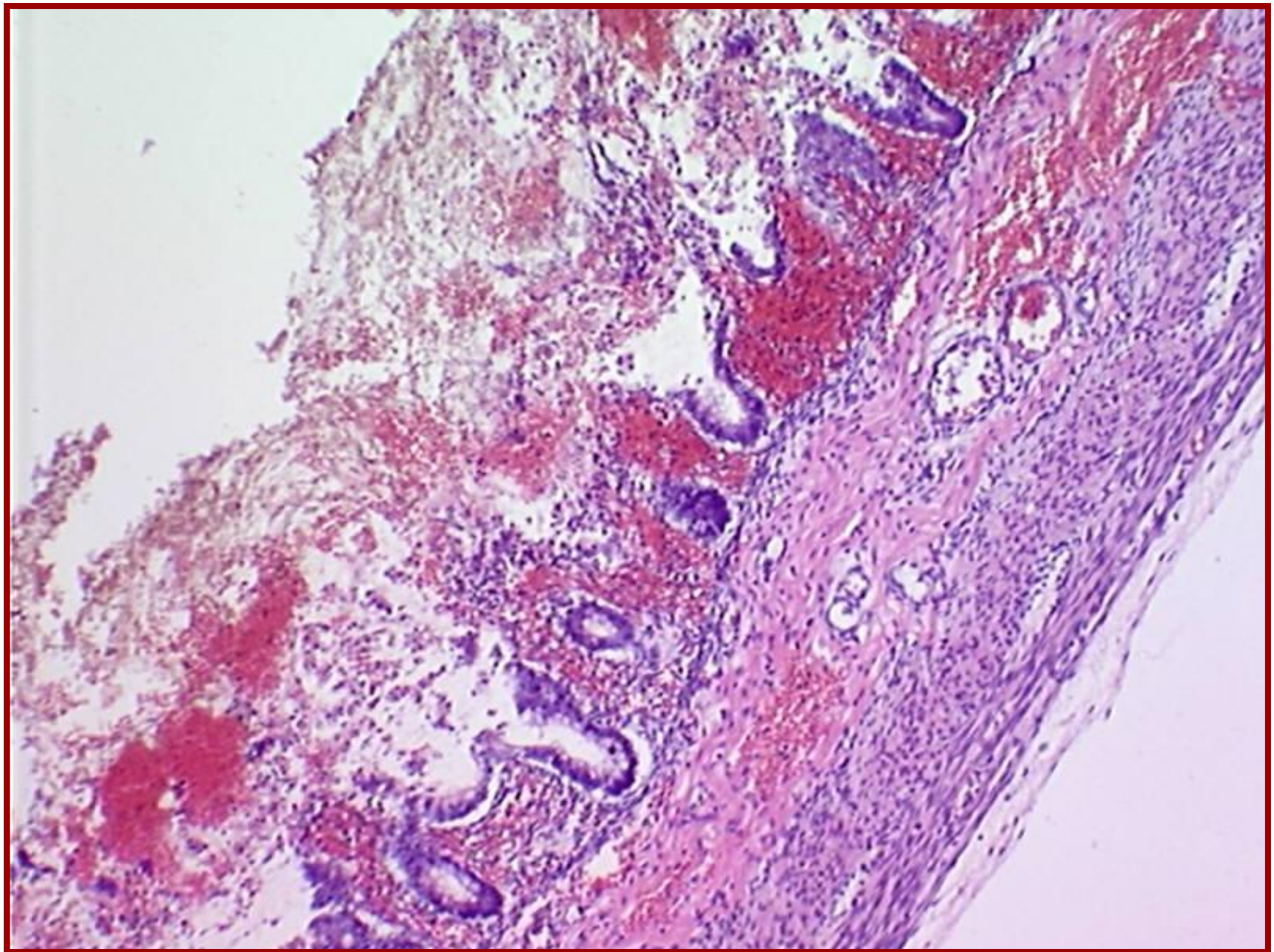


Дистрофия кардиомиоцитов, некроз





Некротизирующий энтероколит



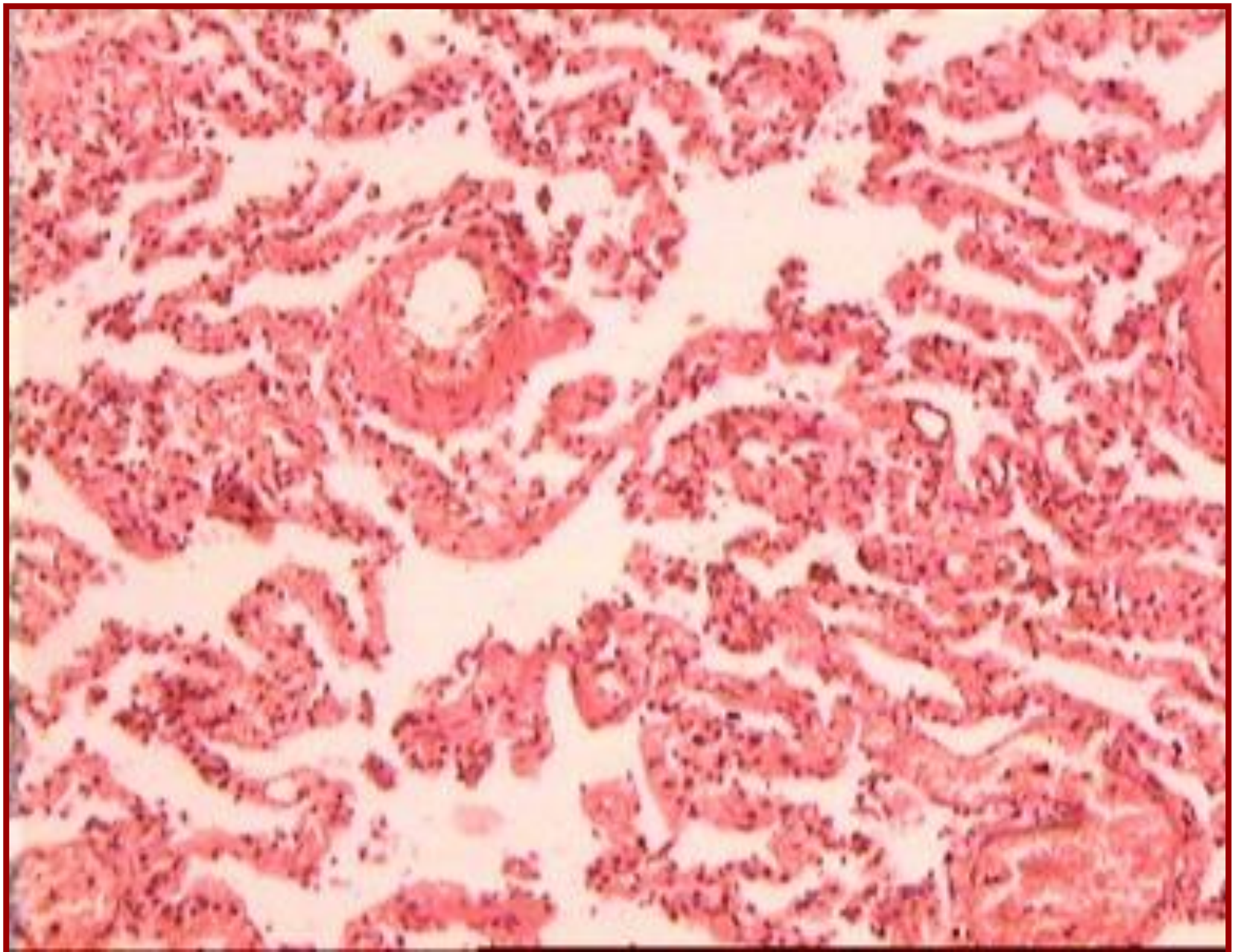
Morphology of shock

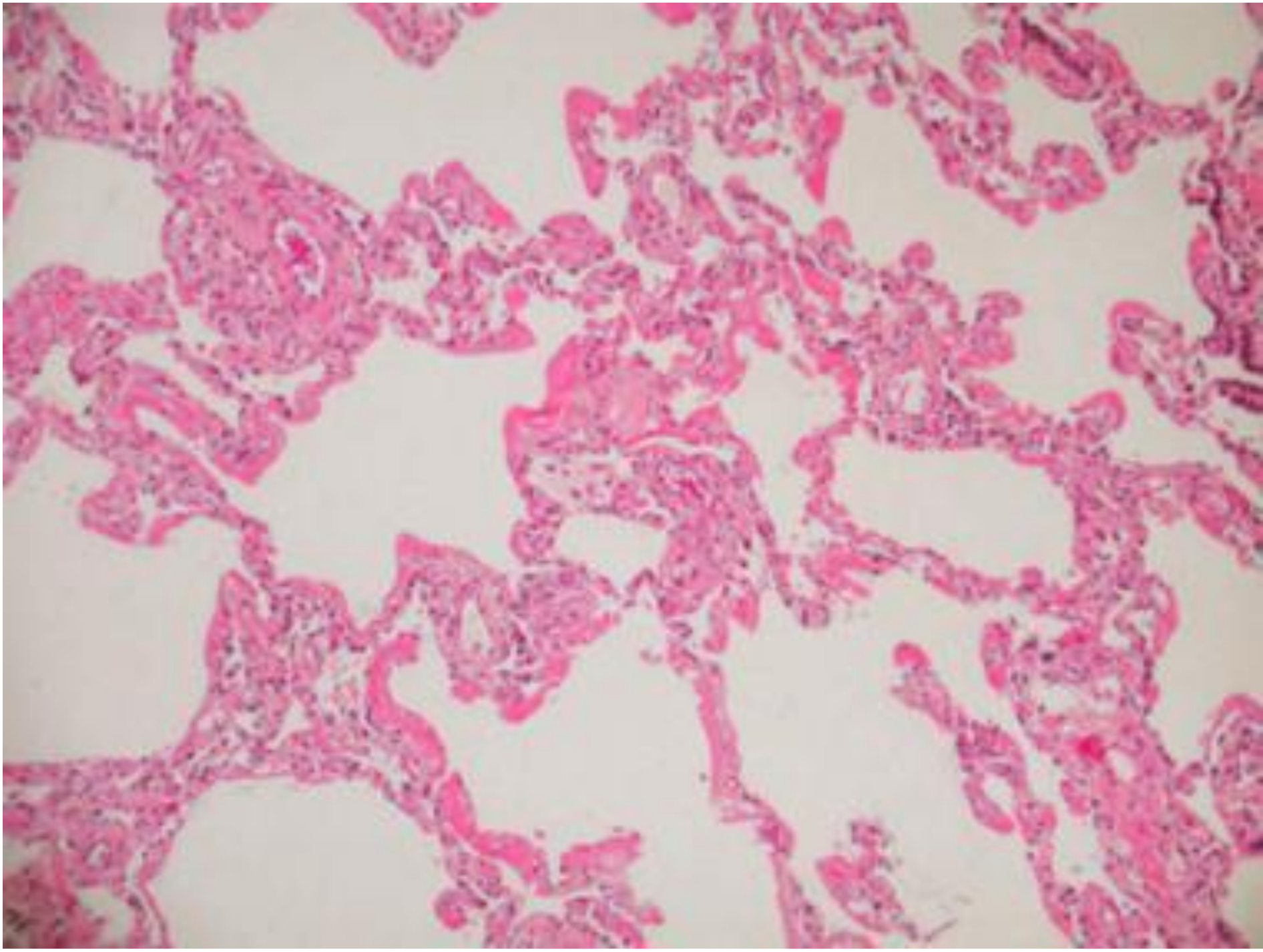
- **Lungs**

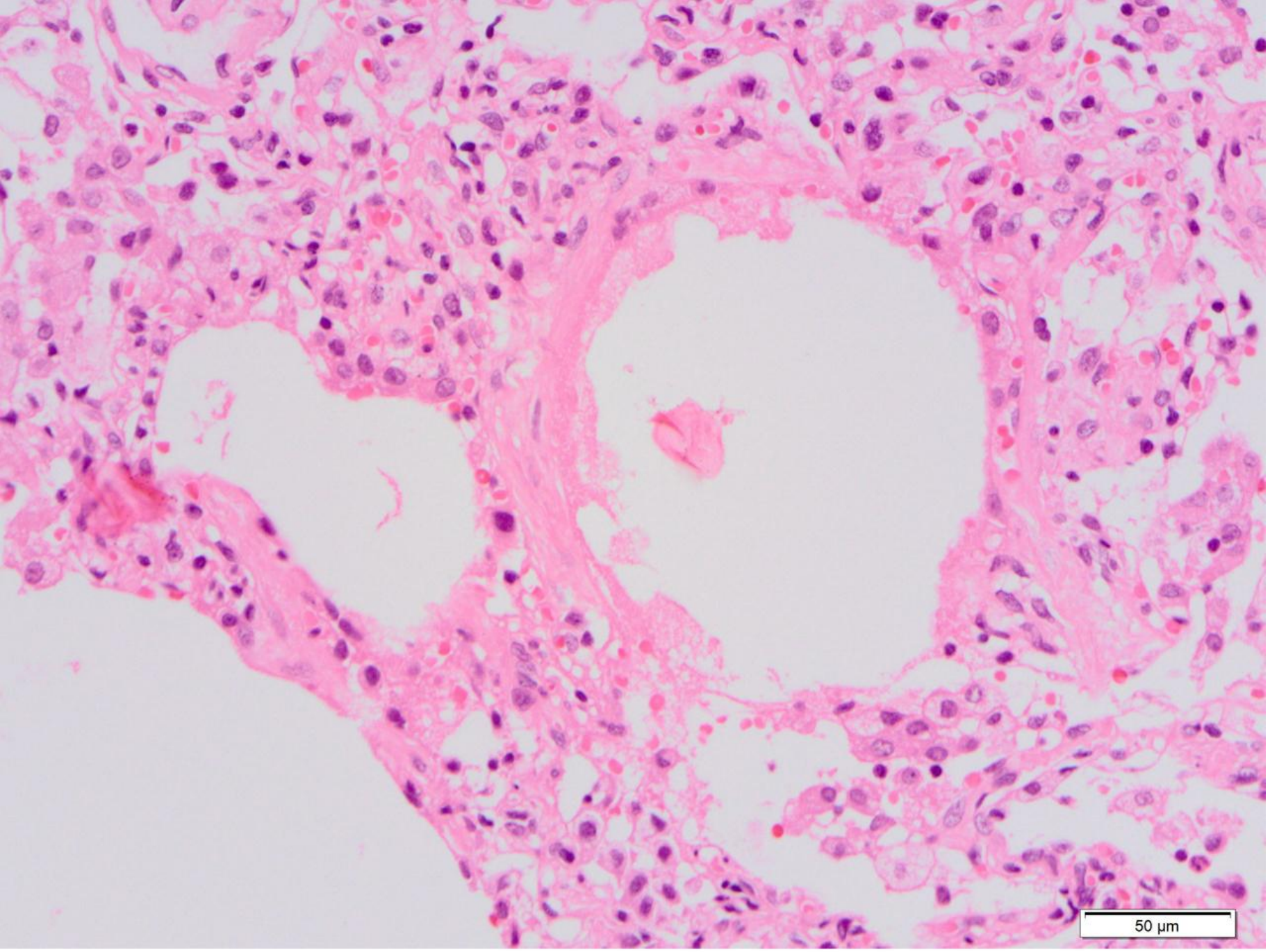
- congestion and edema develops leading later to formation of hyaline membrane and alveolar collapse.

- If patient survives organization and fibrosis occurs leading to emphysema and bronchiectasis

Дисателектазы и ателектазы

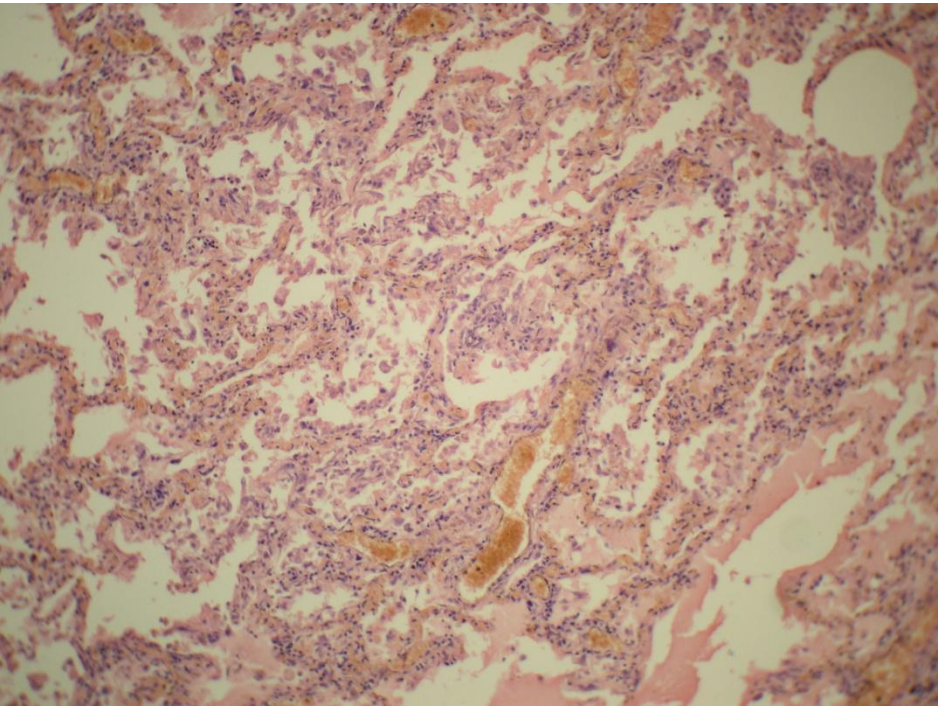


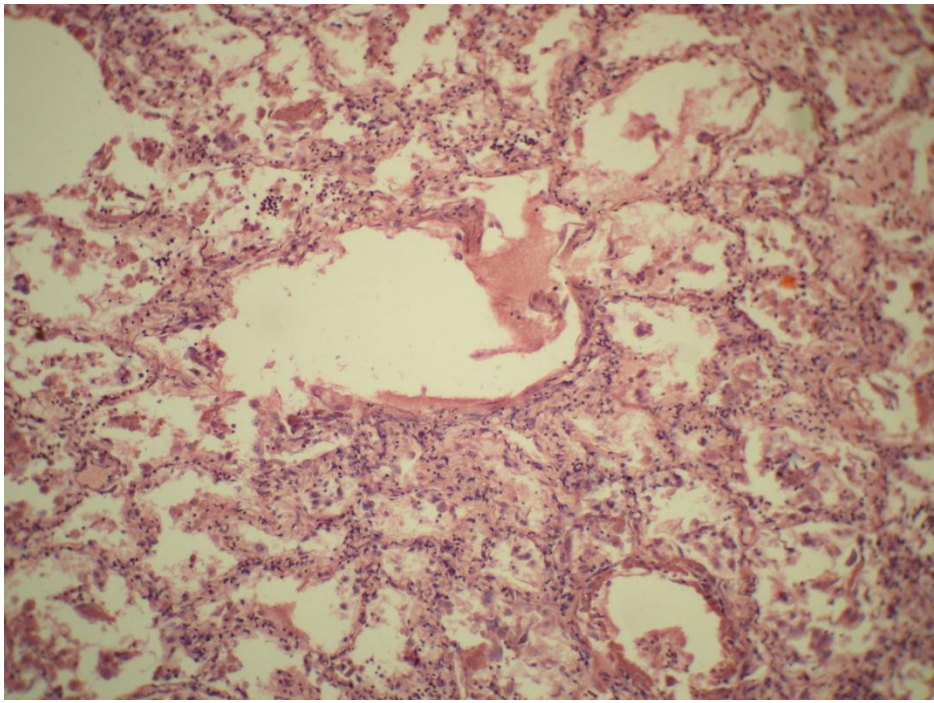




Hyaline membrane

Acute respiratory syndrome (SARS)





Morphology of shock

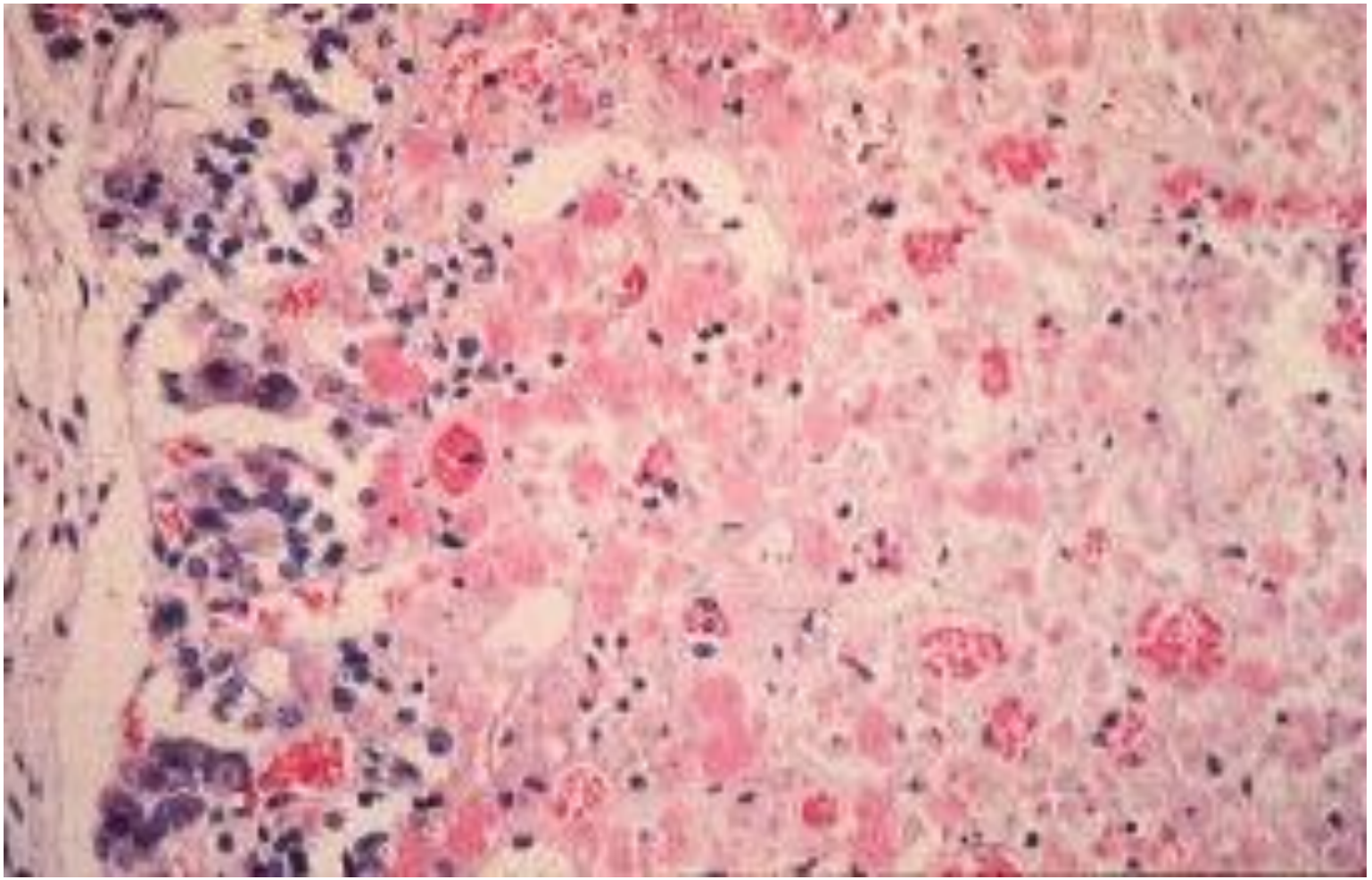
- **Kidney**

- fall in the BP leads to reduction in glomerular filtrate which further produces uremia due to retention of waste products

- Due to tubular ischemia, tubular necrosis develops which leads to anuria further leading to severe progressive uremia

Diffuse cortical necrosis

Necrosis of pituitary gland



Crush syndrome

Acute Compartment and Crush Syndrome

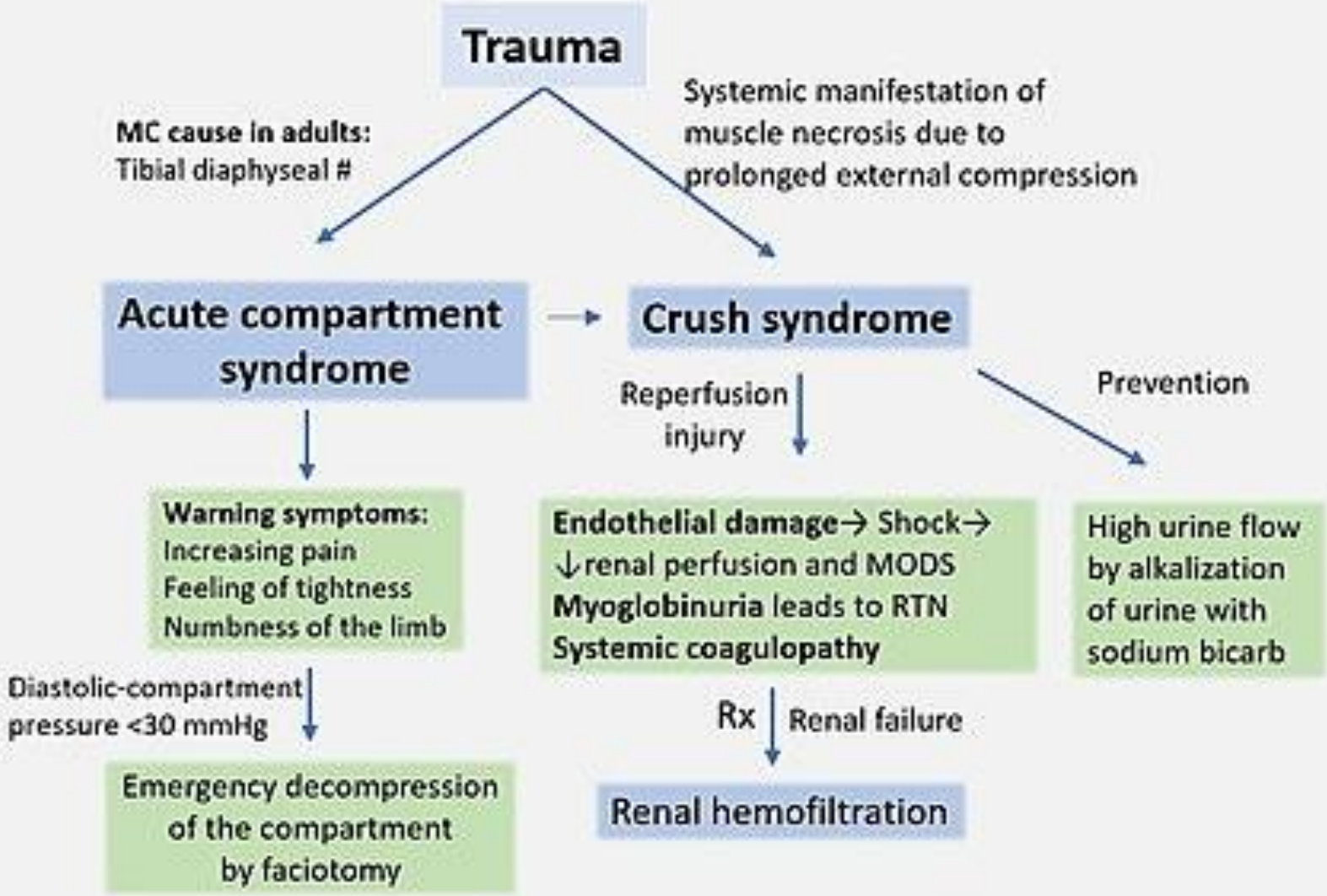
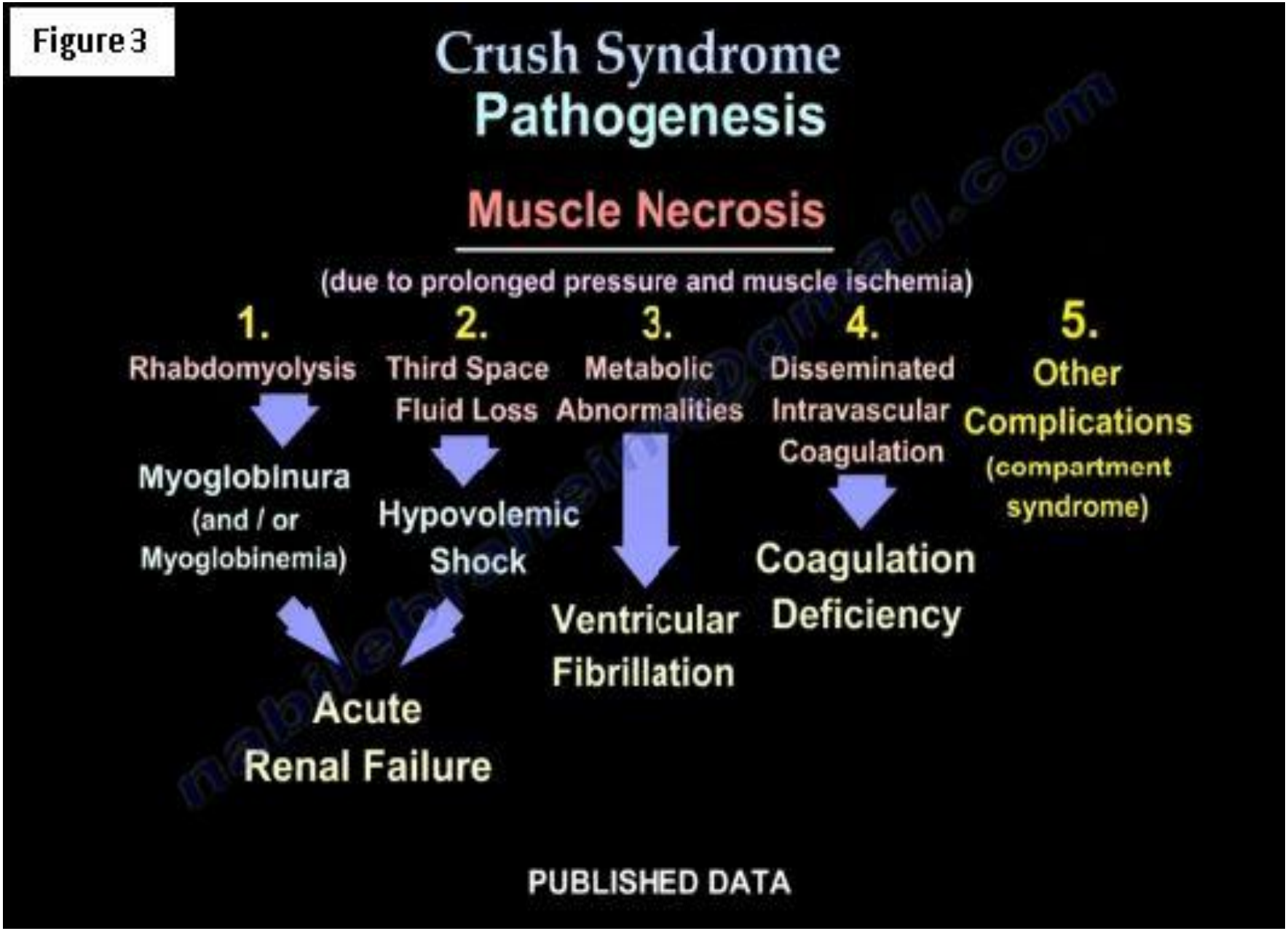
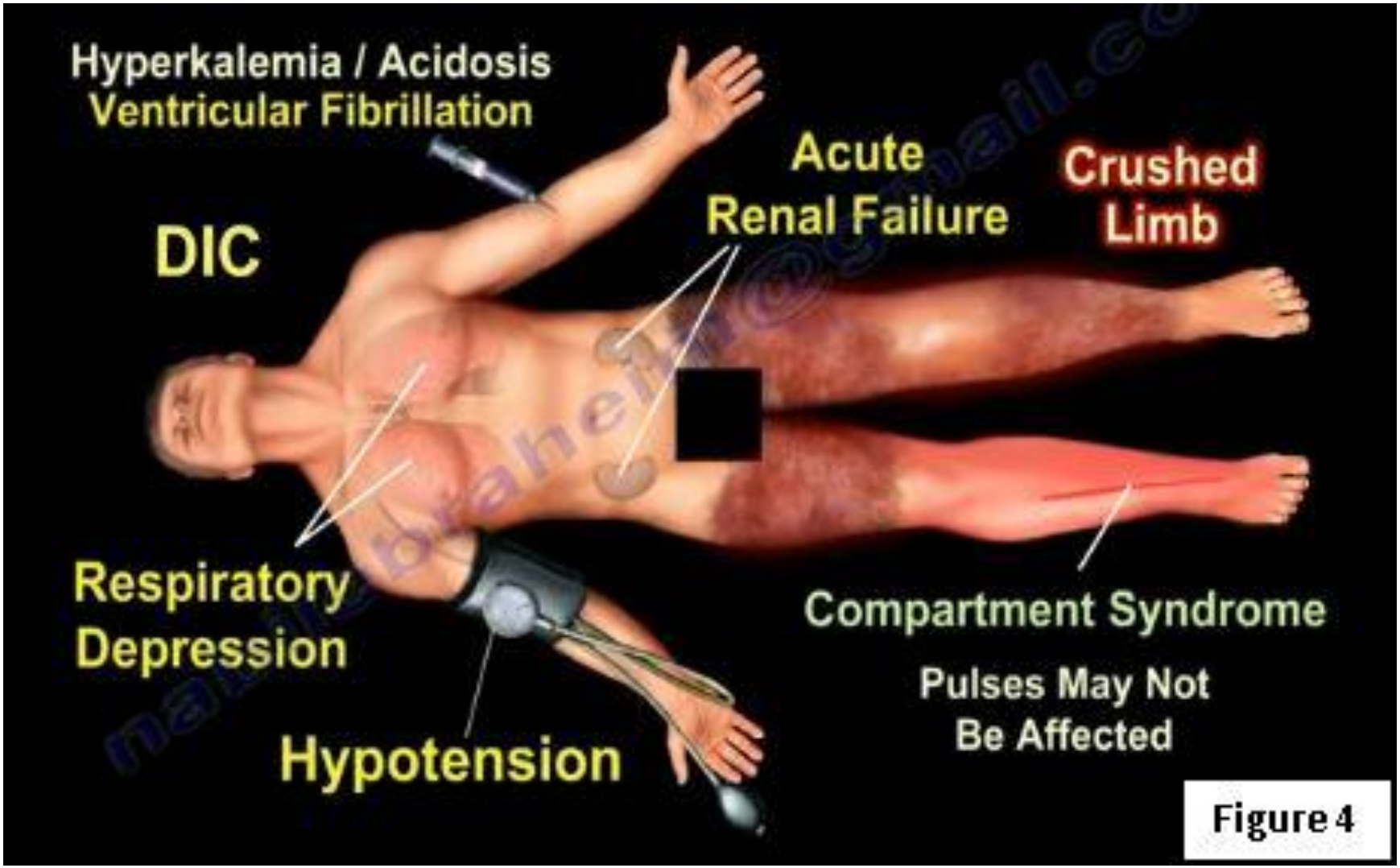


Figure 3


Crush Syndrome
Pathogenesis
Muscle Necrosis
(due to prolonged pressure and muscle ischemia)
1.
Rhabdomyolysis
Myoglobinura
(and / or
Myoglobinemia)
2.
Third Space
Fluid Loss
Hypovolemic
Shock
3.
Metabolic
Abnormalities
Ventricular
Fibrillation
4.
Disseminated
Intravascular
Coagulation
Coagulation
Deficiency
5.
Other
Complications
(compartment
syndrome)
Acute
Renal Failure
PUBLISHED DATA

Crush syndrome



Collapse

Collapse

- Collapse is an acute vascular insufficiency which is characterized by fall of a vascular tone, and also acute reduction of circulating blood volume .

- At the collapse there is a reduction of venous blood inflow to heart, decrease of heart output, fall of arterial and venous pressure, infringement of tissues perfussion and metabolism, comes hypoxia of brain appears, the vital functions of an organism are oppressed.

Collapse

- It is shown in clinics by short-term loss of consciousness, general weakness, features of acute vascular insufficiency with infringements hemodynamics practically in all organs and tissues.

- In a basis of development of collapse discrepancy between volume of circulating blood and capacity of a vascular system lays.

- The reasons may be sudden reduction of blood volume (blood loss, dehydratation), and sudden dilatation of vessels.

- Collapse develops as complication at heard diseases and pathological conditions.

Collapse

- ***The infectious collapse*** develops as complication of acute infectious diseases: meningoencephalitis, and typhoid fever typhus fever, acute dysentery, pneumonia, botulism, the Siberian ulcer, virus hepatites, toxic influenza.

- The reason of such complication is the intoxication by endo- and exotoxins of microorganisms, mainly that influence on central nervous system, or receptors of pre- and postcapillaries.

Collapse

- ***Hypoxic collapse*** may appear in conditions of reduced partial pressure of oxygen in air.

- The direct reason of circulation infringements thus is insufficiency of adaptive reactions of an organism to hypoxia.

- To development of collapse in these conditions may promote also hypocapnia owing to hyperventilation which leads to expansion of capillaries and vessels, and from here to deposition and decrease of circulating blood volume.

Collapse

- ***Ortostatic collapse*** appears at fast transition from horizontal position in vertical, and also at long time of standing.
- Thus there is a redistribution of blood with increase of total amount of a venous system and decrease of inflow to heart.
- In a basis of this condition insufficiency of a venous tone lays.
- Ortostatic collapse may be observed at recovers after heard diseases of endocrine and nervous system, in the postoperative period, at fast removal of ascitic liquids or as a result of spinal and peridural anesthesias.
- Iatrogenic ortostatic collapse sometimes appears during wrong use of neuroleptics, ganglioblockers, adrenoblockers, sympatolytics.
- Among pilots and cosmonauts ortostatic collapse may be caused by redistribution of blood at action of acceleration when blood from vessels of the upper half of body and a head moves into vessels of organs of abdominal cavity and inferior extremitus, causing hypoxia of brain.
- Also it may be observed at practically healthy children and teenagers.

Collapse

- Progressing changes lead to infringement of functions of a brain, deepening of regulatory and hemodynamic disorders.

- The death at a collapse comes owing to an exhaustion of power resources of brain, intoxication and disturbances of metabolism.

Coma

Coma

- Coma is a pathological condition which is characterized by deep oppression of functions of the central nervous system and it is shown by loss of consciousness, absence of reflexes on external irritators and disorders of the vital functions regulation of an organism.

Coma

- By origin distinguish:

1. Comas at initial injury and diseases of the central nervous system (insult, craniocerebral trauma).

2. Comas during the endocrine diseases which apper as at insufficiency of some glands of internal secretion (diabetic, hypocorticoid, hypopituitary, hypothyreoid), and at their hyperfunction (thyreotoxic, hypoglycemic).

3. Toxic comas are observed at endogenic (uraemia, hepatic insufficiency, toxicoinfections, pancreatitis) and exogenic intoxications (alcoholic poisonings, barbiturate poisoning, phosphororganic poisoning and by other substances).

4.Comas, caused by infringements of gas exchange at various kinds of hypoxias.

5. Comas, caused by loss of electrolytes, water and energetic substances.

Coma

- **Exogenous factors**– pathogenic agents of environment, as rule , extraordinary forces, toxicity or break down of characteristic.

- **Examples:**
- -
  Variaty traumatic (as rule, brain) factors (electrical charge, mechani cal trauma of head.
- - Thermal action (overheat, overcooling, sun stroke).
- - Considerable fluctation of barometric pressure (hypo- and hyperbaria).
- - Neurotropic toxins (alcohol and its supstitutes, ethylene glycol).
- -
  Infectious agents (neurotropic viruses, toxins of botulinus and tet anus, agents malaria, typhus fever, cholera).
- - Exogenous hypoxia and anoxia.
- - Ionizing radiation (large dose of radiation).

Coma

- **Endogenous factors** - leading to coma development, are resultate of hard disorders of vital activaty of organism. They are observed at unfavourable course variaties illnes.

- **Examples:**
- - Pathological processe in brain (ischemia, insult, tumor, absces, edema).
- - Insuficiency of circulation blood (hypoxia of brain).
- - Respiratory insuficiency (asthmatic states, asphyxia, edema lung).
- - Patology of blood system (hemolysis of erythrocytes, hard anemia).
- - Endocrinopathies (hypoinsulinism, hypo- and hyperthyrosis, superrenal insuficiency).
- - Liver insuficiency, disorder of digestiv system (syndrome of malabsorbtion, intestinal autointoxication).
- - Renal insuficiency
- - Comatous state develops at hard progressive course of collaps and shock.

Coma

- Coma is a stage of development of some diseases.

- Conducting in their pathogenesis is defeat of the central nervous system with infringement of function of cortex brain, subcortex formations and trunk brain that results in loss of consciousness.

- A special role in development of coma plays infringement of reticular formations function with loss of its activating influences on cortex brain and oppression of subcortex formations function and centres of vegetative nervous system.

Pathogenesis of comatose states

The main importance :

toxic damage to the central nervous system cells.

circulatory disorders in the brain

Most often, coma observed in acute cerebral circulatory disorders, diabetes, chronic nephritis, increasing liver failure, severe poisoning poisons.

Coma

1. Infringement of cellular breath and an exchange of energy in brain.

A basis of them is hypoxia, anemia, disorders of brain blood circulation, blockade of respiratory enzymes by cytotoxic poisons, acidosis (at diabetic and uraemic coma), deficiency of power substances or blockade of their recycling (starvation hypoglycemis coma).

In development of brain hypoxia disorders of microcirculation play role. Owing to hypoxia it is broken oxidizing phosphorelation, the content and use ATP and creatinphosphate decreases.

2. Infringement of synaptic transmission to the central nervous system. They may be connected with:

a) infringement of synthesis, transport, deposition and secretion of neuromediators;

b) replacement of neuromediators by pseudomediators;

c) excessive activation of inhibition postsynaptic receptors;

d) blockade stimulating postsynaptic receptors. This mechanism has the great value in development of hepatic, uremic and toxic comas.

Coma

3. Infringement of electrolyte balance with changes of cellular potentials and process of polarization of neurons membranes, and also infringement of osmotic pressure.

Disorders of metabolism of K, Ná, Mg, Ca in a combination with infringements of the acid-base balance (diabetic, uraemic, chlorinehydropenie, hepatic etc. comas) have the greatest value.

4. Changes of physical properties and structures of brain and intracranial formations.

Pathogenetic value has swelling and edema of brain and brain membrane, increase of intracranial pressure which strengthens infringement of haemodinamics and liquordynamic, make hypoxia of nervous cells heavier and oppress their physiological activity.

Mechanical damage of brain matters cells at a craniocerebral trauma, tumours, hemorrhage in brain.

At separate kinds of comas whom each of the listed factors may have leading mean, however they act together more often.

At deep coma disorders of regulation of vegetative functions result in addition in heavy infringements of metabolism in an organism, including brain, and create vise circle in pathogenesis of coma.

Glasgow Coma Scale

EYE OPENING			VERBAL RESPONSE			MOTOR RESPONSE		
								
Spontaneous	>	4	Orientated	>	5	Obey commands	>	6
To sound	>	3	Confused	>	4	Localising	>	5
To pressure	>	2	Words	>	3	Normal flexion	>	4
None	>	1	Sounds	>	2	Abnormal flexion	>	3
			None	>	1	Extension	>	2
						None	>	1

GLASGOW COMA SCALE SCORE

Mild	Moderate	Severe
13-15	9-12	3-8

Hypervitaminosis

Hypervitaminosis

- Hypervitaminosis occurs when the storage levels of vitamins are abnormally high.

- Hypervitaminosis can lead to toxic symptoms and diverse health effects.

Hypervitaminosis E

- Vitamin E is present in a great many foods, particularly vegetable oils, unprocessed cereal grains, nuts and seeds.
- There is no evidence of any adverse effects from consuming vitamin E in food.
- However, high doses of alpha-tocopherol supplements can affect blood clotting, inhibit platelet aggregation and cause haemorrhage.
- Studies have also shown an increase in all-cause mortality associated with vitamin E supplements.
- Supplementation with vitamin E may also significantly increase the risk of prostate cancer among healthy men

Hypervitaminosis A

- Vitamin A is present as fatty-acid esters in food sources such as liver, kidney, and milk, and as provitamin A carotenoids in plants, usually as beta-carotene.

- High intake of beta-carotene (hypercarotenaemia) can colour the skin yellow, sparing the eyes (in contrast to jaundice where the sclera are also yellow).

Hypervitaminosis A

- The body stores excess amounts of vitamin A, primarily in the liver.
- Although excess preformed vitamin A can have significant toxicity, large amounts of beta-carotene and other provitamin A carotenoids are not associated with major adverse effects.
- The features of hypervitaminosis A depend on the size and timescale of the excess intake.

Hypervitaminosis A

- Hypervitaminosis A following sudden, massive intake of vitamin A causes acute toxicity.

- More sustained intake of excess vitamin A leads to increased intracranial pressure (pseudotumour cerebri), dizziness, nausea, headaches, skin irritation, pain in joints and bones, coma, and even death.

Hypervitaminosis A

- Excess intake of preformed vitamin A and some topical synthetic retinoids (eg, isotretinoin and etretinate) can cause congenital birth defects, including malformations of the eye, skull, lungs, and heart.
- Women who might be pregnant should therefore not take high doses of vitamin A supplements.
- Unlike preformed vitamin A, beta-carotene is not known to be teratogenic.
- Even large doses of supplements of beta-carotene or diets with high levels of carotenoid-rich food for long periods are not associated with toxicity.
- The most significant effect of long-term, excess beta-carotene is carotenodermia, a harmless condition in which the skin becomes yellow-orange, which can be reversed by stopping ingestion of beta-carotene.

Acute hypervitaminosis A

- This occurs after large overdosage of the vitamin. This can occur with unusual dietary intake such as, for example, ingestion of polar bear liver, which has a very high vitamin A content.

Symptoms include:

- Headache
- Abdominal pain
- Nausea or vomiting
- Lethargy
- Visual changes
- Impaired consciousness

Chronic hypervitaminosis A

- This requires in excess of 50,000 units/day for more than three months.
- Symptoms often include bone pain and bony swelling due to increased bone resorption and periosteal bone formation, often associated with hypercalcaemia.

Other symptoms can be quite nonspecific:

- Scaly seborrhoeic eczema
- Patchy hair loss
- Stomatitis
- Loss of appetite
- Nausea
- Vomiting
- Malaise
- Hepatosplenomegaly
- Liver failure
- Raised intracranial pressure

Hypervitaminosis D

- Vitamin D toxicity can cause nonspecific symptoms such as anorexia, weight loss, polyuria, and heart arrhythmias.

- More serious effects include raised blood calcium leading to urinary tract stones and also vascular and tissue calcification, causing damage to the heart, blood vessels and kidneys.

- Excessive sun exposure does not result in vitamin D toxicity because the sustained heat on the skin is thought to degrade previtamin D3 and vitamin D3 as it is formed.

Hypervitaminosis D

- Long-term intake of high-dose supplements has been shown to be associated with an increased risk of adverse health effects, with an increase in all-cause mortality, greater risk of some cancers (eg, pancreatic), greater risk of cardiovascular events, and more falls and fractures in the elderly

Hypervitaminosis D

- Most symptoms occur because of secondary hypercalcaemia with increased bone resorption and hypercalciuria.

- Features of hypercalcaemia include polyuria, polydypsia, vomiting, anorexia, lethargy, dehydration, constipation, hypertension, tetany and seizures.

- The traditional description of hypercalcaemia is *stones, bones and groans.*
- Hypervitaminosis D is also recognised as a cause of depression.

- In children it can result in dental enamel hypoplasia and focal pulp calcification.

Hypervitaminosis D

Complications:

1. *nephrolithiasis*,
2. *nephrocalcinosis* (calcium oxalate and calcium phosphate are radio-opaque stones),
3. *calcinosis* of the joints and periarticular tissues, and
4. *chronic kidney disease*.

Hypervitaminosis E

- Vitamin E is present in a great many foods, particularly vegetable oils, unprocessed cereal grains, nuts and seeds.
- There is no evidence of any adverse effects from consuming vitamin E in food.
- However, high doses of alpha-tocopherol supplements can affect blood clotting, inhibit platelet aggregation and cause haemorrhage.
- Studies have also shown an increase in all-cause mortality associated with vitamin E supplements.
- Supplementation with vitamin E may also significantly increase the risk of prostate cancer among healthy men

Hypervitaminosis B6

- High intakes of vitamin B6 from food sources have not been reported to cause adverse effects.
- However, long-term use of supplements can cause severe and progressive sensory neuropathy with ataxia.
- The severity of symptoms is dose-dependent and the symptoms usually stop when the supplements are discontinued.
- Other adverse effects of excessive vitamin B6 intake include painful skin rashes, photosensitivity, nausea and heartburn
-

Hypovitaminosis

Hypovitaminosis

- Avitaminosis (vitamin lack) may be encountered when there areЖ

1. increased losses of vitamins such as occur with chronic severe diarrhea or
2. excessive sweating or when there are increased requirements for vitamins during periods of rapid growth, especially during childhood and pregnancy.

Hypovitaminosis C (scurvy)

- **Scurvy** is a condition caused by a dietary lack of vitamin C (ascorbic acid), hence is also called **hypovitaminosis C**, and is characterized by an increased bleeding tendency and impaired collagen synthesis resulting in osteoporosis and impaired wound healing.

VITAMIN C DEFICIENCY

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anxiety and depression

dry and dull hair

dry skin

weak immune system

bleeding gums

tooth loss

joint pain

slow wound healing

Bleeding from gum

Hypovitaminosis C (scurvy)

Primary vitamin A deficiency

- This is caused by prolonged dietary deficiency, particularly where rice is the staple food (doesn't contain carotene).

- Vitamin A deficiency occurs with protein-energy malnutrition (marasmus or kwashiorkor) mainly because of dietary deficiency (but vitamin A storage and transport are also impaired).

Secondary vitamin A deficiency

- This occurs where there are problems in converting carotene to vitamin A, or reduced absorption, storage, or transport of vitamin A.

- This occurs in coeliac disease, tropical sprue, giardiasis, cystic fibrosis, other pancreatic disease, cirrhosis, duodenal bypass surgery and bile duct obstruction.

Vitamin A deficiency

- Mild forms of vitamin A deficiency may cause no symptoms. However, there may still be an increased risk of developing respiratory infections and gastroenteritis, and delayed growth and bone development.

- There is also a risk of infertility secondary to impaired spermatogenesis, and an increased risk of miscarriage. Fatigue may present as a consequence of vitamin A deficiency anemia.

Eye and vision in Vitamin A deficiency

1. Poor adaptation to darkness - night blindness.
2. Keratomalacia (thinning and ultimately ulceration of the cornea - colliquative necrosis).
3. Conjunctival dryness, corneal dryness, xerophthalmia.
4. Bitot's spots (areas of abnormal squamous cell proliferation and keratinisation of the conjunctiva, causing oval, triangular or irregular foamy patches on the white of the eye).
5. Corneal perforation.
6. Blindness due to structural damage to the retina.
7. Reduced vitamin A concentration increases the risk of blindness in children infected with the measles virus.

Skin and hair in Vitamin A deficiency

1. Dry skin, dry hair, pruritus.
2. Broken fingernails.
3. Follicular hyperkeratosis secondary to blockage of hair follicles, with plugs of keratin.

Other less specific changes in Vitamin A deficiency

1. Keratinisation of mucous membranes.
2. Increased susceptibility to infection (due to impairment of the humoral and cell-mediated immunity).
3. Skin changes (follicular hyperkeratosis), which are also common.

Vitamin D deficiency

- Vitamin D is a fat-soluble vitamin used by the body for normal bone development and maintenance by increasing the absorption of calcium, magnesium, and phosphate.

- The first and best characterized phenotype of vitamin D deficiency is the development of skeletal disorders, notably rickets and osteomalacia.

Vitamin D deficiency: etiology

1. Decreased dietary intake and/or absorption.
2. Decreased sun exposure.
3. Decreased endogenous synthesis.
4. Increased hepatic catabolism.
5. End organ resistance.

Vitamin D deficiency: pathophysiology

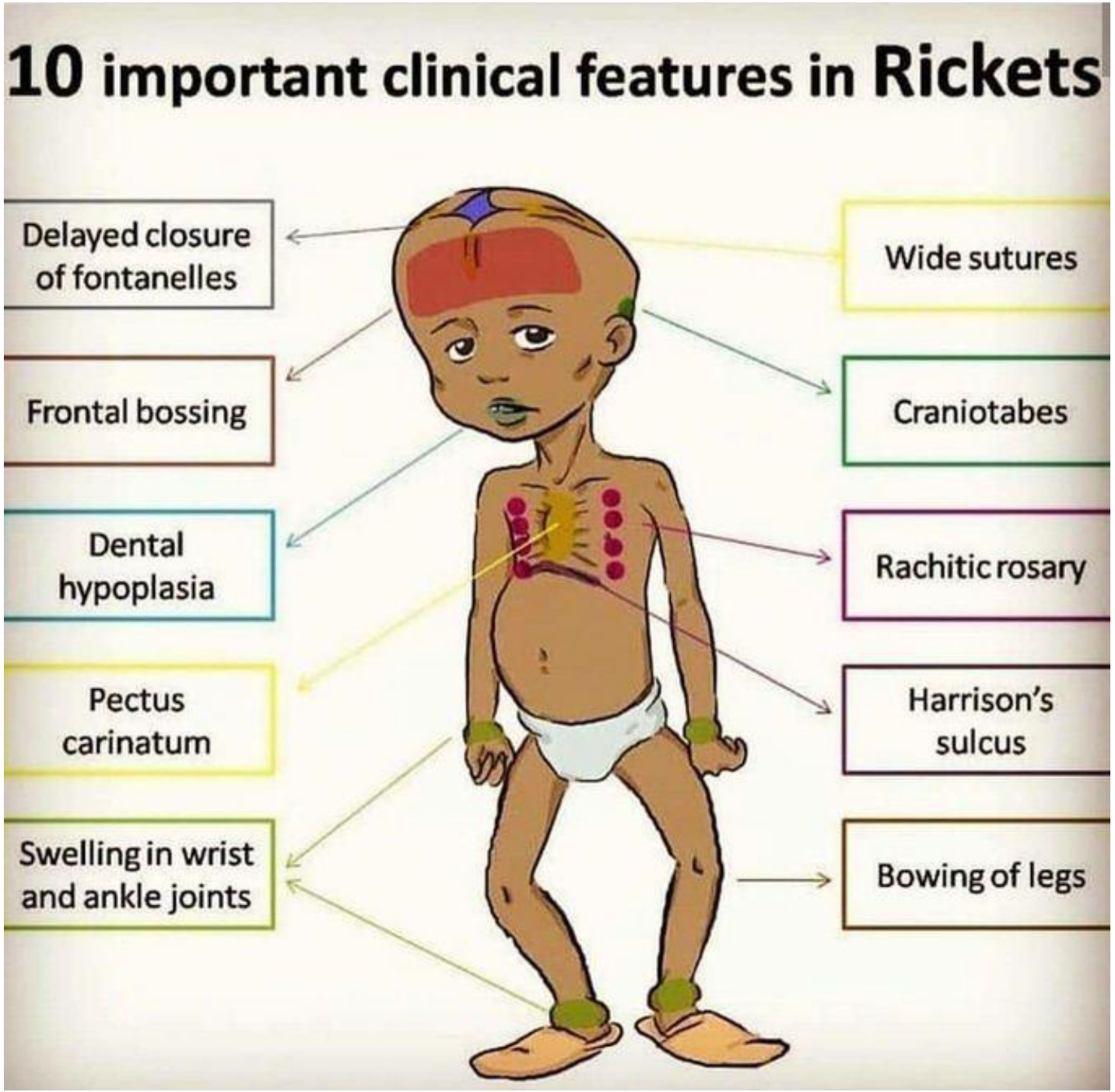
- Vitamin D plays a crucial role in calcium homeostasis and bone metabolism.
- With chronic and/or severe vitamin D deficiency, a decline in intestinal calcium and phosphorus absorption leads to hypocalcemia leading to secondary hyperparathyroidism.
- This secondary hyperparathyroidism then leads to phosphaturia and accelerated bone demineralization.
- This can further results in osteomalacia and osteoporosis in adults and osteomalacia and rickets in children.

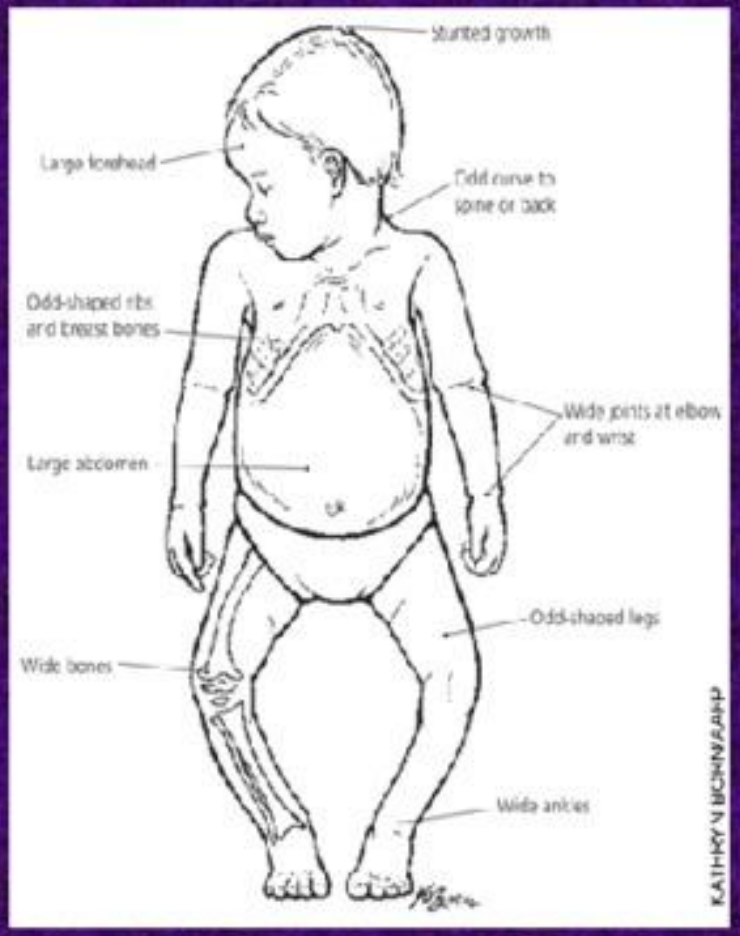
Vitamin D deficiency

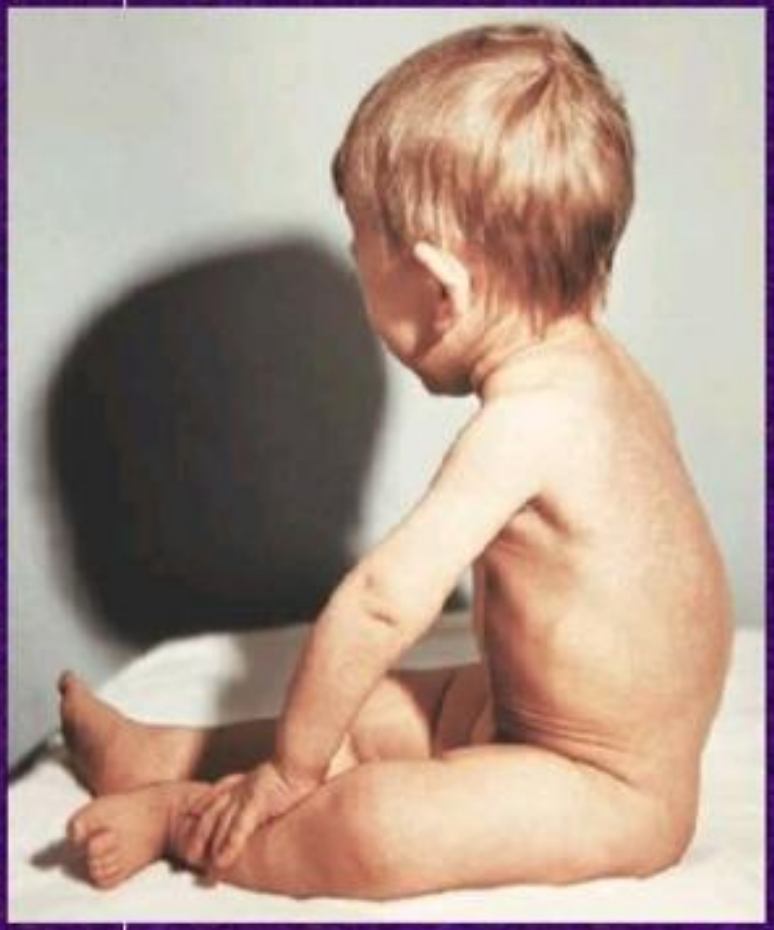
- The majority of patients with vitamin D deficiency are asymptomatic.
- However, even mild chronic vitamin D deficiency can lead to chronic hypocalcemia and hyperparathyroidism which can contribute risk of osteoporosis, falls and fractures especially in the elderly population.

- Patients with a prolonged and severe vitamin D deficiency can experience symptoms associated with secondary hyperparathyroidism including bone pain, arthralgias, myalgias, fatigue, muscle twitching (fasciculations), and weakness. Fragility fractures may result from chronic vitamin D deficiency leading to osteoporosis. In children, irritability, lethargy, developmental delay, bone changes, or fractures can be symptoms of vitamin D deficiency.

10 important clinical features in Rickets




Stunted growth
Large forehead
Odd-shaped ribs and breast bones
Large abdomen
Wide joints at elbow and wrist
Odd-shaped legs
Wide bones
Wide ankles



Vitamin K deficiency

- Vitamin K deficiency results from extremely inadequate intake, fat malabsorption, or use of coumarin anticoagulants.

- Vitamin K deficiency decreases levels of prothrombin and other vitamin K–dependent coagulation factors, causing defective coagulation and, potentially, bleeding.

- Worldwide, vitamin K deficiency causes infant morbidity and mortality.

Vitamin K deficiency

- Vitamin K deficiency causes hemorrhagic disease of the newborn, which usually occurs 1 to 7 days postpartum. In affected neonates, birth trauma can cause intracranial hemorrhage.

- A late form of this disease can occur in infants about 2 to 12 weeks old, typically in infants who are breastfed and are not given vitamin K supplements.

- If the mother has taken phenytoin antiseizure drugs, coumarin anticoagulants, or cephalosporin antibiotics, the risk of hemorrhagic disease is increased.

Vitamin K deficiency

- In **healthy adults,** dietary vitamin K deficiency is uncommon because vitamin K is widely distributed in green vegetables and the bacteria of the normal gut synthesize menaquinones.

Vitamin K deficiency

- **Neonates** are prone to vitamin K deficiency because of the following:
- The placenta transmits lipids and vitamin K relatively poorly.
- The neonatal liver is immature with respect to prothrombin synthesis.
- Breast milk is low in vitamin K, containing about 2.5 mcg/L (cow's milk contains 5000 mcg/L).
- The neonatal gut is sterile during the first few days of life.

In **adults**, vitamin K deficiency can result from

- Fat malabsorption (eg, due to biliary obstruction, malabsorption disorders, cystic fibrosis, or resection of the small intestine)
- Use of coumarin anticoagulants

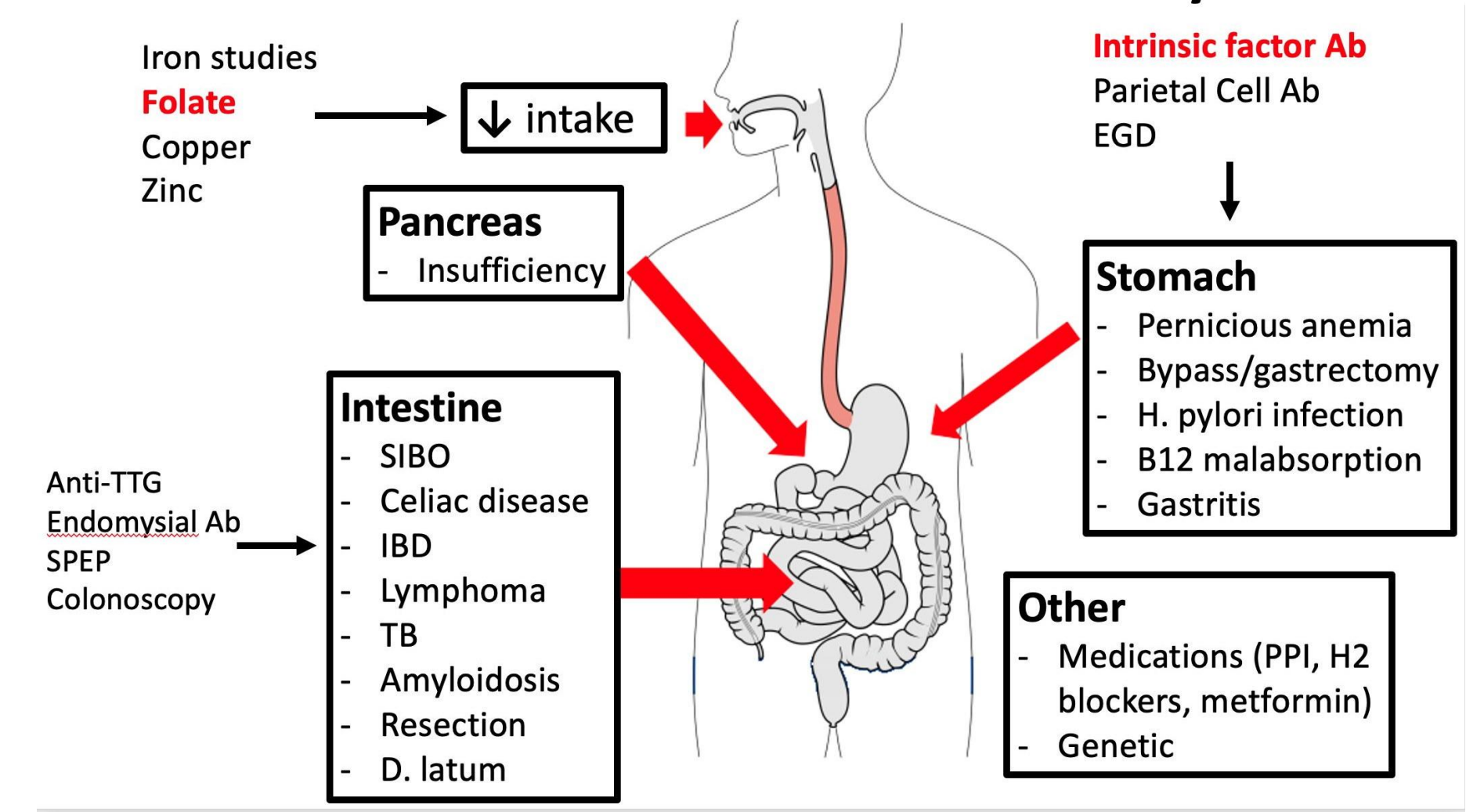
Vitamin K deficiency

- Bleeding is the usual manifestation.
- Easy bruisability and mucosal bleeding (especially epistaxis, gastrointestinal [GI] hemorrhage, menorrhagia, and hematuria) can occur.
- Blood may ooze from puncture sites or incisions.

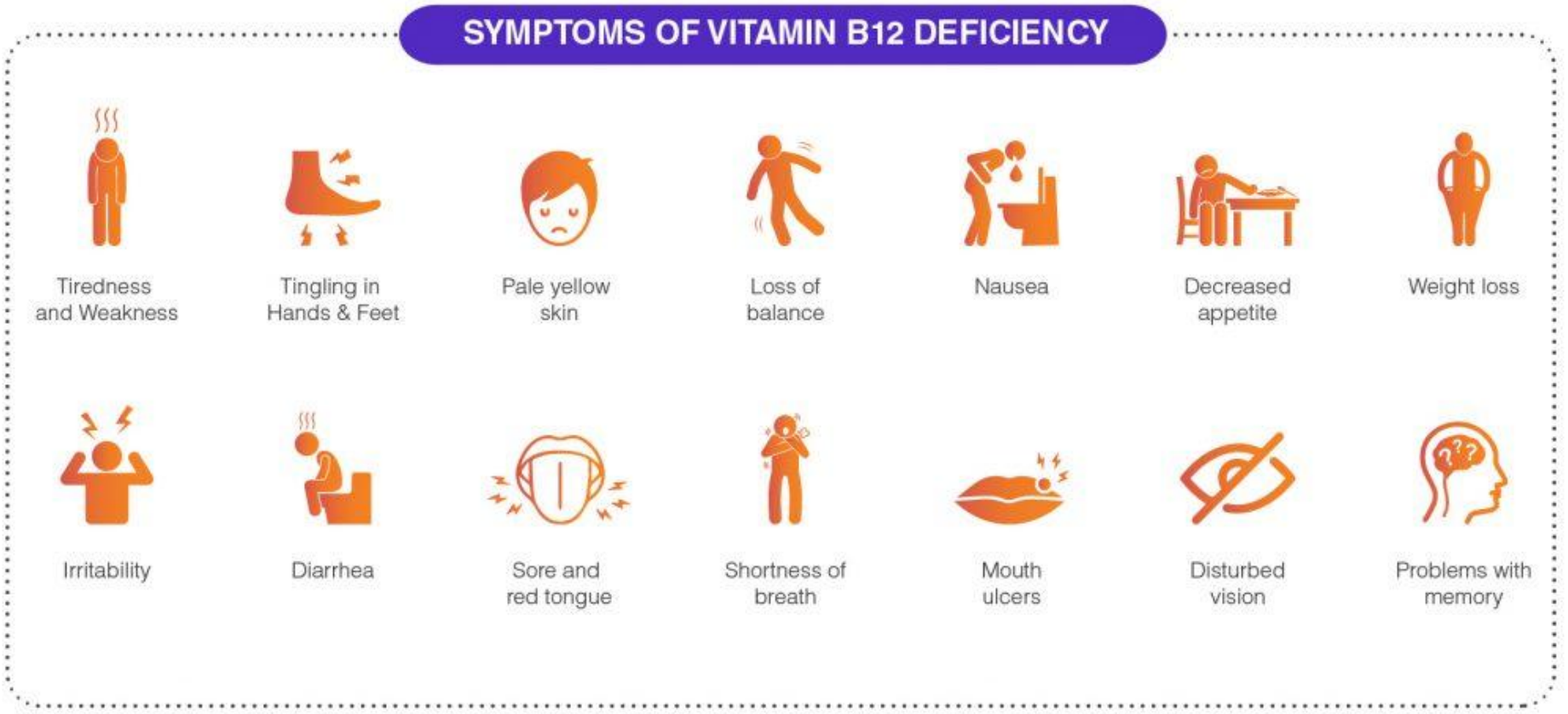
- Hemorrhagic disease of the newborn and late hemorrhagic disease in infants may cause cutaneous, GI, intrathoracic, or, in the worst cases, intracranial bleeding.
- If obstructive jaundice develops, bleeding—if it occurs—usually begins after the 4th or 5th day.
- It may begin as a slow ooze from a surgical incision, the gums, the nose, or GI mucosa, or it may begin as massive bleeding into the GI tract.

Vitamin B12 deficiency

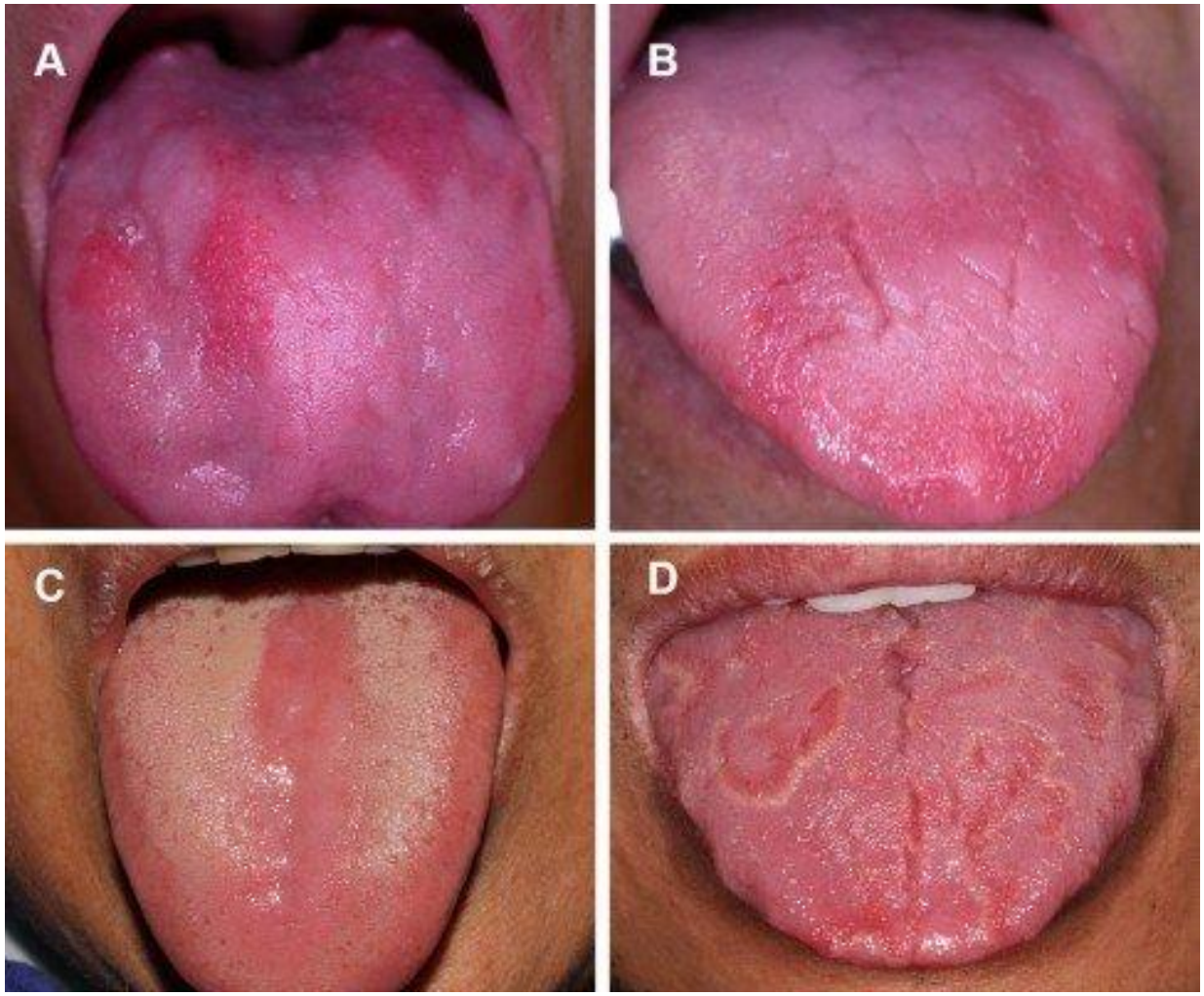
Causes of Vitamin B12 Deficiency



Vitamin B12 deficiency



Vitamin B12 deficiency



Vitamin B6 deficiency

- Because vitamin B6 is present in many foods, the deficiency rarely results from inadequate intake except in severe malnutrition. However, deficiency can also occur, because extensive processing can remove vitamin B6 from foods.
- Vitamin B6 deficiency often results from
- Impaired absorption of food (malabsorption disorders)
- Alcoholism
- Excessive loss of vitamin B6 during hemodialysis
- Use of drugs that deplete vitamin B6 stored in the body

Vitamin B6 deficiency

- In adults, vitamin B6 deficiency can cause inflammation of the skin (dermatitis) and a red, greasy, scaly rash.
- The hands and feet may feel numb and prickling—like pins and needles.
- The tongue may become sore and red, and cracks may form in the corners of the mouth.
- People may become confused, irritable, and depressed.
- They may have seizures.
- Rarely, vitamin B6 deficiency causes seizures in infants.
- Antiseizure drugs may be ineffective in treating these seizures in infants.
- Because vitamin B6 is needed to form red blood cells, deficiency can cause anemia.