

**MINISTRY OF HEALTHCARE OF UKRAINE
HSEEU "Ukrainian Medical Stomatological Academy"**

"Approved"
at the meeting of internal
medicine №1 department
Head of Department
Prof. Skrypnyk I.M.

Protocol № 4 from 13.10.2016

**GUIDELINES
FOR STUDENTS
INDEPENDENT WORK
IN THE PRACTICAL CLASSES PREPARING**

<i>Academic discipline</i>	Internal medicine
<i>Module</i>	Current practice of internal medicine
<i>Content module</i>	Management of the patients with main symptoms and syndromes in cardiology clinic
<i>Study subject</i>	Management of the patients with shortness of breath Management of patients with pulmonary hypertension
<i>Course</i>	VI
<i>Faculty</i>	of foreign students training

1. The aims of the training course:

To Know:

1. The main causes of cyanosis.
2. Differential diagnosis of cyanosis.
3. Test plan, the role of radiological, instrumental and laboratory methods of examination.
4. Drug and non-medicamentous treatment.
5. Indications for surgical treatment.
6. Primary and secondary prevention.
7. Weather and performance.

To be able to:

Conduct surveys and examination of patients with cyanosis

- draft examination of patients with cyanosis
- justify the use of basic diagnostic methods in pulmonology, identify indications and contraindications for their conduct, possible complications
- prescribe treatment, determine prognosis and to conduct primary and secondary prevention in patients with cyanosis
- diagnose and assist in patients with cyanosis

Demonstrate knowledge of moral principles

The contents of topic:

Text

Merck Manual Professional Version <http://www.merckmanuals.com/professional>

cyanosis

Raynaud Syndrome

Raynaud syndrome is vasospasm of parts of the hand in response to cold or emotional stress, causing reversible discomfort and color changes (pallor, cyanosis, erythema, or a combination) in one or more digits. Occasionally, other acral parts (eg, nose, tongue) are affected. The disorder may be...

Section/Chapter: Details

Diagnosis

Clinical criteria Examination and testing for underlying disorder Raynaud syndrome itself is diagnosed clinically. Acrocyanosis (see Acrocyanosis) also causes color change of the digits in response to cold but differs from Raynaud syndrome in that it is persistent, not easily reversed, and...

Symptoms and Signs

Sensations of coldness, burning pain, paresthesias, or intermittent color changes of one or more digits are precipitated by exposure to cold, emotional stress, or vibration. All can be reversed by removing the stimulus. Rewarming the hands accelerates restoration of normal color and sensation. ...

Treatment

Trigger avoidance Smoking cessation Ca channel blockers or prazosin Treatment of the primary form involves avoidance of cold, smoking cessation, and, if stress is a triggering factor, relaxation techniques (eg, biofeedback) or counseling. Drugs are used more often than behavioral...

Key Points

Raynaud syndrome is reversible vasospasm of parts of the hand in response to cold or emotional stress. Raynaud syndrome may be primary, or secondary to another disorder, typically one affecting connective tissue. Primary Raynaud syndrome, unlike the secondary form, rarely causes gangrene or...

- [Overview of Congenital Cardiovascular Anomalies](#)

(See also Overview of Cardiac Valvular Disorders .) Congenital heart disease (CHD) is the most common congenital anomaly, occurring in almost 1% of live births. Among birth defects, CHD is the leading cause of infant mortality.

Section/Chapter: Details

Etiology

Environmental and genetic factors contribute to the development of CHD. Common environmental factors include maternal illness (eg, diabetes, rubella, systemic lupus erythematosus) or maternal intake of teratogenic agents (eg, lithium, isotretinoin, anticonvulsants). Paternal age may also be a...

Pathophysiology

Congenital heart anomalies are classified (see Table: Classification of Congenital Heart Anomalies*) as Cyanotic Acyanotic (left-to-right shunts or obstructive lesions) The physiologic consequences of congenital heart anomalies vary greatly, ranging from an asymptomatic heart murmur or...

Symptoms and Signs

Manifestations of CHDs are varied but commonly include Murmurs Cyanosis HF Other physical examination abnormalities may include circulatory shock, poor perfusion, abnormal 2nd heart sound (S 2 —single or widely split), systolic click, gallop, or irregular rhythm.

Diagnosis

Screening by pulse oximetry ECG and chest x-ray Echocardiography Sometimes cardiac MRI or CT angiography, cardiac catheterization with angiography When present, heart murmurs, cyanosis, abnormal pulses, or manifestations of HF suggest CHD. In such neonates, echocardiography is...

Treatment

Medical stabilization of HF (eg, with O₂, diuretics, ACE inhibitors, digoxin, and salt restriction) Surgical repair or transcatheter intervention After medical stabilization of acute HF symptoms or cyanosis, most children require surgical or transcatheter repair; the...

- [Total Anomalous Pulmonary Venous Return \(TAPVR\)](#)

In total anomalous pulmonary venous return, the pulmonary veins do not connect to the left atrium. Instead, the entire pulmonary venous return enters the systemic venous circulation through one or more persistent embryologic connections. If there is no obstruction to pulmonary venous return,...

Section/Chapter: Details

Symptoms and Signs

Neonates with obstructed pulmonary venous return present with severe pulmonary hypertension, pulmonary edema, and cyanosis. Physical examination usually shows a parasternal lift and a single, loud 2nd heart sound (S₂), with no significant murmur. If pulmonary venous return is not...

Diagnosis

Chest x-ray and ECG Echocardiography Diagnosis is suspected by chest x-ray and established by echocardiography. Cardiac catheterization is rarely necessary; occasionally, cardiac MRI or CT angiography may need to be done to better delineate the anatomy of pulmonary venous return. Chest...

Treatment

Surgical repair Medical treatment of HF (eg, diuretics, digoxin, ACE inhibitors) before surgery Neonates with infradiaphragmatic return with obstruction require emergent surgical repair. In older infants, HF should be treated, followed by surgical repair as soon as the infant is stabilized. ...

- Peripheral arterial disease (PAD) is atherosclerosis of the extremities (virtually always lower) causing ischemia. Mild PAD may be asymptomatic or cause intermittent claudication; severe PAD may cause rest pain with skin atrophy, hair loss, cyanosis, ischemic ulcers, and gangrene. Diagnosis is by...

Section/Chapter: Details

Etiology

Prevalence of PAD is about 12% in the US; men are affected more commonly. Risk factors are the same as those for atherosclerosis: increasing age, hypertension, diabetes, dyslipidemia (high low-density lipoprotein [LDL] cholesterol, low high-density lipoprotein [HDL] cholesterol), cigarette smoking...

Treatment

Risk factor modification Exercise Antiplatelet drugs Sometimes pentoxifylline or cilostazol for claudication ACE inhibitors PTA or surgery for severe disease All patients require aggressive risk factor modification, including smoking cessation; control of diabetes, dyslipidemia,...

Key Points

Peripheral arterial disease (PAD) occurs almost always in the lower extremities. 50 to 75% of patients also have significant cerebral and/or coronary atherosclerosis. When symptomatic, PAD causes intermittent claudication, which is discomfort in the legs that occurs during walking and is...

Diagnosis

Ankle-brachial BP index Ultrasonography Angiography before surgery PAD is suspected clinically but is underrecognized because many patients have atypical symptoms or are not active enough to have symptoms. Spinal stenosis may also cause leg pain during walking but can be distinguished...

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Disclosure: Nothing to disclose.

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Cyanosis and the Clinical Assessment of Hypoxemia

Cyanosis is a bluish or purplish tinge to the skin and mucous membranes

Before the era of rapid blood gas analysis, clinicians often assessed hypoxemia on clinical grounds alone, primarily by looking for cyanosis in the perioral area and fingers.^[1, 2] Clinical assessment of hypoxemia is now known to be notoriously unreliable for the following reasons:

- A host of factors, from natural skin pigment to room lighting, can affect detection of cyanosis. As with many other physical examination findings, significant interobserver variation occurs in detecting cyanosis. ^[3]Physicians may diagnose cyanosis as an indicator of hypoxemia when the patient has normal oxygen saturation; alternatively, physicians may miss cyanosis when it should be present (the patient has very low oxygen saturation with normal hemoglobin). ^[4]
- Approximately 5 g/dL of unoxygenated hemoglobin in the capillaries generates the dark blue color appreciated clinically as cyanosis. For this reason, patients who are anemic may be hypoxemic without showing any cyanosis.
- Ancillary signs and symptoms of hypoxemia (eg, tachycardia, tachypnea, mental status changes) are nonspecific and of no value in reliably detecting hypoxemia. For example, patients may be dyspneic at rest for reasons other than hypoxemia (ie, they have normal PaO₂ and SaO₂). Conversely, many patients who are chronically hypoxemic (low PaO₂ and/or low SaO₂) are perfectly lucid and without any obvious physical signs of their low oxygen state (at least while at rest).

The requirement of 5 g/dL of reduced (ie, deoxygenated) hemoglobin in the capillaries translates into a reduced hemoglobin content of 3.4 g/dL in arterial blood. ^[5]For this reason, patients with normal hemoglobin manifest cyanosis at higher SaO₂ values than patients with anemia. Refer to the image below and consider the following examples:

- A patient whose hemoglobin content is 15 g/dL (hematocrit approximately 45%) would not generate 5 g/dL of reduced (ie, deoxygenated) hemoglobin in the capillaries until his/her SaO₂ level reached about 79% (PaO₂ 47 mm Hg).
- When hemoglobin content is 9 g/dL (hematocrit approximately 27%), the threshold SaO₂ level for manifesting cyanosis is lowered to about 65% (PaO₂ 35 mm Hg). At this level of hypoxemia, the patient would certainly have other manifestations of hypoxemia (eg, respiratory symptoms, mental status changes) apart from cyanosis.
- With a hemoglobin content of less than 9 g/dL, the patient would likely succumb from hypoxemia before cyanosis became evident.

If hypoxemia is suspected for any reason, some measurement of the oxygen level is necessary (eg, arterial blood gas determination, pulse oximetry). No reliable alternative is available to measurement of PaO₂ or SaO₂ when diagnosing hypoxemia or assessing the need for supplemental oxygen therapy. ^[6]At the same time, one should not rely on the absence of cyanosis as reassurance that hypoxemia is not present.

Other causes of cyanosis include the following:

- **Methemoglobin**
 - Normal hemoglobin unbound to oxygen is called reduced hemoglobin and is symbolized HbFe⁺². Methemoglobin (metHb), the oxidized form of hemoglobin, is HbFe⁺³. Normally, as much as 2% of hemoglobin is in the form of metHb. Because metHb is unable to bind with oxygen, arterial oxygen saturation is reduced by the same amount that metHb is increased.
 - MetHb imparts an intense bluish tinge to the skin; therefore, the cyanosis that comes with [methemoglobinemia](#) is not related to reduced hemoglobin but to oxidized hemoglobin. ^[8, 9]Methemoglobinemia usually occurs as a drug reaction, especially to nitrite or nitrate-containing compounds (eg, nitroglycerin) and to some topical anesthetics. Dahshan and Donovan report a case of severe methemoglobinemia from topical benzocaine in a toddler. ^[10]Dapsone, a drug used in HIV and non-HIV conditions, can also cause methemoglobinemia.

- Although excess metHb reduces the measured SaO₂, PaO₂ is not affected; this is because metHb does not affect transfer of oxygen from the atmosphere to the lungs. A low PaO₂ in a patient with excess metHb suggests a concomitant pulmonary problem. MetHb can be measured in a co-oximeter, a companion to the blood gas machine available in most hospital blood gas laboratories. The co-oximeter also measures carboxyhemoglobin, hemoglobin content, and SaO₂. Note that standard pulse oximeters, which measure SaO₂ using 2 wavelengths of light, do not measure metHb (or carboxyhemoglobin). However, a new generation of pulse oximeters that uses 8 wavelengths of light does have the ability to measure carboxyhemoglobin and metHb (Barker 2006).of light does have the ability to measure COHb and metHb.^[11]
- Sulfhemoglobin
 - Sulfhemoglobinemia is a rare condition caused by sulfur binding with hemoglobin so that oxygen cannot be bound.
 - Unlike metHb, the iron moiety remains in the reduced state (HbFe⁺²).
 - Sulfhemoglobin is similar to metHb in causing low SaO₂ but not affecting PaO₂ and in imparting an intense bluish color to the skin.
- Peripheral cyanosis
 - Peripheral cyanosis is a dusky or bluish tinge to the fingers and toes and may occur with or without central cyanosis (ie, with or without hypoxemia).
 - When unaccompanied by hypoxemia, as determined by blood gas analysis, peripheral cyanosis is caused by peripheral vasoconstriction.
- Pseudocyanosis
 - Pseudocyanosis is a bluish tinge to the skin and/or mucous membranes that is not associated with either hypoxemia or peripheral vasoconstriction. Most causes are related to metals (eg, silver nitrate, silver iodide, silver, lead) or drugs (eg, phenothiazines, amiodarone, chloroquine hydrochloride). One report describes blue-gray discoloration in a man who for years ingested colloidal silver for a urinary tract infection^[12]; his oxygen levels were normal.
 - One report describes a girl with intensely blue skin from food coloring.^[13] Consider pseudocyanosis when the patient has no cardiopulmonary symptoms and the skin does not blanch under pressure. To be sure of the diagnosis, obtain a pulse oximetry or arterial blood gas measurement.

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10. Dahshan A, Donovan GK. Severe methemoglobinemia complicating topical benzocaine use during endoscopy in a toddler: a case report and review of the literature. *Pediatrics.* 2006 Apr. 117(4):e806-9. [\[Medline\]](#).
11. Barker SJ, Curry J, Redford D, Morgan S. Measurement of carboxyhemoglobin and methemoglobin by pulse oximetry: a human volunteer study. *Anesthesiology.* 2006 Nov. 105(5):892-7. [\[Medline\]](#).
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13. Zillich AJ, Kuhn RJ, Petersen TJ. Skin discoloration with blue food coloring. *Ann Pharmacother.* 2000 Jul-Aug. 34(7-8):868-70. [\[Medline\]](#).

Self preparation at class:

Listen information;

Work with patients;

Ask about the problems that have not been found in information given.

Self preparation at home:

Compose the plan of your answer;

Answer the questions to the topic;

Do the test given above.

Questions

I. A patient has uneasiness in the chest and difficult breathing after physical exertion. Some time later cough with foamy liquid phlegm appears. Significant cyanosis develops in the patient. What is the leading mechanism for edema development in this case?

- A. Hydrodynamic
- B. Colloid
- C. Membranogenous
- D. Lymphogenic
- E. Osmotic

II. Uma Kumar, Praveen Aggarwal, Rohini Handa, Renu Saxena, Jyoti Prakash Self-assessment questions: Central cyanosis in a young man

Wali *Postgrad Med J* 1999;75:693-696 doi:10.1136/pgmj.75.889.693

A 25-year-old man presented with bluish discoloration of body, lips and nails since birth. He denied any other significant complaints. General examination revealed presence of central cyanosis with steel-grey complexion of the body. He did not have clubbing of nails. Systemic examination was unremarkable. Investigations showed a haemoglobin of 17.2 g/dl and a normal blood chemistry. The arterial blood gas analysis while the patient was breathing room air revealed a PaO₂ of 100.9 mmHg and an oxygen saturation of 97.8%.

Questions

1. What is the probable diagnosis?
2. What are the common causes of central cyanosis?
3. How would you approach a patient with central cyanosis?
4. What is the appropriate management in the present case?

Recommended literature:

A. Main:

1. "Harrison's principles of internal medicine", Editors: Anthony S. Fauci, Dennis L. Kasper, Stephen L Hauser, Dan L. Longo, Joseph Loscalzo, McGraw-Hill Education / Medical; 19 edition (April 8, 2015), 1-2 volumes, 3000 p.
2. CURRENT Medical Diagnosis and Treatment 2012, Fifty-First Edition (LANGE CURRENT Series) by Stephen McPhee, Maxine Papadakis and Michael W. Rabow (Paperback - Sep 12, 2011)
3. Davidson's Principles and Practice of Medicine: With STUDENT CONSULT Online Access, 21e (Principles & Practice of Medicine (Davidson's)) by Nicki R. Colledge BSc FRCP(Ed), Brian R. Walker BSc MD FRCP(Ed) and Stuart H. Ralston MB ChB MD FRCP FMedSci FRSE (Paperback - Mar 11, 2010)Kumar and Clark's Clinical Medicine, 7e (Kumar, Kumar and Clark's Clinical Medicine) by Parveen J. Kumar (Paperback - Jul 2, 2009)
4. CURRENT Diagnosis and Treatment Emergency Medicine, Seventh Edition (LANGE CURRENT Series) by C. Keith Stone (May 23, 2011)
5. Goldman's Cecil medicine / [edited by] Lee Goldman, Andrew I. Schafer.—24th ed. Elsevier Sanders. Rev. ed. of: Cecil medicine. 23rd ed. – 2012. p.
6. Sonographer's Handbook of Diagnostic Ultrasound by Jason R. Young M.D. (Feb 23, 2011)

Additional literature:

- 1.Kovalyova O.M., Asheulova T.V. Propedeutics to internal medicine. Part 1, Diagnostics. Vinnytsya, Nova Knyha, 2006, 424 p

ANSWERS

I. A. Hydrodynamic

II. Answers:

- 1) - As this patient had central cyanosis since birth and was asymptomatic, the probable diagnosis is congenital methaemoglobinaemia. This diagnosis is supported by a normal arterial blood gas analysis.
- 2) - A number of cardiac and pulmonary diseases can produce central cyanosis. Rarely, central cyanosis is produced by disorders of haemoglobin.
- 3)Duration of cyanosis (cyanosis present since birth is usually due to congenital heart disease or methaemoglobinaemia), symptoms related to cardiovascular and pulmonary systems, and exposure to drugs or chemicals that may produce methaemoglobinaemia are important points in the history of a patient who presents with central cyanosis. Central cyanosis should be differentiated from peripheral cyanosis, as the tongue is spared in the latter condition. Clubbing, and any abnormality in cardiac and pulmonary systems should be looked for. Clubbing with cyanosis is present in patients with congenital cyanotic heart diseases, and occasionally in patients with pulmonary diseases such as lung abscess or pulmonary arteriovenous shunts. Chest radiograph, electrocardiograph and echocardiograph may be obtained if there are any suggestions of pulmonary or cardiovascular diseases on history and examination. If there is no

evidence of cardiopulmonary disease, a diagnosis of methaemoglobinaemia should be considered. Pulse oximetry may be helpful in detecting methaemoglobinaemia. Pulse oximeter measures the light absorbance changes by arterial pulsations at only two wavelengths, one in the red (660 nm) and the other in the near infrared (940 nm) range. Methaemoglobin has a high absorbance at both wavelengths, tending to drive the ratio of absorbance toward 1, which corresponds to an oxygen saturation of nearly 85%. Hence, with a high level of methaemoglobin in the blood, pulse oximeter readings will tend to be around 85%. In contrast, the saturation as reported on an arterial blood gas is a calculated value based on the partial pressure of dissolved oxygen and assumes no abnormal haemoglobin is present. Therefore, the reported oxygen saturation from the laboratory is generally higher than that measured with a pulse oximeter. This difference is called the saturation gap and is typically more than 5% in patients with methaemoglobinaemia. Qualitative confirmation of methaemoglobinaemia is done by blood spectrophotometry. Once confirmed, electrophoresis of haemoglobin and estimation of methaemoglobin reductase are required to diagnose the cause of methaemoglobinaemia.

In the present case, the oxygen saturation measured by pulse oximetry was 90%, and the oxygen saturation gap 7.8%. Spectrophotometry of the haemolysate of the patient's blood revealed a methaemoglobin band at 630 nm. On quantification estimation, methaemoglobin was found to be 30%. Electrophoresis of the haemoglobin revealed no abnormal haemoglobin. Estimation of NADH-cytochrome b5 reductase could not be done due to the lack of laboratory facilities.

4)The patient was given ascorbic acid tablets (500 mg) twice daily and cyanosis disappeared within a week; it reappeared on cessation of the treatment. However, since the patient was clinically asymptomatic, no further treatment was given and the patient was reassured.

Methodical recommendations consisted by

Kulishov S.K.