

# Cyanosis

## What is cyanosis?

Cyanosis is the abnormal blue discoloration of the skin and mucous membranes, caused by an increase in the deoxygenated haemoglobin level to above 5 g/dL. Patients with anaemia do not develop cyanosis until the oxygen saturation ( $\text{SaO}_2$ ) has fallen to lower levels than for patients with normal haemoglobin levels and patients with polycythaemia develop cyanosis at higher oxygen saturation levels.

Cyanosis can be divided into either central or peripheral. <sup>[1]</sup>

### Central cyanosis

- Central cyanosis is caused by diseases of the heart or lungs, or abnormal haemoglobin (methaemoglobinaemia or sulfhaemoglobinaemia).
- Cyanosis is seen in the tongue and lips and is due to desaturation of central arterial blood resulting from cardiac and respiratory disorders associated with shunting of deoxygenated venous blood into the systemic circulation.
- Patients who are centrally cyanosed will usually also be peripherally cyanosed.
- Associated features of central cyanosis depend on the underlying cause and include dyspnoea and tachypnoea, secondary polycythaemia and bluish or purple discolouration of the oral mucous membranes, fingers and toes. The hands and feet are usually normal temperature or warm but not cold unless there is an associated poor peripheral circulation.

### Peripheral cyanosis

- Peripheral cyanosis is caused by decreased local circulation and increased extraction of oxygen in the peripheral tissues.
- Isolated peripheral cyanosis occurs in conditions associated with peripheral vasoconstriction and stasis of blood in the extremities, leading to increased peripheral oxygen extraction - eg, congestive heart failure, circulatory shock, exposure to cold temperatures and abnormalities of the peripheral circulation.
- Features of peripheral cyanosis therefore include peripheral vasoconstriction and bluish or purple discolouration of the affected area, which is usually cold. Peripheral cyanosis is most intense in nail beds and may resolve with gentle warming of the extremity. The mucous membranes of the oral cavity are usually spared.

Unless the cause is already established, episodes of central cyanosis require urgent assessment, especially infants and young children who require urgent admission.

## Differential diagnosis

### Central cyanosis in neonates

Central cyanosis should clear within a few minutes of the birth. Peripheral cyanosis clears within a few days. Increased sensitivity of the peripheral circulation to cold temperature may persist well into infancy.

- Transient cyanosis after delivery can occur without clear diagnosis. One study suggested that a significant proportion may have gastro-oesophageal reflux.<sup>[2]</sup>

- Cardiac and circulatory causes include:
  - [Transposition of the great arteries](#).
  - [Fallot's tetralogy](#).
  - Stenosis or atresia of the pulmonary valve or tricuspid valve.
  - Total anomalous pulmonary venous return (all four pulmonary veins drain into systemic veins or the right atrium, associated with a right-to-left shunt through an [atrial septal defect](#)).
  - Hypoplastic left heart.
  - Truncus arteriosus (a single great artery leaves the heart and divides into the pulmonary artery and the aorta).
  - Persistent fetal circulation (blood continues to be shunted through the foramen ovale and a [patent ductus arteriosus](#)).
- Respiratory causes include:
  - [Respiratory distress syndrome](#).
  - Birth asphyxia, [birth injury](#) or haemorrhage.
  - Transient tachypnoea of the newborn.
  - [Pneumothorax](#).
  - [Meconium aspiration](#).
  - [Pulmonary oedema](#).
  - [Congenital diaphragmatic hernia](#).
  - Tracheo-oesophageal fistula.
  - [Pleural effusion](#).
  - Obstruction of the upper respiratory tract – for example, in Pierre Robin sequence or choanal atresia.
- Other causes include infection, seizures and metabolic abnormalities – eg, hypoglycaemia, hypomagnesaemia.

## Central cyanosis in adults

- Lung disease: any severe respiratory disease, [pulmonary oedema](#), [pulmonary embolism](#), decreased PO<sub>2</sub> of inspired air (eg, high altitude), [severe pneumonia](#), [chronic obstructive pulmonary disease \(COPD\)](#), [acute severe asthma](#), [acute adult respiratory distress syndrome](#).
- Right-to-left cardiac shunt: eg, cyanotic [congenital heart disease](#), [Eisenmenger's syndrome](#), pulmonary arteriovenous fistulas.
- Abnormal haemoglobins (do not allow adequate oxygen uptake):
  - Methaemoglobinaemia: may be genetic or associated with certain drugs - eg, quinones, primaquine, sulfonamides. [3]
  - Sulphaemoglobinaemia is usually associated with certain drugs, especially sulfonamides.
- [Polycythaemia vera](#) or any other cause of polycythaemia may present with central cyanosis.

## **Causes of peripheral cyanosis**

- All causes of central cyanosis also cause peripheral cyanosis.
- Reduced cardiac output - eg, heart failure, shock.
- [Peripheral arterial disease](#) - eg, thrombosis, atheroma or embolism.
- Vasoconstriction:
  - [Cold exposure](#).
  - [Raynaud's phenomenon](#).
  - Acrocyanosis: benign, caused by spasm of smaller skin arteries and arterioles, causing hands and feet to be cold and mottled. [4]
  - Erythrocyanosis: usually affects young women; blotches of cyanosis occur in the lower legs.
  - Beta-blocker drugs.
- Venous obstruction (eg, lower limb [deep vein thrombosis](#)) can occasionally produce a painful blue leg (phlegmasia cerulea dolens). [Obstruction of the superior vena cava](#) can cause cyanosis, venous engorgement and oedema affecting the face.

# Symptoms and signs of cyanosis (presentation)

## Symptoms

- Associated symptoms may include:
  - Chest pain: cyanosis associated with pleuritic chest pains may be due to pulmonary emboli or pneumonia. Pulmonary oedema may cause dull, aching chest tightness.
  - Dyspnoea: sudden onset of dyspnoea can occur with pulmonary emboli, pulmonary oedema or asthma.

## Signs

- Temperature: pneumonia and pulmonary emboli may be associated with pyrexia.
- Inspection:
  - Central cyanosis produces a blue discolouration of the mucous membranes of the lips and tongue as well as the extremities.
  - Peripheral cyanosis affects the extremities and the skin around the lips but not the mucous membranes.
  - The combination of clubbing and cyanosis is frequent in congenital heart disease and may also occur in pulmonary disease (lung abscess, bronchiectasis, cystic fibrosis) and pulmonary arteriovenous shunts.
  - The jugular venous pressure is elevated with congestive cardiac failure.

- Respiratory examination:
  - Poor chest expansion occurs with chronic bronchitis, and asthma. Unilateral reduced chest expansion may occur with lobar pneumonia.
  - Dullness to percussion occurs over an area of consolidation.
  - Localised crepitation may be heard with lobar pneumonia. Crepitation is more widespread with bronchopneumonia and pulmonary oedema. Air entry may be poor with COPD and asthma. Bronchial breathing may be auscultated over an area of consolidation, and wheezing may be heard with asthma.
- Heart sounds may be abnormal or added heart murmurs may suggest a cardiac origin.
- Localised features suggesting an aetiology of peripheral cyanosis, such as oedema in venous insufficiency or absent peripheral pulses and ischaemia in arterial occlusion.

## Diagnosing cyanosis (investigations)

History:

- Age and nature of onset:
  - Cyanosis due to congenital heart disease causing anatomical right-to-left shunts may have been present since birth or the first few years of life.
  - Acute onset of cyanosis may be due to pulmonary emboli, cardiac failure, pneumonia or asthma.
  - Patients with COPD develop cyanosis over many years and associated polycythaemia may exacerbate the degree of cyanosis.
  - The description may be typical of Raynaud's phenomenon.
  - Past history: cyanosis can result from any lung disease of sufficient severity.
  - Drug history: certain drugs may cause methaemoglobinaemia (eg, nitrates, dapsone) or sulphaemoglobinaemia (eg, metoclopramide).

#### Tests:

- **Arterial blood gases:** oxygen saturation for patients with central cyanosis is usually below 85%. If the oxygen saturation does not increase to above 95% while the patient inhales 100% oxygen then there is likely to be pulmonary intravascular shunting of blood bypassing the alveoli (eg, right-to-left intracardiac shunt or pulmonary arteriovenous fistulae).
- FBC: haemoglobin level is increased with chronic cyanosis. White cell count is increased in pneumonia and pulmonary embolism.
- ECG: features of myocardial infarction; nonspecific ST abnormalities with pulmonary emboli.
- CXR: pneumonia, pulmonary infarction, cardiac failure.
- Sputum and blood cultures: pneumonia.
- Ventilation-perfusion scan - 'VQ scan', or pulmonary angiography: pulmonary embolus.
- Echocardiography: cardiac defects.

- Haemoglobin spectroscopy: methaemoglobinaemia, sulfhaemoglobinaemia.
- Digital subtraction angiography: acute arterial occlusion.
- Duplex Doppler or venography: acute venous occlusion.

## Management

- Oxygen therapy for patients who are hypoxic.
- Treatment of the underlying cause.

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## Further reading

- [Desai K, Rabinowitz EJ, Epstein S](#); Physiologic diagnosis of congenital heart disease in cyanotic neonates. *Curr Opin Pediatr.* 2019 Apr;31(2):274-283. doi: 10.1097/MOP.0000000000000742.

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