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Diagnostic procedures to detect the causes of hypoxic respiratory failure:
is being less invasive necessarily better?

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Educational aims

- To review the diagnostic approach to the most relevant pulmonary causes of hypoxic acute respiratory failure.
- To focus on the use of invasive and noninvasive diagnostic techniques for these diseases.

Summary

Both acute and chronic pulmonary disorders can lead to hypoxic acute respiratory failure (ARF), in which patients are unable to maintain arterial oxygenation despite not retaining carbon dioxide. The three major acute disorders which can underly ARF are (ventilator-assisted) pneumonia (VAP), acute respiratory distress syndrome (ARDS) and pulmonary embolism. Each of these conditions poses its own diagnostic and treatment difficulties. This article will review diagnostic procedures relating to these most relevant causes of this syndrome.

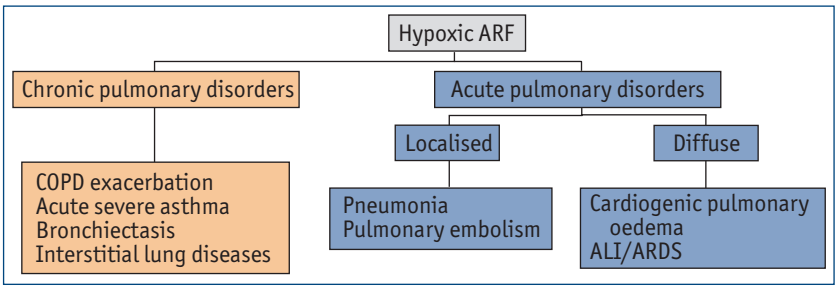


Figure 1
The most important clinical conditions causing ARF. ALI: acute lung injury.

Hypoxic ARF is a syndrome characterised by the inability to maintain correct arterial oxygenation in the absence of carbon dioxide retention [1]. Figure 1 shows the most important clinical conditions causing hypoxic ARF, and may serve as an outline for the first diagnostic approach in this syndrome. This article will review diagnostic procedures relating to the most relevant causes of this syndrome.

Ventilator-associated pneumonia (VAP)

The clinical criteria for the diagnosis of VAP are based on the presence of a new or progressive pulmonary radiographic infiltrate, plus at least two of the following three clinical features: fever; leukocytosis or leukopenia; and purulent respiratory secretions [2]. While these criteria are indicative of suspicion, unfortunately they are not specific to VAP. However, these are the most accurate criteria for the initiation of empirical antibiotic therapy, which should be started only after obtaining a lower respiratory tract sample for culture. Sensitivity to the presence of VAP is increased, at the expense of specificity, if only one criterion is used, whereas the inverse applies if three criteria are applied.

Failure to initiate prompt and effective therapy is consistently associated with increased mortality. It is important to recognise the variability of bacteriology between hospitals and to take local microbiological data into account when adapting treatment recommendations. Tailoring therapy to the results of respiratory tract cultures may avoid the overuse of antibiotics by focusing on accurate diagnosis. The use of sputum and tracheal aspirate Gram staining is of uncertain value, but may help in the selection of initial antimicrobial therapy. A sterile culture of respiratory secretions in the absence of a new antibiotic in the previous 72 hours rules out the presence of bacterial pneumonia in most cases. Blood cultures should be collected from all patients with suspected VAP, but a positive result can indicate the presence of either pneumonia or extrapulmonary infection.

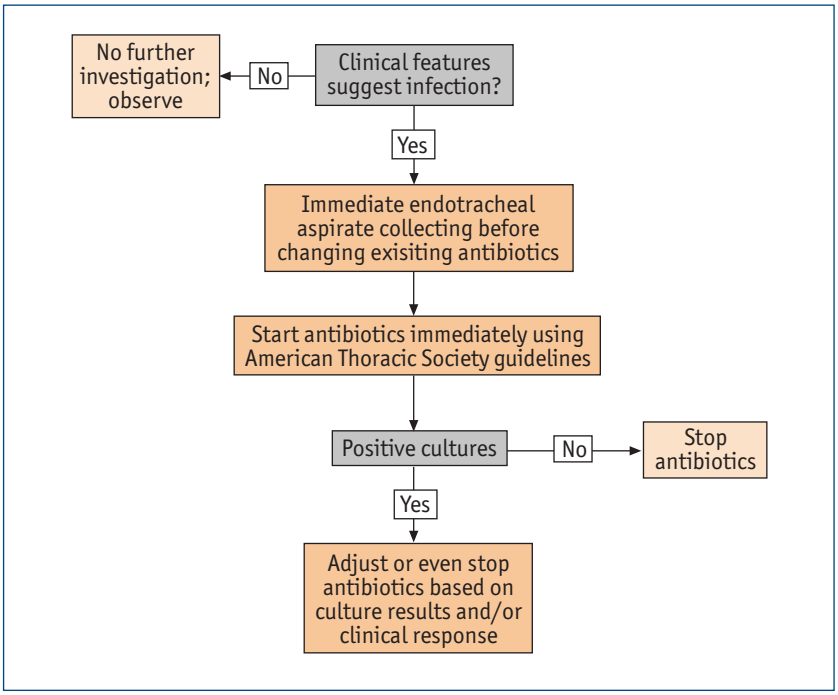
In the management of VAP, two different diagnostic approaches may be recommended, depending on whether invasive diagnostic techniques are used [3]:

> The clinical algorithm is based on the collection of tracheal aspirates prior to initiating empirical antibiotic therapy. Antibiotic therapy is then adjusted or even stopped based on culture results and/or clinical response (figure 2).

> The invasive and quantitative culturing strategy is based on the immediate sampling of distal airways before changing existing antibiotics.

Antibiotic treatment is then adjusted or stopped based on direct specimen examination, the presence or absence of severe sepsis and the results of quantitative cultures (figure 3).

Figure 2
The clinical algorithm for managing VAP.



Acute respiratory distress syndrome (ARDS)

Owing to the differing definitions of ARDS, there are wide variations in incidence estimates. This syndrome consists of an acute, severe alteration in the lung structure and function characterised by hypoxaemia, low respiratory system compliance, low functional residual capacity and diffuse radiographic infiltrates, along with increased lung endothelial and alveolar epithelial permeability.

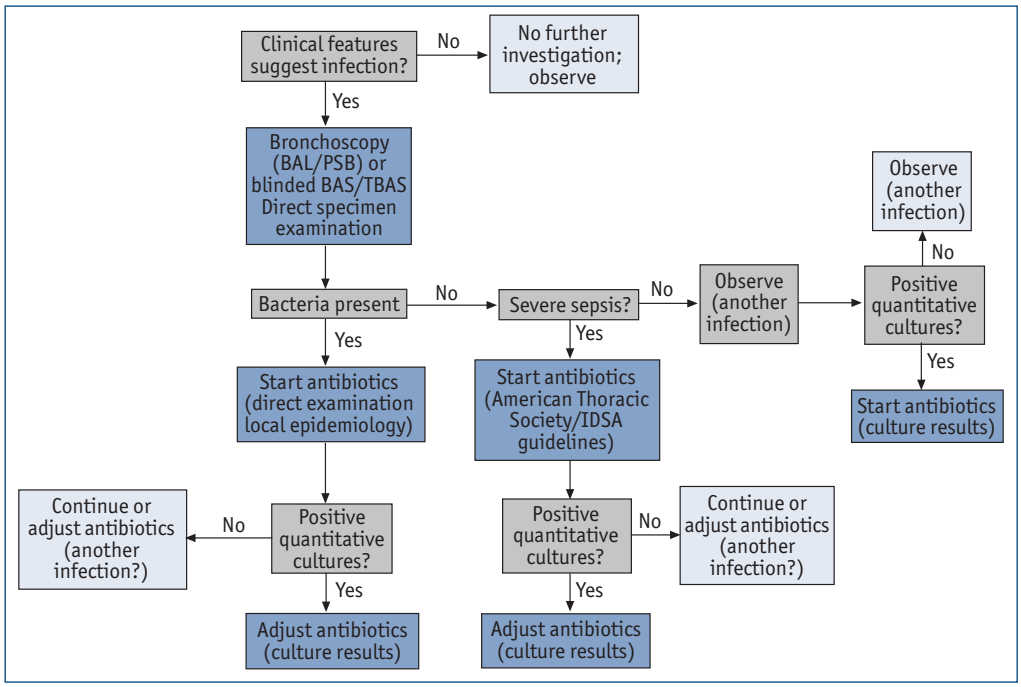


Figure 3
The invasive and quantitative algorithm for managing VAP. BAL: bronchoalveolar lavage; PSB: protected specimen brush; BAS: bronchial aspirate; TBAS: tracheobronchial aspirate; IDSA: Infectious Diseases Society of America.

It is important to recognise the presence of risk factors in the diagnosis of ARDS. The strongest evidence to support a causal relationship between a risk factor and ARDS covers sepsis, trauma, multiple blood transfusions, aspiration of gastric contents, pulmonary contusion, pneumonia and smoke inhalation. There is weaker evidence to suggest that disseminated intravascular coagulation, fat embolism and cardiopulmonary bypass can cause ARDS.

The pathogenesis of ARDS has been divided into pulmonary and extrapulmonary causes. This is an easy distinction in most cases, based on an accurate history and clinical assessment, particularly in the early phases of ARDS. However, the two processes are likely to overlap with time and with the structural changes in the lungs [4].

The original definition of ARDS was based on the presence of severe dyspnoea, tachypnoea, hypoxaemia refractory to oxygen therapy, reduced lung compliance and diffuse alveolar infiltration on chest radiography. Subsequently, cardiogenic pulmonary oedema was explicitly excluded, with suggestions for a quantitative threshold for pulmonary wedge capillary pressure, and this was followed by the introduction of a quantitative measurement of respiratory system compliance. In 1988, the "lung injury score" was proposed to quantify the presence, severity and evolution of acute and chronic damage involving lung parenchyma [5]. An American–European consensus conference on ARDS has since defined ARDS as a syndrome of inflammation and increased permeability that can not be explained by, but may coexist with, left atrial or pulmonary capillary hypertension [6]. The definition of ARDS according to this consensus conference was the presence of arterial hypoxemia with an arterial oxygen tension/inspiratory oxygen fraction ratio <200 mmHg (26.6 kPa), bilateral pulmonary infiltrates and either a clinical judgment or objective evidence of absence of increased pulmonary capillary wedge pressure.

The pulmonary artery catheter (PAC) has been a cornerstone of the haemodynamic monitoring of critically ill patients for many years. The PAC provides information about cardiac output, right- and left-heart filling pressures and pulmonary arterial pressures, and it enables measurement of the oxygen content of mixed venous blood. The pulmonary artery occlusion pressure (PAOP) is a surrogate measure of left atrial pressure and (in the absence of mitral valve disease, increased pulmonary venous resistance or wedging of the catheter in smaller pulmonary arterioles) of left ventricular end-diastolic pressure. As such, it provides an estimate of the fluid filtration pressure in pulmonary vessels. Since compliance of the left heart is extremely variable, PAOP is not a good predictor of end-diastolic volume and hence stroke volume. Several studies have demonstrated the inaccuracy of PAOP as a measure of cardiac preload and fluid responsiveness. The PAC can be diagnostically useful because it generally differentiates specific types of shock (hypovolemic, distributive and cardiogenic) and pulmonary oedema (hydrostatic *versus* permeability).

Table 1 Common symptoms and signs of acute pulmonary embolism

Symptoms	Signs
Dyspnoea (78%)	Tachypnoea (73%)
Pleuritic chest pain (59%)	Crackles (55%)
Cough (43%)	Leg swelling (31%)
Leg pain (27%)	Tachycardia (30%)
Haemoptysis (16%)	Loud pulmonic component of second heart sound (23%)
Wheezing (14%)	Wheezes (11%)
Palpitations (13%)	Diaphoresis (10%)
Angina-like pain (6%)	Fever (7%)

Educational question

1. When are invasive diagnostic techniques indicated in patients with hospital-acquired pneumonia?

a) In patients aged 18–65 years.
b) In case of unfavourable evolution alter 72 hours of empirical antimicrobial treatment.
c) If pneumonia is accompanied by fever and severe worsening of general state.
d) In case of isolation of *Pseudomonas aeruginosa* in blood cultures.
e) If patients can expectorate but a sputum of good quality does not show bacteria in the Gram stain.

The invasiveness of the PAC and the recent controversy about its utility in the care of critically ill patients [7, 8] have renewed interest in alternative minimally invasive haemodynamic monitoring devices. Among other techniques, two-dimensional echocardiography and transoesophageal Doppler monitoring may be useful in patients with suspected ARDS. Although strictly a diagnostic test rather than a monitoring device, its availability in intensive care units has contributed to a decrease in PAC use. Transoesophageal and, to a lesser extent, transthoracic echocardiography allow a rapid differential diagnosis of shock with the assessment of left and right ventricular function, end-diastolic volume and the inspiratory changes in inferior vena cava diameter. The continuous oesophageal Doppler provides monitoring of stroke volume and an estimate of cardiac preload and fluid responsiveness. Although the initial studies performed in critically ill patients demonstrated good correlation of pulse Doppler echo with thermodilution cardiac output with PAC, the need for additional training limits its use in critically ill patients.

Pulmonary embolism

Pulmonary embolism is one of the most common cardiovascular disorders and accounts for substantial morbidity and mortality in hospitalised patients. Recognising the presence of risk-factors for venous thrombosis (and thus pulmonary embolism) is a key in suspecting the diagnosis and identifying prophylactic needs. Most risk factors for venous thrombosis can be derived from the triad of stasis, venous injury and hypercoagulability. The incidence of venous thrombosis increases with the severity of illness and the number of risk-factors. Patients in the ICU are at especially high risk owing to severe underlying disease, immobility and veno-invasive catheters and devices. [9, 10].

Clinical evaluation alone is not sufficient to diagnose and exclude pulmonary embolism, since the clinical manifestations are nonspecific. The most common clinical symptoms are shown in table 1.

The most critical step in diagnosing pulmonary embolism is to have a clinical suspicion of the problem. Careful attention to symptoms and risk factors is essential in raising the suspicion of the disease, as well as in identifying the need for appropriate prophylaxis. Common initial tests in the evaluation for pulmonary embolism include spiral chest computed tomography (CT) or ventilation/perfusion scintigraphic scanning. In critically ill patients, lower extremity ultrasound and echocardiography have important ancillary roles, particularly in the case of patients with massive pulmonary embolism, who may present with extreme hypoxaemia and/or critical hypotension. In these patients, in addition to diagnosis through spiral CT or portable perfusion scans, a right ventricular dilation and dysfunction are also likely to be seen by echocardiography, and subsequent changes after therapy has been initiated may serve as a follow-up control of the efficacy of the treatment.

Also important is the exclusion of pulmonary embolism in patients with clinical suspicion, since anticoagulant therapy carries risks and complications. In this case, D-dimer, as a specific by-product of cross-linked fibrin, has been extensively evaluated in the setting of suspected acute deep-venous thrombosis and pulmonary embolism. The quantitative rapid ELISA D-dimer assay is very sensitive and has a high negative predictive value for excluding deep-venous thrombosis and pulmonary embolism in outpatients, and hence a negative value is as diagnostically useful in excluding pulmonary embolism as a negative lung scan or a negative duplex ultrasonography finding [11]. However, D-dimer is less useful in the complex, critically ill patients, since many conditions are associated with elevated levels in these patients.

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Suggested answer

1. b.