RATIONAL TESTING

Interpreting arterial blood gas results

Nicholas J Cowley,1 Andrew Owen,1 Julian F Bion2

You have been called to see a 69 year old man on a surgical ward because he has become drowsy and short of breath. He had a large bowel resection the previous day, has a background of type 2 diabetes, and is a current smoker. On examination his arterial blood pressure is 104/65 mm Hg, his heart rate 132 beats/min and irregular, and his respiratory rate 22 breaths/min; his oxygen saturations with pulse oximetry are 94% on supplemental oxygen via a 40% Venturi-type mask. He is slightly confused and is complaining of abdominal pain despite using patient controlled analgesia with morphine. His chest is clear on auscultation.

What is the next investigation?

You take a blood specimen for analysis of arterial blood gases for rapid biochemical evaluation to guide diagnosis and initial management. Table 1 shows the results. It is important to adopt a systematic approach to interpreting results of arterial blood gases, as outlined in table 2, preceded by a brief history and focused clinical examination.

Step 1: Assess oxygenation
Arterial oxygen tension (PaO₂) is the partial pressure of oxygen in arterial blood. The main determinants of PaO₂ are the inspired oxygen concentration, alveolar gas exchange, and, to a lesser extent, tissue oxygen consumption. The ratio between the PaO₂ and the inspired oxygen concentration expressed as a fraction (FiO₂) is termed the PaO₂/FiO₂ ratio or the P/F ratio. This is a useful index for determining the presence and severity of impaired alveolar gas exchange and is easier to calculate than alternative indices, such as the alveolararterial gradient. Estimations of FiO₂ based on oxygen flow through a standard facemask are rarely accurate. The FiO₂ will vary according to the oxygen delivery device used, the presence of a reservoir, and the patient’s inspiratory flow rate. A healthy individual would be expected to have a P/F ratio above 50, with lower values signifying impaired gas exchange. Patients with acute lung injury or acute respiratory distress syndrome have values below 40 and 26.7 respectively, in addition to other required diagnostic criteria.1

The PaO₂ in our example patient (8.9 kPa) is below normal, but as he is breathing supplemental oxygen rather than room air, this represents significant impairment of oxygen uptake, probably from intrapulmonary shunting. Intrapulmonary shunting occurs when areas of lung are perfused without adequate ventilation—for example, after atelectasis, consolidation, fluid accumulation, or acute inflammation of lung tissue. In the calculation of his P/F ratio, the inspired oxygen concentration is determined by the Venturi-type mask (in this case 0.4). Thus, his P/F ratio is calculated as (8.9/0.4 = 22.3), representing marked impairment in gas exchange.

Be aware that the measurement of oxygen saturation using standard pulse oximetry and some arterial blood gas analysers may give misleading results. Oxygen saturations are falsely raised in carbon monoxide poisoning (which produces carboxyhaemoglobin) and depressed in methaemoglobinemia, which is caused by various drugs or toxins, including nitrate fertilisers, some local anaesthetics, and sulphonamide antibiotics. These conditions cannot be readily distinguished clinically, and analysers using co-oximetry to analyse haemoglobin oxygen saturations will report levels of carboxyhaemoglobin and methaemoglobin.2 However, if oxygen saturation is not available on the analyser, pay close attention to the patient’s clinical history.

Step 2: Assess pH
The pH is usually maintained within a tight range between 7.35 and 7.45, and a small change in the pH will result in a large change in the hydrogen ion concentration, making even modest derangements in the pH of clinical significance. Our example patient has an acidosis (pH of 7.25) or, more accurately, an acidemia (abnormally low blood pH). In some cases an underlying acid-base disorder can be disguised by

Table 1: Report of arterial blood gases for the hypothetical patient described

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Value (reference range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.25 (7.35-7.45)</td>
</tr>
<tr>
<td>Partial pressure of oxygen (PaO₂) (kPa)</td>
<td>8.9 (11-13)</td>
</tr>
<tr>
<td>Partial pressure of carbon dioxide (PaCO₂) (kPa)</td>
<td>5.9 (4.7-6.0)</td>
</tr>
<tr>
<td>Standard bicarbonate(sHCO₃⁻) (mmol/L)</td>
<td>18.5 (22-26)</td>
</tr>
<tr>
<td>Base excess (mmol/L)</td>
<td>−7.0 (−2 to +2)</td>
</tr>
<tr>
<td>Haemoglobin g/dL</td>
<td>6.1 (13-17)</td>
</tr>
<tr>
<td>Sodium (Na⁺) (mmol/L)</td>
<td>148 (136-145)</td>
</tr>
<tr>
<td>Potassium (K⁺) (mmol/L)</td>
<td>3.0 (3.5-5.0)</td>
</tr>
<tr>
<td>Calcium (Ca²⁺) (mmol/L)</td>
<td>1.2 (1.1-1.4)</td>
</tr>
<tr>
<td>Chloride (Cl⁻) (mmol/L)</td>
<td>108 (98-106)</td>
</tr>
</tbody>
</table>

*61 (130-170 g/L)

Table 2: Guide to systematic approach to analysis of a report of arterial blood gases

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Assess oxygenation</th>
<th>The inspired oxygen concentration. Calculate the P/F ratio,* particularly if patient is receiving supplemental oxygen. Assess haemoglobin saturations, if testing is available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 2</td>
<td>Assess pH</td>
<td>Is the patient acidaemic or alkalaeic?</td>
</tr>
<tr>
<td>Step 3</td>
<td>Assess sHCO₃⁻ and base excess</td>
<td>An abnormal base excess and sHCO₃⁻ indicates a primary or compensatory metabolic acid-base disturbance</td>
</tr>
<tr>
<td>Step 4</td>
<td>Assess PaCO₂</td>
<td>Is there a primary respiratory acidosis or alkalosis? Is low or high PaCO₂ compensating for a metabolic acidosis or alkalosis respectively? The respiratory system will not normally overcorrect a metabolic acid-base disturbance, and so if this is the case, consider a mixed metabolic and respiratory disorder</td>
</tr>
<tr>
<td>Step 5</td>
<td>Review additional analytes</td>
<td>Review electrolytes, and consider calculation of anion gap to further assess any metabolic acidosis. Haemoglobin, glucose, and lactate concentrations may be available and may be helpful in determining the cause of any acid-base abnormality</td>
</tr>
<tr>
<td>Step 6</td>
<td>Reassess</td>
<td>After institution of a management plan, repeat clinical assessment and consider repeat analysis of arterial blood gases to guide further treatment</td>
</tr>
</tbody>
</table>

LEARNING POINTS

Interpretation of arterial blood gases requires a systematic assessment of oxygenation, pH, standard bicarbonate(sHCO₃⁻) and base excess, partial pressure of carbon dioxide(PaCO₂), and additional analytes

The P/F ratio (ratio between the PaO₂ and the inspired oxygen concentration expressed as a fraction) is a useful guide to the presence and severity of impaired alveolar gas exchange. Reassess all acutely ill patients regularly, and consider repeat arterial blood gas analysis to guide further treatment.

Errors in blood gas analysis are dependent more on the clinician than on the analyser.

Cite this as: BMJ 2013;346:f16

doi: 10.1136/bmj.f16

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This series of occasional articles provides an update on the best use of key diagnostic tests in the initial investigation of common or important clinical presentations. The series advisers are Steve Atkin, professor, head of department of academic endocrinology, diabetes, and metabolism, Hull York Medical School; and Eric Kilpatrick, honorary professor, department of clinical biochemistry, Hull Royal Infirmary, Hull York Medical School. To suggest a topic for this series, please email us at practice@bmj.com.
compensatory mechanisms that normalise pH, referred to as a compensated acidosis or alkalosis.

**Step 3: Assess standard bicarbonate (sHCO₃⁻) and base excess**

Most blood gas analysers will calculate values for standard bicarbonate (sHCO₃⁻) and base excess, either of which can be used to isolate metabolic causes of acid-base disturbance. These values are particularly useful when the cause of the acid-base disorder has both metabolic and respiratory components. The contribution of any respiratory acid-base disorder to the acid-base disturbance can be assessed next to identify any ventilatory component in the disturbance.

**Step 4: Assess arterial partial pressure of carbon dioxide (PaCO₂)**

The arterial partial pressure of carbon dioxide (PaCO₂) should be assessed next to identify any ventilatory component in the acid-base disturbance. A raised PaCO₂ value will contribute towards an acidosis, and a low value towards an alkalosis. In our patient the PaCO₂ value is not raised, indicating that the acidosis is not respiratory in origin. If respiratory drive were normal, compensatory hypocarbia would be expected. However, in our example, the patient’s PaCO₂ value is at the upper limit of normal, indicating an inadequate ventilatory response, which could be caused by opioid analgesia, coexistent chronic obstructive pulmonary disease, severe abdominal pain splinting breathing, or incipient ventilatory failure. Thus our patient has a metabolic acidosis without respiratory compensation.

The presence of a normal PaO₂ value, or normal values on pulse oximetry, does not rule out respiratory failure, particularly in the presence of supplemental oxygen. An unexpectedly high PaCO₂ value is a more sensitive marker of ventilatory failure than pulse oximetry or PaO₂, particularly in the presence of supplemental oxygen, as it has a close relationship with depth and rate of breathing.

**Step 5: Assess additional analytes**

Many “point of care” arterial blood gas analysers can now evaluate electrolytes, haemoglobin, glucose, and lactate. The
Sources of error in analysis of arterial blood gases

<table>
<thead>
<tr>
<th>Type of error</th>
<th>Consequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient identification error</td>
<td>Wrong patient treated</td>
</tr>
<tr>
<td>Contamination of sample—eg. by heparin anticoagulant when obtained by flush from indwelling arterial cannula</td>
<td>Inaccurate values</td>
</tr>
<tr>
<td>Incorrect sampling tubes—eg excess heparin anticoagulant</td>
<td>Sample dilution and measurement errors</td>
</tr>
<tr>
<td>Haemolysis of blood</td>
<td>Errors in measurement of electrolytes and packed cell volume</td>
</tr>
<tr>
<td>Air bubbles in specimen</td>
<td>Falsely raises PaCO₂ and pH and lowers PaO₂</td>
</tr>
<tr>
<td>Sample not representative</td>
<td>If supplemental oxygen is added or removed around time of analysis, results may be unrepresentative. Ensure supplemental oxygen is recorded on report</td>
</tr>
<tr>
<td>Delay in processing the sample</td>
<td>Ongoing metabolism within sample falsely raises PaCO₂ and lowers PaO₂ and pH</td>
</tr>
</tbody>
</table>

Analytical errors

- Calibration error: Drift may cause inaccuracy—many machines suppress results if unreliability is detected.
- Interference: Examples: haemolysis, icterus, and lipaemia can cause inaccuracies.
- Measurement method: Example: haemoglobin measured using “conductivity” may be inaccurate in certain situations.
- Hypothemia: Results will differ if analysis is corrected to the patient’s body temperature, although the merits of performing this correction are debated. If this information is inputted, analysers may present results corrected for body temperature, as well as uncorrected.

This is part of a series of occasional articles on common problems in primary care. The BMJ welcomes contributions from GPs.

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A 30 year old woman visits her general practitioner complaining of itchy eyes for six months, aggravated by computer use in her job as a clerk. Dry eye is a common multifactorial condition of the tear and ocular surface. In ambulatory settings it may commonly result from increased tear evaporation (resulting from, for example, blepharitis or contact lens wear); tear hyposecration (from, for example, age related or anticholinergic drugs); and mucous dysfunction (mucus secreting goblet cells in the conjunctiva may be damaged after previous infectious conjunctivitis). Severe dry eye resulting from systemic diseases is uncommon in primary care but conditions predisposing to dry eye should be documented (box).

What you should cover

History

Are the symptoms consistent with dry eye?—Ask about symptoms of dry eye, such as chronic burning, grittiness, and visual fluctuations. Paradoxically, patients may complain of watery eyes owing to eye irritation and reflex tearing. A complaint strongly suggestive of dry eye is worsening of symptoms by prolonged visual tasks, exposure to wind, and air conditioning.

10-MINUTE CONSULTATION

Dry eye

Louis Tong,12 Jeremy Tan,34 Julian Thumboo,45 Gabriel Seow6

A 30 year old woman visits her general practitioner complaining of itchy eyes for six months, aggravated by computer use in her job as a clerk. Dry eye is a common multifactorial condition of the tear and ocular surface. In ambulatory settings it may commonly result from increased tear evaporation (resulting from, for example, blepharitis or contact lens wear); tear hyposecration (from, for example, age related or anticholinergic drugs); and mucous dysfunction (mucus secreting goblet cells in the conjunctiva may be damaged after previous infectious conjunctivitis). Severe dry eye resulting from systemic diseases is uncommon in primary care but conditions predisposing to dry eye should be documented (box).

Step 6: Reassess

After the start of treatment, regular reassessment will be needed. Repeated blood gas analysis can demonstrate response to treatment and guide further treatment. In a high dependency setting, consider inserting an arterial cannula for obtaining repeated specimens to avoid multiple arterial punctures.

Accuracy

With advances in machine performance and quality assurance,4–6 two thirds of errors in point of care analysis of arterial blood gases are now attributable to clinicians.9 10 Attention to detail in sampling technique and processing is thus essential (table 3). If obtaining an arterial sample is difficult, venous blood (taken without a tourniquet) will provide a reasonable substitute for all analytes other than PaO₂, although this should be clearly marked as such to avoid confusion in interpretation.

Outcome

Our patient received adequate analgesia to allow more comfortable breathing and was monitored closely for evidence of bleeding. He received fluid therapy and a blood transfusion, which coincidentally increased the serum potassium concentration. This treatment caused resolution of his acid-base disturbance on subsequent arterial blood gas analysis, as well as spontaneous reversion to sinus rhythm.

Cite this as: BMJ 2012;345:e7533
doi: 10.1136/bmj.e7533

Competing interests: None declared.

Provenance and peer review: Commissioned; externally peer reviewed.

Patient consent not required (patient anonymised, dead, or hypothetical).

References are in the version on bmj.com.
Systemic causes of dry eye

Endocrine
- Post-menopausal state
- Post-ophorectomy
- Diabetes mellitus
- Thyroid disease

Dermatological
- Rosacea
- Stevens-Johnson syndrome
- Mucous membrane pemphigoid

Neurological
- Parkinson’s disease

Drug induced
- Tricyclic antidepressants (anticholinergic effect)
- Antihistamines (anticholinergic effect)
- Lymphoma and leukaemia
- Orbital radiation

Autoimmune
- Primary Sjögren’s syndrome
- Secondary Sjögren’s syndrome

*The most common systemic causes of dry eye found in general practice suggests episcleritis

- Proposisis and lid lag suggest thyroid eye disease
- Red reflex. Irregular pupil suggest uveitis
- Visual acuity should not be severely impaired in dry eye, as blinking helps to maintain normal acuity during examination.

The examination should focus on: the skin (acne, eczema, malar rash, target lesions); finger joints (features of rheumatoid arthritis); neck (goitre); Parkinsonian features (in Parkinson’s disease there is reduced blinking, resulting in excessive tear evaporation between blinks).

Schirmer’s testing, fluorescein dye, and slit lamp microscopes are needed for a formal diagnosis of dry eye, and community optometrists have access to these.

What you should do
- Reassure the patient if no red flags are present. Dry eye is a chronic condition but does not threaten sight.
- Start artificial tears (lubricant eye drops), the mainstay of management. Reassure the patients that preservative-free formulations can be used as often as desired and titrated to visual activities. If initial formulations do not relieve symptoms, consider adding transient gels, or hypomolar eye drops that contain hyaluronate and lipids. Ointments and viscous gels are best used before bedtime as these induce blurring. Some trial and error may be necessary to determine what is most comfortable for each patient.
- Consider aggravating factors, such as (a) contact lenses—these should be removed for the day when dry eye symptoms appear, and patients could consider the newer silicon-hydrogel or rigid gas permeable lenses if they need to continue wearing contact lenses; (b) drugs with antimuscarinic side effects—for patients taking tricyclic antidepressants, consider alternatives such as selective serotonin reuptake inhibitors (also, the use of oral antihistamines should not be prolonged unnecessarily).
- Manage commonly associated conditions. Ocular irritation will improve if allergic conjunctivitis, blepharitis, and rosacea are treated.
- Refer to an ophthalmologist (a) urgently, if the red flags mentioned above are detected; and (b) routinely, if symptoms persist (may need punctal plugs, ciclosporin, and steroids).

Competing interests: LT was supported for the submitted work by the Singapore National Research Foundation under its clinician scientist award NMRC/CSCA/013/2009 and administered by the Singapore Ministry of Health’s National Medical Research Council, and by the Singapore Ministry of Health’s National Medical Research Council under its individual research grant NMRC/1 206/2009 and centre grant NMRC/CGRi/SEBI/2010. All authors have no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

Provenance and peer review: Not commissioned; externally peer reviewed. Accepted: 31 October 2012

USEFUL RESOURCES
- Dry Eye Company (www.dryeyezone.com)—US resource for treatment and relief of severe or chronic dry eye conditions
- Clinical Knowledge Summaries (www.cks.nhs.uk/dry_eye_syndrome)—Diagnosis and management information about dry eye
- Prodigy (http://prodigy.clarity.co.uk/dry_eye_syndrome)—Diagnosis and management information about dry eye

ANSWERS TO ENDGAMES, p 40

STATISTICAL QUESTION
Stratified random allocation
- Statements a, c, and d are true, whereas b is false.

ANATOMY QUIZ
Oblique radiograph of the normal lumbar spine
- This is the pars interarticularis (part between the two articular processes) of the vertebra, also known as the “Scottish terrier dog sign.”
- A: Superior articular process (forms the ear)
- B: Pedicle (forms the eye)
- C: Transverse process (forms the nose)
- D: Pars interarticularis (forms the neck)
- The sign of a “neck break” is indicative of spondylosis
- E: Lamina (forms the body)
- F: Inferior articular process (forms the foreleg)

PICTURE QUIZ A rash in a patient with neutropenia
1. There are two annular macular erythematous lesions overlying the left knee. The largest is about 3 cm in diameter and has a dusky necrotic centre. The smaller 1 cm lesion also has a darker centre.
2. A persistent fever in a neutropenic patient, which does not respond to broad spectrum antibiotics, raises the possibility of an invasive fungal infection. The development of multiple randomly distributed and centrilocally necrotic skin lesions with lung consolidation is classic for disseminated Fusarium infection. Fusarium spp are ubiquitous environmental moulds that are an increasingly common cause of opportunistic infection in immunocompromised patients.
3. The differential diagnosis for multiple macular centrally necrotic skin lesions includes bacterial soft tissue infection (such as ecthyma or ecthyma gangrenosum), other invasive fungal infections (such as Aspergillus or Candida), and cutaneous vasculitis.
4. Perform a comprehensive screen for bacterial and fungal infection. This should include skin swabs from an ulcerated lesion, blood cultures, and skin biopsy (for histology and tissue culture). An echocardiogram should be performed to exclude infective endocarditis. With evidence of lower respiratory tract consolidation, bronchoalveolar lavage could be considered.
5. International and national guidelines exist for the management of invasive fungal infections in patients with haematological cancer. First line empirical antifungal agents primarily target Aspergillus and Candida. Fusarium is typically resistant to echinocandins (such as caspofungin), so if this organism is considered in the differential diagnosis, liposomal amphotericin B would be a suitable first line agent. Specialist local microbiologist advice should be sought.

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