Using quality assured spirometry to support diagnosis

Spirometry is very easy to do, and very easy to get wrong (Martin, 2010; personal communication). Not only is quality assured spirometry dependent on the effort exerted by the patient, and the technical ability of the spirometer operator, but also on the understanding of the results by the person interpreting them. Interpretation of the results is essential if any meaningful decision is to be made about the patient’s care. This article aims to help understand how spirometry fits in to the diagnostic workup of a patient with suspected asthma or chronic obstructive pulmonary disease (COPD). It also looks at why quality assurance is important, and why poor-quality spirometry may lead to misdiagnosis. As well as referring to national guidelines on asthma and COPD, this article takes information published in the Guide to Quality Assured Diagnostic Spirometry in Primary Care (Primary Care Commissioning [PCC], 2013), which is endorsed by the British Thoracic Society (BTS), the Primary Care Respiratory Society (PCRS), and the Association for Respiratory Technology and Physiology (ARTP). This guide provides a summary of spirometry standards as established by Miller et al (2005).

QUALITY

When looking at a spirometry result, the first consideration should be if the data meets quality assurance standards. The reality of a busy clinical environment means that quality spirometry can sometimes be difficult to achieve. Both the volume/time and flow/volume curves should

KEY WORDS:

- Spirometry
- Reversibility
- Asthma
- Chronic obstructive pulmonary disease
- Guidelines
be examined from either the spirometer’s screen or paper printout. The tracings should be smooth, free from irregularities, and in the case of the volume/time curve, be smooth and convex. Ideally, the length of the blow should be six seconds. Blows below six seconds may indicate that the patient has stopped blowing before their lungs are completely empty. There should be three slow vital capacity (VC) readings, the highest two should be within 100mls or 5% of each other, and three forced vital capacity (FVC) readings, the highest two should be within 100mls or 5% of each other. Some guidance suggests that readings within 150mls may be acceptable and that 100mls is too stringent (Levy et al, 2009), which has led to much debate within the respiratory community.

Finally, the higher of either the VC or the FVC should be used to calculate the ‘ratio’. Sometimes the VC can be higher than the FVC, which may indicate air-trapping, where the small airways collapse during the forced manoeuvre. In this case, the VC should be used to calculate the ratio, e.g. FEV1/VC, rather than FEV1/FVC (Figure 1). If the ratio is 0.7 or lower, airways obstruction may be diagnosed.

In practice, during a busy clinic and when patients’ respiratory health may not be at its best, it can be difficult to obtain full quality assurance. Readings that do not meet guideline-defined quality assurance should not be used diagnostically.

Quality assured spirometry enables clinicians to diagnose

- FEV1 1.50
- VC 2.5
- FVC 2.0
- FEV1/VC 0.6
- FEV1/FVC 0.75

FIGURE 1.
In this example, the VC is higher than the FVC. If the FEV1/FVC ratio is used, airways obstruction is not apparent. If the FEV1/VC is used, airways obstruction may be diagnosed.

The tracings should be smooth, free from irregularities, and in the case of the volume/time curve, be smooth and convex. Ideally, the length of the blow should be six seconds. Blows below six seconds may indicate that the patient has stopped blowing before their lungs are completely empty. There should be three slow vital capacity (VC) readings, the highest two should be within 100mls or 5% of each other, and three forced vital capacity (FVC) readings, the highest two should be within 100mls or 5% of each other. Some guidance suggests that readings within 150mls may be acceptable and that 100mls is too stringent (Levy et al, 2009), which has led to much debate within the respiratory community.

Airways obstruction is currently defined as an FEV1/FVC (or FEV1/VC) ratio of 0.7 or less (National Institute for Health and Care Excellence [NICE], 2010; British Thoracic Society [BTS]/Scottish Intercollegiate Guidelines Network [SIGN], 2014). Airways restriction can be defined as a ratio above 0.7 with a FVC of less than 80% predicted (Figure 2). Pure airways restriction is rare, and consideration of referral to specialist care should be considered. Some patients may have both obstructive and restrictive patterns, known as ‘combined.’

As there are many respiratory diseases that can cause obstructive lung function, such as bronchiectasis, cystic fibrosis, inhaled foreign body, oblitterative bronchiolitis, and lung cancer, spirometry on its own cannot diagnose any individual condition. Lung function is just one piece of the diagnostic jigsaw puzzle, and should always be interpreted in context along with clinical history and other signs and symptoms. There is no single diagnostic test for either asthma or chronic obstructive pulmonary disease (COPD), and those tests that are available, such as reversibility, home peak flow, methacholine challenge, exhaled nitric oxide, and sputum eosinophil count, lack complete sensitivity or specificity (BTS/SIGN, 2014).

When examining and recording readings, it is good practice (Primary Care Commissioning [PCC], 2013) to present both actual values in litres, and percentage of predicted values (Table 1).
Both asthma (BTS/SIGN, 2014) and COPD (NICE, 2010) national guidelines suggest that spirometry should be interpreted along with the overall clinical picture. The asthma guidelines (BTS/SIGN, 2014) provided a bullet point list which helps to determine if the patient has a high probability of asthma or a low probability of asthma. Similarly, the COPD guidelines (NICE, 2010) give signs and symptoms that help determine if the patient is more likely to have asthma or COPD. Using the guidelines, clinicians can make assessments to help determine if patients are more likely to have asthma or COPD. On occasions, it may be clear that the presenting patient has one or the other, in which case spirometry may be helpful in providing an objective measurement and thus confirm a diagnosis. At other times, it is less clear, and further investigations, including spirometry, are needed.

The Quality Outcomes Framework suggests that a diagnosis of asthma should be made with ‘measures of variability or reversibility’ (General Medical Services [GMS], 2014). This can provide a challenge as many patients may be asymptomatic at the time of the lung function test, and may have completed normal lung function with no reversibility. In other words, if a reversibility test is performed at the point when a patient is feeling well, there may be little or no change in lung function. An absence of reversibility therefore cannot exclude a diagnosis of asthma.

One of asthma’s defining characteristics is its variability (BTS/SIGN, 2014). A little girl was once asked to draw a picture of her asthma, and she drew a picture of a roller-coaster, indicating that she had good and bad times. This variability can sometimes be demonstrated by significant changes in peak flow. Other objective measures that may be useful in supporting a diagnosis of asthma, are symptom scores, such as those produced by validated, structured symptom tests, e.g. the Royal College of Physicians’ (RCP’s) ‘3 Questions’ (Thomas et al, 2009a), or the Asthma Control Test (ACT) (Thomas et al, 2009b). A trial of treatment with repeated measurements of either peak flow or symptom scores, may be helpful in confirming a diagnosis if either peak flow or symptom scores significantly improve with treatment.

**HOW TO MEASURE VARIABILITY AND REVERSIBILITY**

The evidence behind what constitutes a positive reversibility is complex and unclear. The amount of reversibility which is significant has been described as ‘arbitrary’ (NICE, 2010) and a ‘constant variable’ (Calverley et al, 2003). The sensitivity of reversibility testing has been shown to be poor (Smith et al, 2004). People with COPD can experience a change of 160ml in FEV\(_1\), and a variability of FVC of 330mls (Tweeddale et al, 1987; Calverley et al, 2003). Therefore, it can be difficult to understand if any variation is natural or caused by a disease process. Furthermore, lung function does not correlate closely with symptoms or disease severity (Burge et al, 2003).

National guidelines for asthma have suggested an improvement in FEV\(_1\) of 400mls is suggestive of asthma. In children, the guidelines suggest an improvement in FEV\(_1\) of greater than 12% over baseline indicates reversible airflow obstruction and supports the diagnosis of asthma (BTS/SIGN, 2014: section 3.1.5).

If using peak flow, an increase of 60 l/min or 20% was suggested as a definition of reversibility (BTS/SIGN, 2014: table 8). Peak flow may be more beneficial in monitoring asthma (for example, as part of a personal asthma action plan [PAAP]) than in diagnosis). Also, peak flow cannot identify airways obstruction.

**Table 1: Actual values and percentage of predicted values**

<table>
<thead>
<tr>
<th>Actual value</th>
<th>Percentage of predicted values</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV(_1)</td>
<td>1.75</td>
</tr>
<tr>
<td>FVC</td>
<td>3.50</td>
</tr>
<tr>
<td>FEV(_1)/FVC</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Symptom variability can be measured with a structured symptom questionnaire such as the ACT. This provides a composite score of between five to 25; the higher the value, the more likely the patient’s asthma is to be well controlled. The minimally important difference in ACT score is three, meaning that an improvement of three or more is clinically significant (Schatz et al, 2009). This may be useful in understanding if a trial of treatment has worked. For example, if a patient’s ACT score is 17 before a month’s trial of inhaled steroids, and afterwards their ACT score is 20, this improvement in symptoms can provide confidence that the treatment has worked. This may also be helpful in the diagnostic workup of asthma, for example, if a patient has asthma-like symptoms, where it

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**Practice point**

Although spirometry may be helpful in both diagnosing and monitoring respiratory diseases, results should always be considered in conjunction with the wider clinical picture.

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**Reversibility key points**

- **Spirometric definition:** 400mls increase in FEV\(_1\), in adults (or 12% increase in FEV\(_1\) in paediatrics).
- **Peak expiratory flow rate (PEFR) definition:** 60 litres per minute or 20% or more increase in PEFR.
- **Use:** 400mcg inhaled salbutamol via metered dose inhaler (MDI) and spacer, and wait 20–30 minutes.
- **Treatment trial:** 400mcg inhaled beclometasone dipropionate (BDP) for 6–8 weeks.
- **Lack of response does not exclude asthma.** (BTS/SIGN, 2014: section 3.5)
The only ICS/LABA fixed-dose combination licensed in COPD
in both a pMDI and DPI
(FeV1 < 50% predicted)

Fostair 100/6 and 200/6 prescribing information
Please refer to the full summary of Product Characteristics before prescribing.

Presentation: Each Fostair pressurised metered-dose inhaler (pMDI) 100/6 dose contains 100 micrograms (mcg) of beclometasone dipropionate (BDP) and 6mcg of formoterol fumarate dihydrate (formoterol). Each Fostair pMDI 200/6 dose contains 200mcg of BDP and 6mcg of formoterol. Each Foster NEXThaler 100/6 dry powder inhaler (DPI) dose contains 100mcg of BDP anhydrous and 6mcg of formoterol. Each Foster NEXThaler 200/6 DPI dose contains 200mcg of BDP anhydrous and 6mcg of formoterol.

Indications: Asthma: Regular treatment of asthma is the use of an inhaled corticosteroid/long-acting beta2-agonist (ICS/LABA) combination is appropriate patients not adequately controlled on ICS and as-needed (prn) short-acting beta2-agonist, or patients already adequately controlled on both ICS and LABA. COPD (Fostair 100/6 only): Symptomatic treatment of patients with severe COPD (FEV1 < 50% predicted) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators. Dosage and administration: For inhalation in adult patients (≥18 years). Asthma: Maintenance and Reliever Therapy (Fostair pMDI 100/6 only) taken as a regular maintenance treatment and prn in response to asthma symptoms. 1 inhalation twice daily (bd) plus 1 additional inhalation prn in response to symptoms. If symptoms persist after a few minutes, an additional inhalation is recommended. The maximum daily dose is 8 inhalations. Fostair pMDI 100/6 may also be used as maintenance therapy (with a separate short-acting bronchodilator prn). Fostair pMDI 200/6 and NEXThaler 100/6 and 200/6 should be used as maintenance therapy only. Maintenance therapy: Fostair pMDI and NEXThaler 100/6: 1–2 inhalations bd. Fostair pMDI and NEXThaler 200/6: 2 inhalations bd. The maximum daily dose is 4 inhalations. Patients should receive the lowest dose that effectively controls their symptoms. COPD (Fostair 100/6 only): 2 inhalations bd. Fostair pMDI can be used with the AeroChamber Plus® spacer device. BDPI in Fostair is characterised by an extrinsic particle size distribution which results in a more potent effect than formulations of BDP with a non-extrinsic particle size distribution (100mcg of BDP extrinsically in Fostair are equivalent to 250mcg of BDP in a non-extrinsic formulation). When switching patients from previous treatments, it should be considered that the recommended total daily dose of BDP for Fostair is lower than that for non-extrinsic BDP containing products and should be adjusted to the needs of the individual patient. However, patients who are transferred between Fostair NEXThaler and Fostair pMDI do not need dose adjustment. Contraindications: Hypersensitivity to the active substances or to any of the excipients. Warnings and precautions: Use with caution in patients with cardiac arrhythmias, aortic stenosis, hypertrophic obstructive cardiomyopathy, ischemic heart disease, severe heart failure, congestive heart failure, oesophageal varices, arterial hypertension, severe arterial hypertension, aneurysm, thyrotoxicosis, diabetes mellitus, pheochromocytoma and untreated hypokalaemia. Caution should also be used when treating patients with known or suspected prolongation of the QTc interval (QTc > 0.44 seconds). Formoterol itself may induce QTc prolongation. Potentially serious hypokalaemia may result from beta2-agonist therapy and may also be potentiated by concomitant treatments (e.g. sartan derivatives, steroids and diuretics) and increase the risk of arrhythmias. Formoterol may cause a rise in blood glucose levels. Fostair should not be administered for at least 12 hours before the start of anaesthesia, if halogenated anaesthetics are planned. Use with caution in patients with pulmonary tuberculosis or fungal/viral airway infections. Fostair treatment should not be stopped abruptly. Treatment should not be initiated during exacerbations or acutely deteriorating asthma. Fostair treatment should be discontinued immediately if the patient experiences a paradoxical bronchospasm. Systemic effects: Systemic effects of ICS may occur, particularly at high doses for long periods, but are less likely than with oral therapy. Corticosteroids may be associated with the development or exacerbation of existing conditions, such as Cushing’s syndrome, Cushingoid features, adrenal suppression, decreased in bone mineral density, cataract and glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression and aggression. Prolonged treatment with high doses of ICS may result in adrenal suppression and acute adrenal crisis. Lactose contains small amounts of milk proteins, which may cause allergic reactions. Interactions: Beta-blockers should be avoided in asthmatic patients. Concomitant administration of other beta-agonistic drugs may have a potentially additive effect. Concomitant treatment with quinidine, disopyramide, procarbazone, phenothiazines, antiarrhythmics, monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants can prolong the QTc interval and increase the risk of ventricular arrhythmias. L-dopa, L-thyroxine, oestrogen and alcohol can impair cardiac tolerance towards beta-sympathomimetics. Hypertensive reactions may occur following co-administration with MAOIs including agents with similar properties (e.g. furazolidone, procarbazone). Concomitant treatment with sartan derivatives, steroids or diuretics may potentiate a possible hypokalaemic effect of beta-agonists. Hypokalaemia may increase...
has been difficult to obtain significant reversibility or variation in lung function.

When performing reversibility, it is important to ensure that the patient has not taken any bronchodilator therapy before the test. This includes inhaled beta2 agonist and muscarinic antagonists. Short-acting bronchodilators last for four to six hours, and long-acting bronchodilators last between 12 and 24 hours. Knowledge of the duration of action of the individual bronchodilator is therefore an important consideration, as these may affect test results.

Although reversibility is a useful test for confirming the diagnosis of asthma, it is of little value in excluding asthma. Also, reversibility is of little use in diagnosing COPD. Guidelines suggest that diagnostic spirometry for COPD should be performed post-bronchodilator, in other words, after the patient has received inhaled bronchodilators. The subtle difference between ‘post-bronchodilator spirometry’ and ‘spirometry with reversibility’ may be slightly confusing, and it is important to understand not only the difference between the two, but when one should be used over the other (Table 2).

### WHAT COULD POSSIBLY GO WRONG?

The Guide to Quality Assured Diagnostic Spirometry in Primary Care (PCC, 2013) provides examples of common errors in spirometry. Errors such as these can lead to misdiagnosis, or even the prescribing of incorrect treatment. It is essential that not only is the numerical data scrutinised, but also that the tracings provided are closely examined, as in the examples given.

### FUTURE DEVELOPMENTS

The arbitrary FEV1/FVC ratio of less than 0.7 given to diagnose airways obstruction, may be replaced by a ‘lower limit of normal’ value (Levy et al, 2009; PCC, 2013). It is thought that the fixed ‘less than 0.7’ definition may under-diagnose COPD in younger people, and over-diagnose COPD in old people (Swanny et al, 2008). Therefore, there is a move toward using a lower limit of normal value, which can be derived from appropriate reference equations, which are already being provided by some modern spirometers (Levy et al, 2009; PCC, 2013).

Draft asthma guidelines from NICE have suggested that up to 30% of people with asthma may have no clear evidence of their diagnosis (NICE, 2015). The draft guidelines have called for better tests to be developed, to improve the accuracy of asthma diagnosis. One such test is fractional exhaled nitric oxide (FeNO), a breath test that can detect eosinophilic inflammation inside the airway, such as that produced in some people with asthma. The suggestion is that this test can be performed in primary care as an addition to spirometry and reversibility testing. How this additional cost, training, and workload will be organised in primary care is not yet understood.

The draft asthma guidance from NICE has also suggested accepting a reversibility of 200mls as being indicative of asthma. This is contrary to the COPD guidelines published by NICE (2010) and the BTS/SIGN (2014) asthma guidelines. Previous

### Table 2: Differences between reversibility testing and post-bronchodilator spirometry

<table>
<thead>
<tr>
<th>Test Type</th>
<th>FEV1/FVC ratio**</th>
<th>Suggests asthma</th>
<th>Suggests COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversibility*</td>
<td>&lt;0.7</td>
<td>Significant</td>
<td>Insignificant</td>
</tr>
<tr>
<td></td>
<td>May become normal following treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-bronchodilator spirometry</td>
<td>&lt;0.7</td>
<td>Insignificant</td>
<td>Significant</td>
</tr>
</tbody>
</table>

* Significant reversibility = increase FEV1 >400mls or PEF >60 l/min or 20%
** Use FEV1/VC if VC is greater than FVC

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Example one

This 76-year-old lady is 168cm tall. Her FEV1 is 2.27 litres or 121% of predicted. The spirometer has provided an interpretation of ‘normal spirometry’ and a ‘lung age’ of 55 years. Superficially, these results may show a patient who is in excellent health, is at low risk of exacerbation, and has perhaps excelled at sport at a high level.

However, closer examination of the inter-blow variability (labeled ‘VAR’) shows huge differences in FEV1 and FVC as high as 51%, suggesting spirometry that is not within quality standards.

The volume/time curve appears normal with a smooth, convex tracing of sufficient duration. However, it is only upon examination of the flow/volume curve, that a better understanding of the reading can be obtained.

The flow/volume curve reveals a covert extra breath taken by the patient during the manoeuvre. Only by examining the tracing can a full understanding be gained.
versions of the BTS/SIGN asthma guidelines have suggested a 200ml change as being diagnostic of asthma, and there would appear to be evidence to support both readings (Levy et al, 2009). Consensus is essential if a consistent and reliable approach to asthma diagnosis is to be reached.

CONCLUSION

Spirometry is very easy to perform, and very easy to get wrong. Ensuring spirometry is quality assured will help to facilitate a diagnosis that is as accurate as possible. While spirometry may appear easy to perform, assuring quality standards are met in clinical practice can be challenging. It should always be interpreted in the context of a full clinical picture. If suspecting COPD, guidelines suggest post-bronchodilator spirometry may be helpful in identifying airways obstruction and in classifying severity. If suspecting asthma, reversibility testing (including treatment trials) may be useful for including an asthma diagnosis, but not for excluding an asthma diagnosis.

REFERENCES


Example two

The flow/volume curve (left) appears relatively normal, with the tracing appearing to almost match the area of prediction (shaded). However, the volume/time tracing shows a ‘slow start’, indicating that the patient did not start to exhale at their highest rate until nearly two seconds had elapsed.

In this case, the FEV1 would be hugely reduced, along with a false FEV1/FVC ratio, potentially leading to an inaccurate diagnosis of airways obstruction. The reduced FEV1 may also lead to a COPD severity classification much worse than reality, which in turn could lead to an incorrect prescription of inhaled steroid/long-acting β2 agonist.