Lung Function Testing

The following is a guide on which test will benefit your patients.

Flow Volume Loop (Spirometry)	Asthma COPD monitoring First presentation sleep patient
Full Lung Function **(aka Complex Lung Function) Includes Pre & Post bronchodilator Flow volume loops, Lung Volumes and Gas Transfer.**	First presentation respiratory patient Emphysema with decreased diffusion capacity Reduced SpO2 Smoker/Ex-smoker new shortness of breath Emphysema for valve insertion (EBV) Interstitial Lung Disease Pulmonary Fibrosis Medico-Legal / Work Cover assessments Patient is on Prednisolone On or about to commence chemotherapy/Stem Cell Transplant. Occupational exposure to harmful substance Bird Fanciers Lung - Hypersensitivity pneumonitis Pulmonary Arterial Hypertension
Bronchial Provocation – Mannitol	Normal CLF but patient has asthmatic symptoms Defense/Police Force Recruitment, SCUBA Diving medicals
Respiratory Muscle Strength - MIPs MEPs	Motor Neuron Disease, Muscular Dystrophy
6MWT	Evaluate for home oxygen (MASS) Pulmonary Arterial Hypertension
Allergen Skin Prick Test	Quantify atopy Asthma Differentiate between allergic and vasomotor rhinitis Food reactions

Flow Volume Loops, before and after bronchodilator

Flow volume loops are a physiological test that measures inhaled and exhaled volumes of air as a function of time. The primary signal measured is volume and flow. Parameters obtained are, vital capacity (VC), the largest volume of air that can either be inspired or expired from the lungs. VC measured from a maximal forced exhalation is called the forced vital capacity (FVC). The most commonly measured parameters from the FVC manoeuvre are the FVC itself and the forced expiratory volume in one second (FEV1). Various flows can be measured in conjunction with an FVC manoeuvre, either at specific points or across specific intervals.

Many of the flow measurements from the forced expiration can also be obtained during forced inspiration. The forced inspiratory vital capacity (FIVC) is often measured in conjunction with the FVC, and like the FVC, various inspiratory flows can be measured [e.g., peak inspiratory flow (PIF) and forced inspiratory flow when 50% of the FIVC has been inhaled (FIF50%)].

The graphic display of the FVC manoeuvre is useful during testing for assessing patient effort and cooperation. The spirogram is also helpful for assessing the quality of the manoeuvre and for interpretative purposes. Two common spirogram displays are used: volume-time and flow-volume.

Since the FVC manoeuvre includes measurements of both volume and flow, it is useful in the assessment of both restrictive and obstructive diseases. Diseases that interfere with the

bellows action of the chest wall or lungs result in a reduction of vital capacity. A reduced FVC or VC, without a disproportionately greater reduction in flows, suggests a restrictive disorder. This “restrictive” pattern predicts a reduced total lung capacity (TLC) only about half the time; the absence of the restrictive pattern strongly predicts a normal TLC. Measurement of additional lung volumes, such as TLC, are required to confirm the presence of a restrictive pattern.

Spirometry is the diagnostic tool for evaluation of obstructive lung disease. Maximal air flow depends primarily on the elastic recoil of the lungs, the compliance and calibre of the airways. During forced expiration from TLC, airflow limitation begins in the large airways (trachea and mainstem bronchi) with the development of turbulent flow. As the forced expiration continues, the site of air flow limitation moves to smaller airways where flow is laminar. Flow is limited by the compression of the airways downstream from the "equal pressure point". As the lungs empty, the equal pressure point moves into smaller airways. Measurements of flow at different lung volumes allows assessment of the status of the airways. Loss of elastic recoil (as in emphysema) results in increased compression of the airways and markedly reduced flows at all lung volumes. A decrease in the calibre of the airways (as in asthma or bronchitis) directly limits flow developed for a given driving pressure.

The pattern of flow reduction can be used to assess the site of flow limitation. Large airway obstructions, such as tumours, usually limit flow across a wide range of lung volumes. By measuring maximal flows during both inspiration and expiration, the nature of central airway obstruction can often be identified (i.e., fixed versus variable, intrathoracic versus extrathoracic). Measured flows are compared to those of healthy individuals to determine the severity of airway obstruction.

A comparison of erect and supine spirometry has been advocated as a clinical test for diaphragmatic weakness and is a useful adjunct to measuring maximum respiratory pressures, especially in those patients too ill or unable to perform mouth pressure manoeuvres.

Indications:

Diagnostic

- To evaluate symptoms, signs, or abnormal laboratory tests
- To measure the effect of disease on pulmonary function
- To screen individuals at risk of having pulmonary disease
- To assess preoperative risk
- To assess prognosis
- To assess health status before enrolment in strenuous physical activity programs

Monitoring

- To assess therapeutic intervention
- To describe the course of diseases affecting lung function
- To monitor those exposed to injurious agents
- To monitor for adverse reactions to drugs with known pulmonary toxicity

Disability/Impairment Evaluations

- To assess patients as part of a rehabilitation program
- To assess risks as part of an insurance evaluation
- To assess individuals for legal reasons

Public Health

- Epidemiological surveys
- Derivation of reference equations
- Clinical research

Contraindications:
The following conditions may pose a relative danger to the patient or affect the validity of performance of spirometry:

- Haemoptysis of unknown origin
- Recent pneumothorax
- Unstable cardiovascular status
- Thoracic, abdominal, or cerebral aneurysms
- Recent eye surgery
- Presence of an acute disease that might interfere with test performance (e.g., nausea, or vomiting, chest or abdominal pain)
- Recent surgery of thorax or abdomen

Lung Volumes (Body Plethysmography)

The measurement of static lung volumes generally refers to measuring the various lung "capacities" and "volumes." The capacities include: functional residual capacity (FRC), total lung capacity (TLC), vital capacity (VC), and inspiratory capacity (IC).

These four capacities can be divided into sub-volumes which are also measured and include: inspiratory reserve volume (IRV), expiratory reserve volume (ERV), tidal volume (TV), and residual volume (RV). The sum of two or more lung volume subdivisions comprises a lung capacity.

FRC is the volume of gas from which a normal breath is taken, or alternatively, the volume of gas present in the lung at end-expiration during tidal breathing. The term “thoracic gas volume” (generally referred to when measuring this volume of gas using the body plethysmograph and abbreviated TGV or VTG) is nonspecific and refers to the absolute volume of air in the thorax at any point in time and at any alveolar pressure, and the use of this term is not recommended and it should be replaced with more specific terminology (e.g., FRCpleth). The FRC increases with aging and may also increase in the presence of lung diseases that cause air-trapping (e.g., asthma, chronic bronchitis and emphysema). Conversely, the FRC can be reduced in the presence of restrictive lung disease processes such as interstitial lung disease (ILD) and pneumonectomy.

TLC is the total or greatest volume of gas in the lungs at the end of a full inspiration. TLC is calculated by either summing FRC and IC, or VC and RV. TLC may be normal or increased with obstructive lung diseases and tends to be reduced with restrictive lung diseases or neuromuscular disorders. IC is the maximal amount of gas inspired from a normal end-expiration (FRC). It is also the sum of IRV and TV.

VC is the volume change at the mouth between the positions of full inspiration and complete expiration. It is also the sum of TV, IRV, and ERV. As compared to the forced expiratory vital capacity (FVC), the slow vital capacity (SVC) is an untimed manoeuvre and may also be referred to as the "relaxed vital capacity", or simply as VC. The inspiratory vital capacity (IVC) is also performed in a relaxed manner from a position of full expiration to full inspiration. The VC may be maintained within the normal range with certain pulmonary diseases but is often reduced in the presence of obstructive lung diseases. It is also reduced in the presence of restrictive lung diseases or neuromuscular disorders.

ERV is the volume of gas that can be maximally exhaled from the end-expiratory level during tidal breathing (i.e., FRC). TV (also denoted as V_T) is the volume of gas inhaled or exhaled with the respiratory cycle. If it is measured under conditions other than quiet relaxed breathing, then this should be indicated. The IRV is the maximal volume of gas that can be inhaled from the end-inspiratory level during tidal breathing.

RV is the volume of gas remaining in the lungs after maximal (complete) exhalation regardless of the lung volume at which expiration was started. It requires maximal expiratory efforts and cannot be obtained in non-cooperating subjects. It is indirectly determined by subtracting the ERV from FRC, or VC from TLC. It is usually elevated in obstructive lung diseases and reduced with restrictive lung diseases.

Assessment of lung volumes is used to establish or confirm a "restrictive ventilatory defect" or in diagnosing hyperinflation and abnormal distensibility as may occur in patients with emphysema. Static lung volumes are also useful for differentiating types of lung disease processes characterized by airflow limitation that have similar forced expiratory configurations. Additional indications for testing include the need to:

- Establish or confirm a diagnosis of a restrictive ventilatory defect
- To distinguish between obstructive and restrictive process
- Assess response to therapeutic intervention
  E.g. lobectomy, chemotherapy, transplantation.
- Evaluation of pulmonary disability
- Aid in the interpretation of other lung function tests
- Preoperative assessment
- Quantify the amount of non-ventilated lung

Gas Transfer

The diffusing capacity of the lung for carbon monoxide (DLCO), also referred to as the transfer factor of the lung for carbon monoxide (TLCO), is used to evaluate the transfer of gas from the distal air spaces into the pulmonary capillaries. It can be measured when known and very low concentrations of carbon monoxide (CO) are inspired. The rate of CO disappearance is calculated from the ratio of the CO concentrations of the inspired and expired gas and then expressed as a function of the driving pressure (mL CO/min/mmHg).

Breath-hold with alveolar sample collection: In this technique, the patient inhales a volume of test gas containing 0.3% CO, 18% He (CH4 with some equipment) and 21% oxygen with the balance nitrogen. The test gas is held in the lungs for approximately 10 seconds, and then enough gas is exhaled to wash out the mechanical and anatomical dead space and to collect a sample for analysis.

Increases in DLCO occur in:

- Polycythemia
- Pulmonary hemorrhage
- Diseases associated with increased pulmonary blood flow
- Exercise
- Asthma
- Mueller manoeuvre

Decreases in DLCO occur in:

- Emphysema
- Parenchymal lung diseases (e.g., interstitial pulmonary fibrosis)
- Pulmonary involvement in systemic diseases
- Cardiovascular diseases
- Pulmonary embolism
- Anemia
- Haemoglobin binding changes (e.g., increased COHb)
- Valsalva manoeuvre

Indications:
Some indications for DLCO are:

- Evaluation and follow-up diseases which involve lung parenchyma (e.g., those associated with dusts, drug reactions, or sarcoidosis)
- Evaluation and follow-up of emphysema
- Differentiating among chronic bronchitis, emphysema and asthma
- Evaluation of pulmonary involvement in systemic disease
- Evaluation of cardiovascular diseases
- Prediction of arterial desaturation during exercise in some patients with lung disease
- Evaluation and quantification of impairment and disability associated with interstitial lung diseases and emphysema
- Evaluation of the pulmonary effects of chemotherapy agents or other drugs known to induce pulmonary dysfunction
- Evaluation of pulmonary haemorrhage
- As an early indication of certain pulmonary infections that cause diffuse pneumocystis (e.g., pneumocystis pneumonia)

Contraindications:

- The presence of acute disease that might affect test performance i.e. any condition causing pain on inspiration e.g. pleurisy
- The presence of any abnormality that might affect test performance e.g. mouth deformities causing leakage of air around the mouthpiece or a cracked rib causing pain
- Any mental or physical condition that affects the ability of the patient to cooperate and follow instructions

Bronchial Provocation Test

Variable airways obstruction can either be demonstrated either with a bronchodilator or be induced by bronchoprovocation testing. The assessment of whether lung function improves after a bronchodilator drug is administered is one of the respiratory laboratory's most requested tests. It provides an indication of treatment and can be used for confirming a diagnosis of asthma. A change in forced expiratory volume in one second (FEV1) of >12% and 200 ml is considered significant.

Sensitivity of the airways to provoking stimuli is a method used to confirm the diagnosis of asthma. There is a range of provoking stimuli but most protocols utilize a dose response curve. A positive test is one where there is a significant decrease in FEV1 and is classified as hyper-responsive. The FEV1 is the lung function index of first choice in clinical practice to monitor bronchial responsiveness.

Mannitol
Mannitol (Aridol) is an indirect osmotic bronchial challenge test indicated for identifying bronchial hyperresponsiveness to assist in the diagnosis of Asthma. A positive Mannitol challenge can be achieved by a fall in FEV1 of 15% from baseline or an incremental fall of 10% in FEV1 between consecutive Mannitol doses. Mannitol is classed as the Gold Standard of bronchial provocation testing

6 Minute Walk Test (6MWT)

In the assessment of functional capacity in patients with respiratory disease, objective measures are considered better than questioning patients about their abilities to perform activities (such as asking the number of blocks that can be walked).

The 6-minute walk test (6MWT) is a practical simple test to perform that does not require exercise equipment. The 6MWT measures the distance that a patient can walk quickly on a flat hard surface in a period of 6 minutes (the 6MWD). The 6MWT evaluates the global and integrated responses of all body systems involved during exercise. It does not provide specific information on the function of each of the different organs and systems involved as is possible

with the cardiopulmonary exercise test. Most patients do not achieve maximal exercise capacity during the 6MWT, and instead, choose their own level of intensity.

The most common use of the 6MWT is to measure the response to therapy in patients with a severe cardiopulmonary disease. The patient's pre-treatment 6MWD is compared with their post-treatment value. The 6MWT is also used as a one-time measure of the functional status of patients with COPD. The test if often repeated on oxygen via nasal canula if oxygen desaturation occurs below 88% to assess for benefits of home oxygen use and for MASS benefits.

Respiratory Muscle Strength

The measurement of respiratory muscle forces (or strength), maximum inspiratory pressure (MIP or PImax), and maximum expiratory pressure (MEP or PEmax), are direct tests that are simple to perform. They assess the aggregate force or pressure that respiratory muscles can generate against an occlusion at the mouth. PImax is an index of diaphragm strength, while PEmax measures the strength of abdominal and intercostal muscles.

Indications

- Assess and quantify the degree of respiratory muscular weakness that may occur with neuromuscular diseases (e.g., amyotrophic lateral sclerosis, myasthenia gravis, and polymyositis), obstructive lung disease causing hyperinflation (e.g., emphysema, chronic bronchitis, and cystic fibrosis), and conditions requiring chronic steroid use, conditions with chest deformities, and unexplained dyspnea.
- Abnormal diagnostic test results [e.g., decreased forced vital capacity (FVC), peak flow, maximal voluntary ventilation (MVV), or abnormal chest radiograph].
- The PEmax gives information about the potential for effective cough and ability for secretion clearance.
- Diagnosis and management of a patient with actual or suspected injury to the diaphragm or other respiratory muscles.
- Evaluate the effectiveness of therapy designed to improve respiratory muscle strength.

FeNO: Fractional Exhaled Nitric Oxide

FeNO, a marker of Th2-mediated airway inflammation, is particularly useful as an indicator of ICS-responsive airway inflammation and, perhaps more importantly, for identifying airway inflammation that will not respond to corticosteroids.

Measurement of fractional nitric oxide (NO) concentration in exhaled breath (FeNO) is a quantitative, noninvasive, simple, and safe method of measuring airway inflammation that has been standardized for clinical use and provides a complementary tool to other ways of assessing airways disease. Nitric oxide (NO) is now recognized as a biological mediator in humans. NO is produced by the human lung and is present in the exhaled breath. NO has been implicated in the pathophysiology of lung diseases, including asthma. Advantages for FeNO include the noninvasive nature of the test, ease of repeat measurements, and the relatively easy use in patients with severe airflow obstruction where other techniques are difficult to perform. By providing information about airway inflammation, FeNO adds a new dimension to the traditional clinical tools (history, physical exam, and lung function tests).

Asthma is a heterogeneous, chronic disease characterized by two fundamental and interrelated abnormalities: airway inflammation and airway hyper-responsiveness. Asthma is a clinical diagnosis and there is no single diagnostic test for the disease. There are several inflammatory phenotypes in asthma most commonly described as eosinophilic, neutrophilic, mixed, and paucigranulocytic. FeNO is associated with eosinophilic airway inflammation. FeNO

production is more accurately defined as a marker of Th2-mediated inflammation, which often includes airway eosinophilia. In asymptomatic individuals, including patients with well-controlled asthma, low FeNO suggests that ICS dose could be reduced or even withdrawn altogether. FeNO is also useful for assessing adherence with corticosteroid therapy in patients with established asthma.

Airway inflammation and hyper-responsiveness associated with asthma can be triggered by exercise and numerous exogenous factors such as aeroallergens, infections, cigarette smoke and other irritants. Airway inflammation results from the activation of mast cells and antigen-specific Th2 cells, resulting in the production of cytokines, including interleukin (IL)-4, IL-5 and IL-13.10. In turn, IL-4 and IL-13 cause epithelial inducible nitric oxide synthase (iNOS) expression to be upregulated via signal transduction and is an activator of transcription (STAT)-6, a process that is corticosteroid sensitive. Exhaled NO is a direct signal of the Th2-mediated, pro-inflammatory cytokine mechanisms in the pathophysiology of allergic airway inflammation.

Patients with asthma have high levels of NO in their exhaled breath and high levels of inducible nitric oxide synthase (NOS2) enzyme expression in the epithelial cells of their airways, suggesting a role for NO in asthma pathogenesis. NO is a highly reactive molecule/free radical and may have oxidant properties directly or in the form of the more noxious peroxynitrite. These properties give NO its bactericidal and cytotoxic effects and may participate in host defense by mediating antimicrobial activity and cytotoxicity for tumor cells.

Allergen Skin Prick Testing

Skin prick testing is a diagnostic aid in atopic detection and can identify a specific allergen. It is generally performed by a prick test on the body's surface (cutaneous). The skin prick test is sensitive in the detection of the skin sensitizing antibody IgE. Small amounts of allergen are introduced into the epidermis and non-vascular superficial dermis and interact with specific IgE bound to cutaneous mast cells. Histamine and other mediators are released, leading to a visible “wheal-and-flare” reaction peaking after about 15 minutes.

The skin prick test has good sensitivity and specificity for the presence of allergen-specific IgE and is in some cases more sensitive than in-vitro testing for specific IgE in serum. The discomfort is small and the risk of systemic reactions is minimal although not negligible. The skin prick test is the gold standard for detection of reactivity to aeroallergens and food proteins. Atopy is a genetically determined tendency to make specific IgE responses to common environmental allergens. A positive reaction to one or more of the allergens in the presence of negative controls, defines the patient as atopic.

Skin prick testing provides information about the presence of IgE to protein and peptide antigens (allergens). Allergens introduced via the skin interact with specific IgE bound to cutaneous mast cells. The nature of the change in the mast cell membrane is probably related to changes in Ca^{2+} permeability, allowing an influx of Ca^{2+} causing histamine and other mediators to be released. These produce the wheal and flare on the skin's surface.

Indications for SPT

1. Quantify atopy
2. Asthma
3. Differentiate between allergic and vasomotor rhinitis
4. Food reactions