Cystic Fibrosis Trust

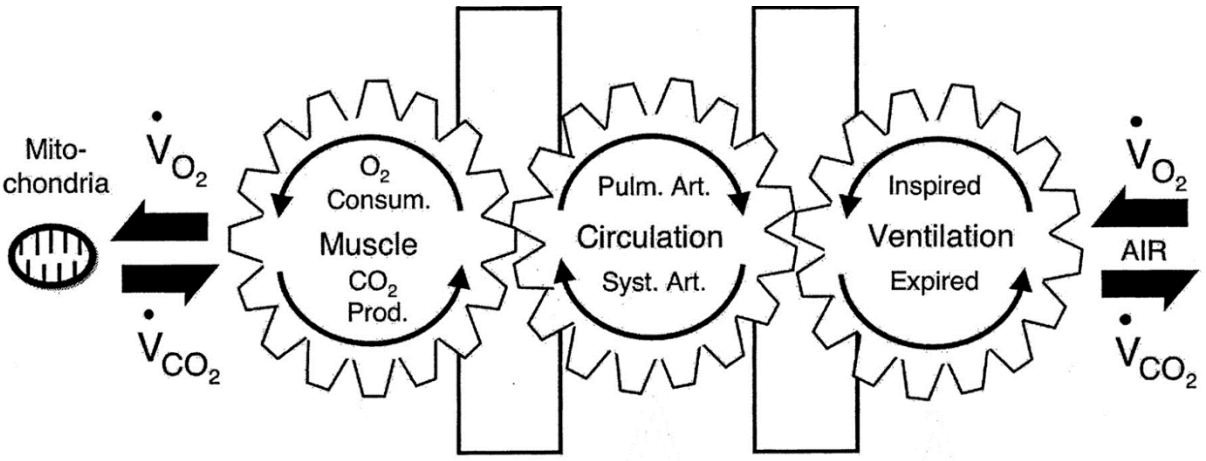
CARDIOPULMONARY EXERCISE TESTING

WHAT, WHY, WHEN, HOW?

WHAT IS A CPET?

A CPET is a ***C**ardio**P**ulmonary **E**xercise **T**est*. It is an exercise test that allows us to simultaneously stress the cardiovascular, ventilatory and muscular systems. Through the examination of gas exchange measurements, we are able to identify limitations to exercise, as well as the energy costs of exercise itself.

A large number of prognostic tests that are performed in a clinic are done at rest, and isolate one system, such as O_2 saturation, spirometry and heart rate. Why is this? How much of our day do we spend sat doing nothing? A lot of the day is spent moving, so it is only sensible to measure the physiology of the body in response to exercise. This is where a CPET is useful.



(Wasserman et al., 2005)

As oxygen moves from the lungs, through the heart, to the working (exercising) muscle; and as carbon dioxide makes the return journey to be exhaled, we can identify how efficiently and effectively the mitochondria of the cell are functioning. Through gaseous exchange observed at the mouth – the measurement of how much O_2 and CO_2 is exhaled with every breath – we can ascertain how well a patient is producing energy, and how 'fit' is a patient is as a result.

A key outcome of any CPET is the volume of oxygen a patient can successfully transport, and utilise, at peak exercise. This is termed the '**VO_{2max}**' – the **maximal volume of oxygen** utilised during exercise.

WHY PERFORM A CPET?

As mentioned, a CPET simultaneously stresses the cardiovascular, ventilatory and muscular systems to identify a patient's fitness. Whilst traditional measures such as lung function and BMI are still clinically relevant tools, these do not provide an overall picture of a patient's clinical profile. Whilst a CPET does not replace these tests, it complements them.

The relationship between FEV_1 and VO_{2max} is not fixed. Research has shown that only 50% of the variation in VO_{2max} is explained by FEV_1 (Pastre et al., 2014). This suggests that:

- There is another 50% that is left unexplained. What are the other factors that may limit a patients ability to exercise?
- We can, and do, see patients with low FEV_1, but a high VO_{2max}; and vice-versa, patients with a high FEV_1, but a low VO_{2max}.

Importantly, VO_{2max} is also a clinically useful measure. Patients with a low VO_{2max} are at greater risk of early death (Nixon et al., 1992, Pianosi et al., 2005), a greater risk of being hospitalised (Pérez et al., 2014) and have a lower quality of life (Hebestreit et al., 2014).

In addition to the clinically useful measure we can obtain, CPET serves an additional purpose for patients that are typically fit and well. Due to the nature of shuttle-walk tests, an increasing number of patients are actually completing these tests, and ever earlier ages. Whilst this is undoubtedly good news for patients, showing they are physically capable of meeting these challenges, it makes it difficult to identify when patients are declining in function. As a CPET **cannot be 'completed'**, it is an increasingly useful tool for fitter patients.

WHEN TO PERFORM A TEST

Currently, it is recommended that all patients with CF undertake an exercise test once per year, ideally in line with their annual review (Cystic Fibrosis Trust, 2017). Whilst this has typically been a shuttle walk in the past, recent recommendations from the European CF Society and European Respiratory Society suggest that clinics should utilise CPET as the methodology of choice (Hebestreit et al., 2015).

A CPET can also be performed at any point where there may be a change in their function, either due to the onset of an exacerbation, or the intervention of new treatment.

Previous researchers and clinicians have undertaken CPETs in a variety of situations, to add to the clinical profile of a patient. For example:

- Before, and after, exercise training programmes (Gruber et al., 2014)
- Before, and after, a course of IV anti-biotics (Alison et al., 1994)
- Before, and after, a percutaneous endoscopic gastrostomy (Tomlinson et al., 2016)
- Before, and after, CFTR potentiator therapy (e.g. Ivacaftor) (Saynor et al., 2014)

Therefore, the utility of a CPET is not only confined to annual review, but any time when the clinical team require further information about a patient's clinical status.

HOW TO PERFORM A TEST

There are many different ways in which a CPET can be performed. Fundamentally, the principles remain the same between all test types and devices.

Bike or Treadmill?

A CPET can be undertaken using either an exercise bike, or a treadmill. As with any process, there are advantages and disadvantages to each. The use of a treadmill typically produces a higher VO_{2max}, as the body is using a greater amount of muscle; however, it requires a greater level of familiarisation for those that are not used to maintaining a constant speed. Furthermore, the use of a treadmill is not ideal for younger patients, or those on supplemental oxygen.

An exercise bike, or cycle ergometer, can be utilised with all patients. Young children, deconditioned patients and those who struggle to walk/run (i.e. overweight/obese, patients with joint issues) are all able to use the bike with greater ease, and therefore this is the recommended equipment.

Protocol

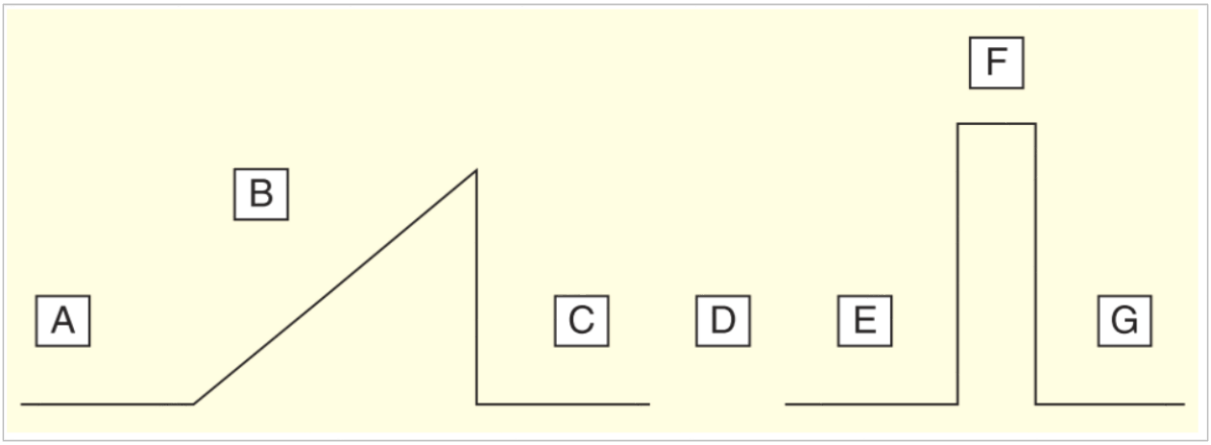
There are numerous protocols that can be used to elicit VO_{2max}. For use on a treadmill, the 'Bruce' protocol is frequently employed. This uses 3-minute stages at foxed speeds and gradients to progressively increase the amount of work done. Eventually, the increased speed (and steepness) of the treadmill will cause patients to fatigue. On cycle ergometers, the 'Godfrey' protocol has been widely used. This bases increases in work rate upon a patients height, and is a 'step test' design, whereby the work rate aggressively increases at the end of every minute-long stage until a patient becomes fatigued and cannot continue.

However, a 'ramp' design is favourable for use on a cycle ergometer due to its smooth, linear, profile. The protocol described and displayed below has been shown to be valid and reliable in people with CF (Saynor et al., 2013a, Saynor et al., 2013b). This protocol is a two-stage test that initially starts with a warm-up (A). Then the patient exercises at an increasing intensity (B) until they cannot maintain a set speed. This produces a sensation of cycling uphill, with patients working harder,

using greater muscle mass and oxygen until they finally fatigue. This ‘ramp’ stage can increase resistance gradually by 10-30 watts every minute, and typically lasts between 8-12 minutes. Once they have cycled to **exhaustion**, they undertake a cool-down (C).

After this five-minute cool down, patients come off the bike for ten minutes (D). This is an ideal opportunity for patients to have a quick drink, cool down further, clear airways and check blood sugars if necessary. This period even presents a time where clinical staff can discuss exercise and undertake physiotherapy reviews.

After this ten minute period, patients get back on the bike, and after a brief warm-up (E), exercise at 110% of their previous power output achieved in part B (F). This is designed to be a verification bout, to ensure that the highest VO_2 observed in the first test is indeed the true VO_{2max}. This stage typically lasts 1-4 minutes, and is far shorter than the first bout (due to its increased intensity). Finally, a further cool-down is performed (G), once the patient is **exhausted** from stage F.



(Williams et al., 2014)

Why a two-stage test?

Initially, a two-stage test may seem unnecessary. However, it is important to consider how we define what makes a test ‘maximal’ and whether a patients has truly achieved. VO_{2max}. Throughout exercise testing, there are several criteria that can be used to determine if someone has exercised maximally. Many are common-sense: sweating, flushing, tiredness and breathlessness. However, there are a series of ‘secondary criteria’ that can be used. These include heart rate, ratings of perceived exertion and dyspnoea, and a ventilatory parameter called the respiratory

exchange ratio (an indirect marker of whether someone is working aerobically, or anaerobically).

However, these 'secondary criteria' that have often used to verify tests have now been consistently shown to be invalid. It is quite possible to have patients fail to reach the specified secondary criteria, yet actually be at maximum; and vice-versa, patients can exceed these secondary criteria, but not yet be at maximum. Therefore, to ensure an accurate test, this two-stage test is used. Its design of exercising at a slightly higher intensity serves to corroborate the first VO_{2max} score. If a higher score is obtained in the second bout, then that is take to be VO_{2max}. Previous research in children with CF has shown ~30% of children will obtain a higher VO_2 in the second phase (Saynor et al., 2013a).

Measurements

Throughout the entire test, patients will be required to wear a facemask. This is in turn connected to a gas analyser, which measures the volume of oxygen and carbon dioxide exhaled with each breath. Alongside the volumes of each gas, the analyser will also measure to the total amount of air exhaled, to provide measures of ventilation. Patients can also wear a heart rate monitor, pulse oximeter and sphygmomanometer if needed.

When to stop?

Ideally, patients exercise until volitional exhaustion. For some patients, this is a very strange sensation and some will be hesitant to work to such a level. Muscular fatigue (particularly in the quadriceps) and dyspnoea will begin to limit exercise, but unless there are clear contraindications to continuing the test, patients should be actively encouraged to continue. Such contraindications include (but are not limited to):

- Chest pain
- Haemoptysis
- Reduced SpO_2 (ECFS/ERS recommend 80% as a lower limit).
- Systolic blood pressure over 250 mmHg
- Confusion, dizziness, faintness

WHAT DATA TO COLLECT

There are many variables that can be collected during the course of a CPET. Some have immediate clinical significance, some will be useful for future prescription of exercise programmes, and some will be of relevance to research partners.

VO_2

This is one of, if not the most, important variables to obtain from a CPET. As noted before, it is related to a patients risk of early death, hospitalisation and quality of life. It is a marker of the volume of oxygen a person is able to breathe in, transport to working muscle and utilise. This can be recorded as an absolute score in litres per minute, or as a score that accounts for a patients body mass (measured in millilitres, per kilogram, per minute). Depending on age and sex, normal values will vary but can range between 15 – 60 ml/kg/min. As yet, there are no extensive normative values for patients with CF, and therefore all values are compared to individuals without CF.

V_E

Minute ventilation is the absolute amount of air exhaled each minute. This measure is naturally related to a patients lung capacity, however the way in which patients increase their ventilation varies. Some patients will utilise a static volume, but hyperventilate from the start of the test to compensate for the additional demands of exercise. Other patients will increase tidal volume, and then increase breathing frequency to produce increased minute ventilation.

Heart Rate

Heart rate will increase during the course of the CPET, up to a value in excess of 200 beat per minute in some individuals. Once VO_{2max} is known (as well as the heart rate at VO_{2max}), heart rates at certain maximal and submaximal points can be utilised to prescribe training zones for patients.

Power Output

The maximal power obtained during the course of a CPET provides an indication of muscular strength. This can also be used to prescribe training zones for patients, as

the power output at certain maximal and submaximal points can be used to elicit specific metabolic responses. In addition, power output achieved can provide an indicator of efficiency – does VO_2 change for a set power output? Finally, the maximal power output achieved can be utilised to predict VO_{2max} when patients are unable to wear facemasks for any reason (e.g. size, claustrophobia or culture of certain bacteria).

Gas Exchange Threshold

The gas exchange threshold (GET) is an indication of when the body starts to rely on an increased anaerobic contribution to maintain exercise. When the volume of carbon dioxide production (VCO_2) begins to increase disproportionately relative to oxygen uptake (VO_2), this is the GET. It also represents the boundary between moderate intensity, and heavy intensity, exercise domains – an important consideration for exercise prescription.

Numerous other variables can, and will be collected. For a more comprehensive overview, please refer to recent ECFS/ERS Statement on Exercise Testing (Hebestreit et al., 2015).

WHAT DOES IT MEAN?

A common question from patients undergoing CPET will inevitably be “Is my VO_2 good?”

There are numerous equations to calculate VO_2 as a percent of predicted, however these are all based on healthy individuals, and there is minimal data on what is considered ‘normal’ for somebody with CF.

As a result, we *also* need to consider how a patients VO_2 changes over time relative to their own prior performances. To determine if a change is meaningful (either due to deconditioning, training, or other interventions), we must now the typical variation associated with the test.

In children with CF, we know this ‘normal’ variation is a VO_2 of ~0.15 mL/min (Saynor et al., 2013b). Therefore, any VO_2 that increases (or decreases) beyond this value can be considered meaningful, and can assist with clinical decisions.

CLINICAL CONSIDERATIONS

There are numerous considerations for clinical teams with regards to CPETs. Some of these are outlined below.

Safety during CPET

As mentioned previously, there are numerous criteria for terminating a test. However, all patients should undergo an initial screening to ensure they are healthy enough to perform maximal exercise.

In addition, some patients will require supplemental oxygen during, or following, exercise – always ensure that this is on hand. Furthermore, ensure appropriate emergency procedures are in place (each trust/clinic will have their own process/protocol). Serious adverse events during CPETs are exceptionally rare.

Infection Control

As per any infection control procedure, it is recommended that all exercise equipment is thoroughly cleaned following a CPET, and any gym or testing space is ventilated for a minimum of one hour. A recommended cleaning procedure for face-masks is a two-stage process, using a decontaminant detergent (e.g. Neutracon, Decon Laboratories) and then a soak in sterilising fluid (e.g. Milton, Ceuta Healthcare). Any free-standing equipment such as bikes and gas analysers can be cleaned using detergent wipes.

Any patients culturing nontuberculous mycobacteria (NTM), can still undertake a CPET as bikes can be cleaned using stronger detergents/wipes. Some gas analysers cannot be as thoroughly cleaned, and so ‘non-gas’ CPETs may have to be run on patients culturing NTM, with VO_{2max} predicted as a result of the power output achieved.

Staffing

There is a level of training required to become competent in administering CPETs. However, this is a relatively easy process to learn and staff can be fully competent and independent after observation, assistance and supervision of 5-20 CPETs

(dependent on prior skill, knowledge and experience). The use of CPETs has minimal impact upon the running of services within the CF MDT. As patients will often be required to undergo an exercise test at annual review, there is always a need for staff, time and space to run these tests; a CPET just take a bit longer to complete fully.

In addition, if additional staff are employed to administer CPETs, they can also be used to prescribe exercise programmes and assist with physiotherapy duties such as review, airway clearance and spirometry. Furthermore, clinicians value such exercise testing and training (Stevens et al., 2010), due to the enhanced clinical profiles it produces.

Costs

There is a level of cost associated with the equipment needed to run a CPET. Whilst there are always variations between makes, models and supplying companies, a typical cycle ergometer will cost approximately £5k, and a gas analyser is £15k. In addition, there are costs for facemasks, calibration gases and servicing.

This may seem a large investment. However, the additional physiological data is clinically relevant, and complements a patient profile with greater detail than a shuttle walk would. In addition, CPET equipment can utilised by other clinical departments (e.g. general respiratory, cardiology, anaesthesiology, renal services) to reduce costs; or collaborations can be sought with existing exercise science departments at universities nationwide.

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CPET Data Collection					
Name:		Height			cm
D.O.B:		Weight			kg
Patient number:		Mask		Ramp rate:	W/min
NHS Number:		Seat			RPM
Date of test:		Peak power		Max	
				110%:	

Pre-test (resting)	
HR	
Sats	
RPE	
RPB/RPD	

Post-test (Immediate)	
HR	
Sats	
RPE	
RPB/RPD	

Post test	(5min)	(10min)
HR		
Sats		
RPE		
RPB/RPD		

During test						
Time (min)	**Watts**	**Sats**	**HR**	**RPE**	**RPB**	**Notes**
Warm up						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						
Post						Reason for finishing the test
5 min						
10 min						
Supra Max						
Warm up						
3						
1						
2						
3						
4						
5						
Post						Reason for finishing the test
5 min						
10 min						

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