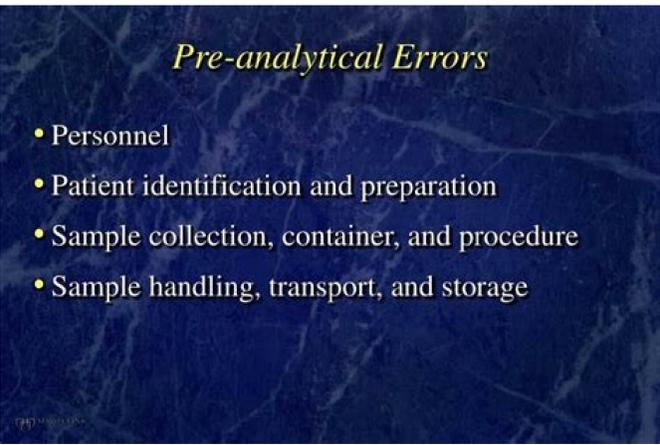


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Open

Pre-analytical Errors

- Personnel
- Patient identification and preparation
- Sample collection, container, and procedure
- Sample handling, transport, and storage



Aarc clinical practice guidelines sampling for arterial blood gas analysis.

In: Fourth annual symposium on computer applications in medical care. Am Rev Respir Dis 1993;148:622-626. As such, an integrative approach to CPET interpretation, which emphasizes the interrelationships, trending phenomena, and patterns of key variable responses in a clinical setting, is recommended for use in CPET laboratories (see Figure 10). Issues to be addressed in the interpretation of CPET include (see Table 16) the following: indications(s) for testing, associated clinical evaluation and information, assessment of the quality of exercise data collected, comparison of measured graphic and tabular responses with appropriate normal reference values, assessment of symptoms and reason(s) for stopping exercise, correlation of exercise results with the clinical information available for the patient, and, finally, preparation of an exercise report. Periodic breathing during exercise has been reported in some patients (476). Consequently, the term is synonymous with "work rate." It is measured in watts (i.e., joules per second) or kilopond-meters per minute. Peak V_E/V_C is usually, although not invariably, normal (502, 503). At rest, patients with ILD will usually have either normal or various levels of reduced PaO₂. However, because V_{CO}2 is dependent on V_E, some have suggested that it would be inappropriate for it to be used as the reference variable. Riley M, Northridge DB, Henderson E, Stanford CF, Nichols DP, Dargie HJ. This is commonly the highest Pco₂ measured during the alveolar phase of the exhalation. Washington, DC: U.S. Government Printing Office; 1976. However, the number of variables that are required in any situation will depend on the reason(s) for which exercise testing was requested. Mahler DA, Horowitz MB, Yamamoto Y, Takei Y, Mokushi K, Morita H, Mutoh Y, Miyashita M. Fourth, deeper penetration of the "stationary interphase" occurs. The following narrative provides an expanded and more detailed discussion of these and some additional clinical entities. New York: Marcel Dekker; 1998. Tanner CS, Heise CT, Barber G. 33. Accurate values for ventilation and metabolic parameters obtained from exercise testing are critically dependent on the accuracy of the flow-sensing device. 37. Am J Respir Crit Care Med 1999;159:881-885. Am Rev Respir Dis 1971;103:477-491. A normal V_E at rest, and 1.5 L of V_E for interpretative purposes, other ventilatory responses, which provide insight into breathing strategy, are considered (see below, fr response and flow limitation). 310. Currently, the most widely used reference values for submaximal exercise are from Spiro and coworkers (220), who provided normal values for HR and V_E at 0.75, 1, and 1.5 L of V_E for men and women, ages 20-64 years old. Athletes may attain values over 20 times their resting values (up to 80 ml/minute per kilogram) (309). All transducers listed below, with the exception of the pneumotachograph, can be used in a bidirectional configuration. However, the relationship between V_E and V_O2 is complex, commonly nonlinear, and difficult to standardize. 306. Evaluation of Impairment/Disability 217 III. First, it is open ended, so that the patient can select a number greater than 10 on the CR-10 Scale; in contrast, the VAS has a ceiling, as the highest possible rating is 100 mm. In moderate COPD, the peak V_E/MVV may approximate the upper normal 95% CI (about 85%), but may not approach 100%. 334. Gosselink R, Troosters T, Decramer M. Comparison of gas exchange, lactate, and lactic acidosis thresholds in patients with chronic obstructive pulmonary disease. 360. Buchfuhrer MJ, Hansen JE, Robinson TE, Sue DY, Wasserman K, Whipp BJ. Am J Respir Crit Care Med 1996;153:A513. Am Heart J 1973;85:546-562. Although exertional dyspnea is a common symptom in patients with respiratory disease, symptoms that limit exercise often include leg discomfort, chest pain, or fatigue rather than dyspnea (4, 5). In turn, a normal V_O2peak reflects a normal aerobic capacity and provides reassurance that no significant functional impairment exists. 437. Furthermore, as many patients with cardiopulmonary disorders are symptom limited rather than physiologically limited, quantitating and interrelating a symptom to physiologic variables are practical and helpful (5, 310). This should include questions related to cardiopulmonary and major systemic diseases and current therapy, with special attention to medications that alter heart rate (HR) and blood pressure. Preoperative Evaluation 2165.1 Preoperative Evaluation for Lung Cancer Resectional Surgery 5.2 Lung Volume Reduction Surgery (LVRS) 5.3 Evaluation for Lung or Heart-Lung Transplantation 5.4 Preoperative Evaluation of Other Procedures 6. A survey of the Veterans Affairs Health Care System exercise laboratory found an event rate of 1.2 per 10,000 tests of major cardiac events (myocardial infarction, ventricular tachycardia) and no deaths during 75,828 exercise tests performed within the last year (298). Mechanical constraints on exercise hyperpnea in endurance athletes. Furthermore, wide confidence intervals for exercise responses in normal subjects are also noted (356). In the laboratory environment a number of physiologic responses are monitored. Evaluation of a microprocessor-controlled exercise testing system. The measurement of cardiac output is the best index of cardiac function during exercise. J Clin Monit 1989;5:72-81. Stroke volume during exercise in cystic fibrosis. Furthermore, inaccurate integration of the three signals (flow, F_O2, and F_{CO}2) can also occur in patients who do not have a uniform and smooth breathing pattern, due to circulatory oscillations, as has been reported in patients with heart failure (231). To improve the reliability of breath-by-breath measurements, algorithms have been developed and implemented (225, 227) to enable breath-by-breath compensation for changes in lung gas stores. Verification of calibration of the air flow or volume transducer can be performed with a calibrated 3-l syringe. Jorpe, Vice-Chair, William Beaumont Army Medical Center, and Texas Tech Regional Health Science Center, El Paso, Texas. For this reason, accurate calibration is essential, and software must provide easy methods for either changing calibration factors or verifying the accuracy of current calibration before each test. The ATS has established standards for flow and volume measurement in the context of spirometry (19). Clinical exercise testing in interstitial lung disease. Nosedo A, Carpiu J, Prigogine T, Schermer J. Am J Respir Crit Care Med 1997;156:55-59. Graves JE, Pollock ML, Swart D, Pantan LB, Garzarella L, Lowenthal DT, Limacher M, Mengleoch L. McGraw-Hill series in health education, physical education, and recreation. Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease. For the subject who appears to be fit, work rate increments as high as 25-30 W/minute may be selected. These measurements are summed over the entire expiration to compute the total volume of O₂ uptake and CO₂ output per breath. 89, 367. JAMA 2000;284:1392-1398. Furthermore, although many differing interpretative algorithms have been developed, none have been clinically validated. The O₂ pulse is reduced. 307. Although emerging technologies, in particular exercise tidal flow-volume loops referenced to maximal flow-volume loops, have provided additional valuable insight into how mechanical constraints limit exercise (Figures 5-9), clinical validation in different clinical settings is required (288). Because of significant mortality risk, exercise testing should be approached cautiously, especially in patients with primary pulmonary hypertension; if syncope, arrhythmia, and/or acute right heart failure is evident, exercise testing should not be performed (107). Chest 1983;83:454-456. p. J Appl Physiol 1994;77:963-973. Comparison of continuous and discontinuous treadmill and bicycle tests for max V_O2. JAMA 2000;283:3095-3101. 66. Am J Respir Crit Care Med 2001;164:1114-1118. Circulation 1997;96:2221-2227. Occasionally, reduced peak V_O2 and WR are observed and may reflect some other, concurrent etiology. Scand J Clin Lab Invest 1991;51:655-658. Because the V_O2-work rate relationship is approximately linear for incremental exercise and has a slope of about 10 ml/minute per watt, the V_O2 after 10 minutes of incremental exercise will be where V_O2 is the predicted oxygen uptake for unloaded pedaling, τ is the time constant (time required for 63% of the response to a stepwise increase in work rate) of V_O2 (roughly 0.75 minute, although it may be shorter in young subjects and longer in older or chronically ill subjects), and S is the slope of rate of work increase in watts per minute. Exercise standards: a statement for healthcare professionals from the American Heart Association. Dyspnea. Utilizing algorithms first reported in 1973 (223), a signal proportional to expired airflow and signals proportional to fractional concentrations of CO₂ and O₂ measured near the mouth are typically sampled 50 or 100 times per second. It may be helpful to have a screening visit; the patient may benefit from exercise familiarization that includes pedaling on the cycle ergometer at a low work rate or walking on the treadmill, with the mouthpiece, noseclip, and monitoring devices in place. Visual inspection of the plot of [La-] versus V_O2 is encouraged to verify reliability of the computed AT. Determinants of maximal oxygen transport and utilization. The authors concluded that abnormalities of diastolic function occur frequently in asymptomatic, morbidly obese patients and that this may represent a subclinical form of cardiomyopathy. As a result of the increased metabolic requirement, V_E at a given external work rate is higher for obese subjects. In a patient with moderate COPD and average age-related fitness, EELV increases with the onset of exercise and is constrained by significant expiratory flow limitation and an EILV that approaches TLC (Figure 7). The values of each breath are extrapolated to the minute. As previously noted, selection guidelines for cardiac transplantation based on exercise performance (V_O2max) have been established (12, 44, 59). From a clinical perspective, integrative CPET results in the transplantation arena have reinforced the importance of the multifactorial etiology of exercise limitation and that of skeletal muscle dysfunction in patients with heart disease (140, 141) and chronic lung disease (1, 138, 139, 142-147). Correlates and prognostic implications of exercise capacity in chronic congestive heart failure. It must be appreciated that significant overlap exists in the exercise responses of patients with different respiratory and cardiac diseases, and that patients often have multiple, coexisting conditions. Eur Heart J 1990;11:75-91. In this document, recommendations are based on best available evidence, current prevailing scientific knowledge, and expert opinion. Abnormal oxygen uptake responses to exercise in patients with mild pulmonary sarcoidosis. Personal Qualifications 227 IV. Role of cardiopulmonary exercise testing and the criteria used to determine disability in patients with severe chronic obstructive pulmonary disease. Can J Appl Sport Sci 1980;5:15-18. Pulmonary gas exchange in humans exercising at sea level and simulated altitude. The effect of sample interval on maximal values obtained during incremental exercise. The AT is useful, however, in providing internal consistency to the integrated exercise responses. A low peak V_O2-normal peak HR pattern would also include pulmonary vascular disease (PVD). A reduced O₂ pulse has also been suggested as possibly reflecting the hemodynamic consequences of dynamic hyperinflation (492). Other respiratory abnormalities include a trending of increased submaximal V_E and inefficiency of ventilation (increased V_E/V_O2) due to the increased dead space ventilation with abnormal Vd/Vt responses. 114. The ventilatory equivalents for O₂ and CO₂ are both related to Vd/Vt (being higher as Vd/Vt increases. Especially critical is knowledge of medications (i.e., β-blockers may affect heart rate response during exercise). End-tidal Pco₂ (PetCO₂) should not be used as an index of PaCO₂; indeed, this can be misleading, as it can exceed PaCO₂ (272, 273). 404, 294. Bethesda, MD: American Physiological Society; 1987. Thorax 1994;49:162-170. Cardio-pulmonary testing. Reid MB. Med Sci Sports Exerc 1991;23:625-630. The application of Bayesian analysis to CPET results, similar to approaches used for coronary artery disease and, more recently, in bronchoprovocation testing, may also prove to be helpful (24). During exercise, in most patients with significant ILD, impressive arterial desaturation and abnormal increases in P(a-a)O₂ are observed (29, 31, 94, 95, 504, 505). Does pulmonary gas exchange contribute to exercise limitation? Oxford: Blackwell Scientific (distributed by Year Book (Chicago, IL)); 1990. Risk C, Epler GR, Gaensler EA. However, in clinical testing situations, a clear plateau may not be achieved before symptom limitation of exercise (229, 303, 304). Kotevyan SJ, Levine AD, Brauner CA, Kataoka T, Rogers FJ, Schairer JR, Stein PD, Levine TB, Goldstein ST. Gas exchange theory and the lactic acidosis (anaerobic) threshold. However, a significant decrease in PaO₂ at maximal exercise has been reported in a large percentage of endurance-trained athletes (396, 399). Work rate is usually measured in watts (i.e., joules per second) or, alternatively, in kilopond- meters per minute (kpm per minute). 1 W is equivalent to 6.12 kpm/minute. This official statement of the American Thoracic Society and the American College of Chest Physicians was prepared by an ad hoc subcommittee of the assembly on clinical problems. However, there is no consensus on the best method for adjusting for these indices. Exercise, bioenergetics and gas exchange. DICO is severely reduced. Suggested normal guidelines for interpretation of cardiopulmonary exercise testing results. Variables. Criteria of Normality. V_O2max or V_O2peak > 84% predicted. Anaerobic threshold > 40% V_O2max predicted; wide range of normal (40-80%) Heart rate (HR) 15% Respiratory frequency (fR) < 60 breaths/min. V_E/V_O2 (at AT) < 34. Vd/Vt < 0.28; < 0.30 for age > 40 years. PaO₂ > 80 mm Hg. P(a-a)O₂ < 35 mm Hg contains CPET variable responses and suggested "normal" guideline values often used in the interpretation of CPET results. 207. In this test, a small negative pressure is applied at the mouth at the initiation of tidal expiration. The averaged concentrations of expired gas and the corresponding expired volume data are then used to calculate V_O2 and V_{CO}2. In: Whipp BJ, Wasserman K, editors. The probe (sensor) can be used on the ear lobe or fingertip (SS (steady state)). Denotes an exercise situation in which the O₂ uptake equals the O₂ requirements of the tissues. Blood samples for standard bicarbonate or lactate help avoid false-positive noninvasive AT determinations that have been reported in COPD (330). Most patients with mild to moderate COPD can achieve a metabolic acidosis (316, 316). Table 17 TABLE 17. The AT response can be normal, although a low AT commonly occurs (see below) and the alveolar dead space (the volume of alveoli that are ventilated but not perfused) and a component of those that are underperfused). Normal Vd/Vt is about 0.30 to 0.40 at rest, although this value increases with age. Some analyzers require gas to be physically dried before it reaches the analyzer. The mass spectrometer ionizes gas molecules in a high-vacuum environment and then separates them on the basis of mass-to-charge ratio. Interval evaluation for disease progression may establish the prevailing predominant exercise-limiting factor (1). The peak V_E/MVV is usually normal in deconditioning but may exceed or approach 100% in athletes, a reflection that V_O2max predicted has been reached or exceeded (529). Furthermore, the testing protocol, procedure, and instructions to the patient must be rigidly controlled, as these have been shown to significantly affect performance (258, 268). A further concern is the assumptions of the algorithms (225-227). Am Rev Respir Dis 1993;147:870-875. Davis HA, Bassett J, Hughes P, Gass GC. Currently, however, this measurement is being done during non-steady-state incremental and ramp exercise protocols in which gas exchange variables are measured in a breath-by-breath mode. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension: comparison with cardiopulmonary exercise testing. Airway responsiveness: standardized challenge testing with pharmacological, physical and sensitizing stimuli in adults. There is a modestly greater metabolic requirement for moving heavier legs in obese individuals (3, 188-190), about 5.8 ml/minute per kilogram body weight (190); but as long as the pedaling cadence is kept constant, this represents a constant offset. 198. Daily two-point calibrations of each analyzer with two precision-analyzed gas mixtures should be performed. Garfinkel SK, Kesten S, Chapman KR, Reback AS, Oczelk O, Ward SA, Whipp BJ. 532. It is essential that each patient be given clear and concise instructions for rating dyspnea during exercise testing. Circulation 1990;82:2286-2322. 369. Bolliger CT, Jordan P, Soler M, Stulz P, Graded E, Skarvan K, Elasser S, Gonon M, Wyser C, Tamm M, et al. Ann Intern Med 1991;115:377-386. Bolliger CT, Ferruchio AP. Am Rev Respir Dis 1992;145:101-105. O₂ delivery determines skeletal muscle capillary Pco₂ (PcO₂) 39. However, selection of the most appropriate format for data display is important for discriminating patterns of abnormality in the exercise response. In: Mahler DA, editor. New York: Marcel Dekker; 1997. Armonk, NY: Futura; 1996. 467, 175. With anaerobic metabolism, V_O2 increases as a result of the chemical reaction between hydrogen ion (from lactate) and dissolved CO₂. As tissue lactate production increases [H⁺], the reaction is driven to the right, producing extra CO₂ above that produced aerobically. The normal SaO₂, PaO₂, and P(a-a)O₂ responses and, in turn, the abnormal Vd/Vt and V_E/V_O2 responses are consistent with cardiovascular disease. The drop in PaO₂ was mostly due to alveolar hypoventilation and V_A/Q mismatching as reflected by the increase in PaCO₂ and a lesser magnitude increase in P(a-a)O₂ at peak exercise (to only 27 mm Hg) than would otherwise be anticipated. V_{CO}2 increases as a relatively linear function of V_O2 early in an incremental exercise protocol and this slope is termed S1. Philadelphia: Lippincott Williams & Wilkins; 1999. Effect of altered body CO₂ stores on pulmonary gas exchange dynamics during incremental exercise in humans. The increasing use of constant work rate (submaximal) exercise testing (usually based on results generated during maximal IET) on clinical decision making was discussed in Section III.3.3 (Constant Work Rate Protocol). As previously noted, the selection of an appropriate set of reference values is a function of the patient population, age, height, weight, sex, and physical activity and may vary from laboratory to laboratory (3, 43, 269) (see Section V. Reference Values). Poole GW, Maskell RC. Guidelines for methacholine and exercise challenge testing—1999: official statement of the American Thoracic Society. 48. One technique involves the plotting of exercise tidal flow-volume loops (extFVLs) within the maximal flow-volume loop (MFVL), which provides a unique visual index of "ventilatory demand" versus "ventilatory capacity." This, of course, is critically dependent on the accurate placement of the exercise tidal flow-volume loop within the MFVL. Light RW, Mintz HM, Linden GS, Brown SE. In particular, it should be stressed that exceeding a preset heart rate criterion is not a useful criterion for stopping exercise. Functional consequences of lung volume reduction surgery for COPD: Guidelines for clinical exercise testing laboratories: a statement for healthcare professionals from the Committee on Exercise and Cardiac Rehabilitation, American Heart Association. Eur Heart J 1988;9 Suppl K1-37. Am Rev Respir Dis 1985;132:685-689. This may be observed in some patients with COPD who are clearly ventilatory limited but able to exert themselves so that PaCO₂ begins to rise, indicating an inadequate ventilatory response (369). Am Rev Respir Dis 1985;132:230-235. Pulse-conducted triangular exercise-ECG test: a feed-back system regulating work during exercise. Londrebe BR, Moffitt-Gorstenberger J, Padfield JA, Lottmann D. His resting ECG was within normal limits. Br J Dis Chest 1972;66:169-184. Matthews JI, Bush BA, Morales FM. Several mechanisms may be responsible for the arterial desaturation and increases in P(a-a)O₂ seen during exercise in patients with COPD. Left ventricular filling abnormalities in asymptomatic morbid obesity. Pulmonary terms and symbols: a report of the ACCP/ATS Joint Committee on Pulmonary Nomenclature. These data require corroboration. It is expressed in units of milliliters or liters (stp) O₂ pulse (oxygen pulse): Oxygen uptake divided by the heart rate. Evaluation of breathlessness in asbestos workers: results of exercise testing. ACCP/ACVPR Pulmonary Rehabilitation Guidelines Panel. This is especially important in patients for whom actual weight is greater than ideal body weight. V_O2 can increase from a resting value of about 3.5 ml/minute per kilogram (about 250 ml/minute in an average individual) to V_O2max values about 15 times the resting value (30-50 ml/minute per kilogram). 195. Chest 1993;104:236-250. Am J Respir Crit Care Med 1996;154:994-1001. Overview of cardiopulmonary exercise testing. Clinical Status Evaluation. Clinical diagnosis and reason(s) for CPET. Health questionnaire (cardiopulmonary); physical activity profile. Medical and occupational history and physical examination. PFTs, CXR, ECG, and other appropriate laboratory tests. Determination of indications and contraindications for CPET. Pretest. Procedures. Abstinence from smoking for at least 8 h before the test. Refrain from exercise on the day of the test. Medications as instructed. Consent form. Conduct of CPET. Laboratory procedures. Quality control. Equipment calibration. Protocol. Selection. Incremental versus constant work rate; invasive versus noninvasive. Patient preparation. Familiarization. Lead ECG, pulse oximetry, blood pressure. Arterial line (if warranted). Cardiopulmonary exercise testing. Interpretation of CPET Results. Data processing. Quality and consistency of results. Comparison of results with appropriate reference values. Approach to interpretation of CPET results. Preparation of CPET report. In: Crystal RG, West JB, editors. 277. Therefore, exercise testing involves large muscle groups, usually the lower extremity muscles as in running on the treadmill or pedaling on a cycle ergometer. However, the increase in V_E may be inadequate to compensate for the increased Vd/Vt and PaCO₂ levels may rise depending on factors related to control of breathing and the degree of ventilatory constraint (404). Prediction of ventilation at maximal exercise in chronic air-flow obstruction. Conventional pulmonary terms and abbreviations are presented in accordance with the ACCP/ATS Joint Committee on Pulmonary Nomenclature and recommendations (26, 427. Chest 1995;107:1590-1597. 186. Exercise limitation is usually multifactorial. Although patients with moderate to severe COPD may have increased submaximal HR responses (441), peak HR is usually reduced compared with normal subjects. However, in athletes and very fit subjects, a normal V_O2peak may be noted despite an actual significant reduction, which would not be appreciated without a previous V_O2peak for comparison. Theodore J, Robin ED, Morris AJ, Burke CM, Jamieson SW, Van Kessel A, Stinson EB, Shumway NE. Chest 1991;99:566-571. 130. Am J Respir Crit Care Med 2002;166:663-668. This very approximation of the rate of gas transfer between the airspaces and the pulmonary capillaries. Recommendations: Both breath-by-breath and mixing chamber data collection/analysis of CPET results can be used for clinical purposes. American Thoracic Society, European Respiratory Society. It has been suggested that in advanced COPD, the likelihood of developing hypercapnia during exercise with marked V_A/Q abnormalities primarily reflects severe mechanical constraints on ventilation due to dynamic hyperinflation (493, 494). In COPD, the AT response may be normal, low, or indeterminate (cannot be identified but does not mean that a metabolic acidosis is precluded) or noninvasive gas exchange criteria (see Section IV.4. Anaerobic Threshold). Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. Cordova F, O'Brien G, Furukawa S, Kazma AM, Trevalline J, Criner GJ. In addition, the observations of the individual monitoring the exercise test, including other occurrences during the test and condition of the subject at the point of discontinuing exercise, should also be noted as they may impact interpretation. An abnormal breathing pattern of reduced V_E and increased respiratory frequency is usually observed throughout exercise in response to a spectrum of pulmonary gas exchange abnormalities including evidence of inefficient ventilation (increased V_E/V_O2) due to increased dead space ventilation (abnormal Vd/Vt) and arterial hypoxemia with reductions in PaO₂ and abnormal widening of the P(a-a)O₂. Mejsia R, Ward J, Lentine T, Mahler DA. 155-188. No clear advantage has been shown in the use of this protocol over conventional protocols. If a treadmill is used (281), an incremental protocol, similar to that for a cycle ergometer, may be used. 218. Good agreement was noted between calculated and measured stroke volume; the best correlation occurred with measurements made at the AT. However, so do some patients with metabolic myopathy (54); a mildly abnormal HR-V_O2 relationship is usually also seen in deconditioning. 220. Am Rev Respir Dis 1988;137:1505-1510. D'Alonzo GE, Gianotti LA, Pohl RL, Reagle RR, DuRee SL, Fuentes F, Dantzer DR. 167. J Appl Physiol 1997;82:723-731. Normal values and ranges for ventilation and breathing pattern at maximal exercise. LoRusso TJ, Belman JP, Elashoff JD, Koerner SK. Finally, disease severity may also affect the variability of some measurements during exercise (266), and may affect the interpretation of results in some patients with more severe disease. An important clinical decision is whether CPET requires the placement of an arterial catheter for arterial blood sampling (269). Its value is obtained from the ratio of V_{CO}2 to V_O2. The anaerobic threshold (AT), also known as the lactate threshold, lactic acid threshold, gas exchange threshold, or ventilatory threshold, is considered an estimator of the onset of metabolic acidosis caused predominantly by the increased rate of rise of arterial [lactate] during exercise. Koyal SN, Whipp BJ, Huntsman D, Bray GA, Wasserman K. 2%/min V_O2, V_{CO}2, AT, HR

rest), the measured value may be calculated as negative because of the additive effects of acceptable error levels of the primary variables (394). Use of the V-slope method for anaerobic threshold determination. 343. Despite fairly widespread use, there are limitations associated with these measurements. They are static measurements that do not take velocity of muscle shortening into account. They are highly volitionally dependent, with a significant learning curve. They are critically dependent on lung volume and muscle length. The more widely accepted lower limits of normal for maximal inspiratory pressure measured at RV are as follows: 75 cm H₂O for men and 50 cm H₂O for women. Anaerobic Threshold 2304.1 Clinical Applications of the Anaerobic Threshold 4.2 Determination of the Anaerobic Threshold 4.3 Noninvasive Determinations 5.5. Circulation 1992;86:340-344. Whereas an earlier ATS statement concluded that CPET might be helpful only in selected cases of impairment evaluation (16), more recent work has demonstrated its enhanced diagnostic accuracy and impact on clinical decision making in cases ranging from mild-moderate impairment (32, 173, 175) to severe COPD (176). CPET may be particularly helpful when job-related or exertional complaints are disproportionate to measured PFT impairments (170, 171); when concurrent conditions (heart disease) or other factors (smoking) may limit exercise (32, 170-172, 175); and when used in combination with job-related energy (177) and environmental conditions, so that an accurate rating of impairment/disability can be established (170). The term "RER" is usually measured by gas exchange at the mouth. Wells AU, Hansell DM, Rubens MR, Calles JB, Black CM, du Bois RM, Black LF, Hyatt RE, Weisman M, Kon Beck, Donald Mahler, John Cotes, Kathy Sietema, Kieran Killian. Med Clin North Am 1996;80:565-587. 539, 386. However, patients with combined cardiovascular and pulmonary disease may demonstrate abnormal P(a-a)O₂ and PaO₂ responses (276, 443). This could be due to mechanical derangement of the lungs and/or chest wall or to respiratory muscle fatigue or inadequate respiratory control mechanisms. Section III. Vol. Because of the greater decrease in T_e, the increase in mean expiratory flow rate is greater than the increase in mean inspiratory flow rate. Whether ventilatory limitation causes or contributes to exercise intolerance has traditionally been evaluated by the ventilatory reserve, which reflects the relationship of ventilatory demand to ventilatory capacity. Although a spectrum of respiratory abnormalities can be seen in patients with pulmonary vascular disease, exercise is usually limited by impaired cardiovascular function and also skeletal muscle dysfunction (see Section VIII.4. Patterns of Exercise Response in Different Clinical Entities). Exercise limitation in patients with respiratory disease is complex, multifactorial, and may be difficult to establish and clearly quantitate (74, 310). Powers SK, Martin D, Cicalo M, Collop N, Huang D, Criswell D, Robinson TE, Sue DY, Huszczuk A, Weller-Ravell D, Hansen JE. Role of exercise stress testing in preoperative evaluation of patients for lung resection. Mancini DM, Walter G, Reichel N, Lenkinski R, McCully KK, Mullen JL, Wilson JR, Gift AG. The most commonly evaluated symptoms are chest pain, exertional breathlessness, general fatigue, and leg fatigue. Controversy persists as to whether a deficiency of oxygen delivery versus oxidative capacity also contributes to the onset of lactic acid production, hence the term "anaerobic threshold." It is possible that both processes, that is, the pattern of muscle fiber recruitment and a potential imbalance between oxygen supply and oxidative metabolism, contribute to the increase in lactic acid as exercise intensity increases. Furthermore, there is no convincing evidence to substantiate that anaerobiosis at the cellular level is responsible for the increased arterial lactate above the AT; lactate accumulation may occur above and below a critical P_O2, which suggests that other factors (i.e., glycolytic enzymes) may also be involved (314). Am J Respir Crit Care Med 1997;156:1023-1028. Use of arm crank exercise in the detection of abnormal pulmonary gas exchange in patients at low altitude. Exercise testing of patients with coronary heart disease: principles and normal standards for evaluation. Chest 1992;101(5 Suppl):242S-247S. J Clin Invest 1979;63:665-676. Chest 1994;105:168-174. Archer GJ, Hoyle JL, McCluskey A, Macdonald J, Casaburi R. Because Pco₂ is determined by O₂ delivery, there is a strong interaction between O₂ delivery (convective O₂ delivery) and the diffusion capacity of the muscle (O₂ tissue diffusion). Med Sci Sports Exerc 1982;14:339-343. Am Rev Respir Dis 1989;140:1373-1380. Am J Cardiol 1985;55:1037-1042. 441. Martinez FJ, Orens JB, Whyte RI, Graf L, Lynch JP III, Becker FS. Contrasting cardiovascular and respiratory responses to exercise in mitral valve and chronic obstructive pulmonary diseases. Graded comprehensive cardiopulmonary exercise testing in the evaluation of dyspnea unexplained by routine evaluation. 166. Am Rev Respir Dis 1991;143:219-225. Eur Respir J 1995;8:306-313. They feature a reciprocating piston; injection of a precision gas mixture at a precisely metered rate yields simulation of known V_E, V_{CO}2, and V_O2. Leblanc P, Summers E, Inman MD, Jones NL, Campbell EJ, Killian KJ. Advances in pulmonary laboratory testing. Chest 1995;107:144-149. The authors postulated that obese patients might have relatively less efficient cardiac performance, relying on greater tissue extraction during exercise compared with normal subjects. Prediction of maximum exercise tolerance in patients with COPD. Jones NL, Summers E, Killian KJ. Lung volume reduction surgery: official statement of the American Thoracic Society. The focus of this document is on clinical indications, standardization issues, and interpretative strategies for CPET in adults. Weisman IM. 144. Detection of expiratory flow limitation during exercise in COPD patients. Am Rev Respir Dis 1991;144:1240-1244. Med Sci Sports Exerc 1993;25:S186. Dillard TA, Piantadosi S, Rajagopal KR. 162. It is this profile that separates this response from the onset of hyperventilation from other causes (e.g., anxiety, pain, or hypoxemia), in which case both V_E/V_O2 and V_E/V_{CO}2 would increase in concert. Am J Respir Crit Care Med 1995;159:1277-1283. J Am Coll Cardiol 1993;22(4 Suppl A):93A-96A. In addition, CPET permits the detection of clinically occult heart disease and provides a more reliable estimate of functional capacity postoperatively compared with PFTs, which routinely overestimate functional loss after lung resection (122). Am Rev Respir Dis 1986;133:581-586. Weber KT, Janicki JS. Redefining the lowest exercise peak oxygen consumption acceptable for lung resection of high risk patients. American Thoracic Society. Chest 1992;102:169-175. Moque LR, Rantala B, Finucane KE, Egan BA, Dawson SA. Anthropomorphic data, PFTs, and peak exercise results appear in Table 20 TABLE 20. Yeh MP, Gardner RM, Adams TD, Yanowitz FG, Crapo RO. Preoperative evaluation of cardiac failure and ischemia in elderly patients by cardiopulmonary exercise testing (see comments). Blackie SP, Fairbairn MS, McElvaney GN, Morrison NJ, Wilcox PG, Parly RL. If necessary and based on the criteria of the physician, admission to the hospital may be warranted. J Med Syst 1993;17:227-231. However, as noted, exercise limitation is most probably multifactorial. Work has shown that CPET is helpful in

people younger than 40 years. Consequently, the ventilatory equivalents for O₂ and end-tidal O₂ reach their nadir and begin to rise in concert with the S1–S2 transition, without an increase in the ventilatory equivalent for CO₂ and/or decrease in end-tidal Pco₂. 82. Exercise tolerance in chronic airway obstruction. Eur Respir J 2000;15:617–618.

Functional evaluation of the lung resection candidate. A hyperbolic ergometer for cycling and cranking. Reference values for gas exchange during exercise in healthy nonsmoking and smoking men. 53. Slivka WA, Sciarba FC. Skin color and ear oximetry. J Cardiopulm Rehabil 2000;20:251–258. Ideally, independent reference laboratories would validate CPET systems akin to the process available for spirometers. However, it must be stressed that the user bears the responsibility for assuring that measurements remain accurate. 34. For example, peak HR = 90% predicted but with 20 beats of heart rate reserve, while a borderline peak Ve/MVV = 80% but with likely flow limitation because fr = 66. A pulmonary angiogram demonstrated significant persistent bilateral pulmonary vascular abnormalities. Zarich SW, Kowalchuk GJ, McGuire MP, Benotti PN, Mascioli EA, Nesto RW. Circulation 1988;77:552–559. A low, unchanging, flat O₂ pulse with increasing work rate may therefore be interpreted as resulting from a reduced SV and/or as a failure for further skeletal muscle O₂ extraction. xviii. Performance, ventilation, and oxygen consumption in three different types of exercise test in patients with chronic obstructive lung disease. Am Rev Respir Dis 1991;144:520–525. Sturani C, Papiris S, Galavotti V, Gunella G. Ventilatory and cardiovascular responses to inspired He-O₂ during exercise in chronic obstructive pulmonary disease [see comments]. Rahn H, Fenn WO. Measurement of breathlessness during exercise in asthmatics: predictor variables, reliability, and responsiveness. And although the values can vary by up to 50% in normal subjects, a lower limit of a 15% difference between Ve and MVV appears to be a reasonable reserve, based on 95% confidence limits of normative data. Moderate reduction in aerobic capacity was noted (Figure 13A). Controlled trial of physical training in chronic heart failure: exercise performance, hemodynamics, ventilation, and autonomic function [see comments]. Dickstein K, Barvik S, Aarsland T, Snapinn S, Karisson J. The minimal value (which occurs near maximal exercise) should be less than 0.20 in younger individuals, less than 0.28 in individuals less than 40 years of age, and 0.30 for those older than 40 years; higher values are seen in many forms of lung disease. 173–185. Several factors can also introduce additional errors in the measurements. In the final analysis, the assessment of subject motivation and effort requires attention to several factors including physiologic variables, observation of the patient, and quantification of symptom(s). Reason(s) for stopping the exercise test, using the modified Borg Scale or VAS and the subject's own words, should be included and reported with the variable responses.

Likewise, although CPET has been used to demonstrate the value of early exercise training after heart transplantation on quality of life and increased capacity for physical work, its routine use in this setting also remains uncertain and requires additional investigation (69). 128. Reproducibility of cardiopulmonary parameters during exercise in patients with chronic cardiac failure: the need for a preliminary test. 299. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Unexplained exertional limitation: characterization in a large cohort discovered to have mitochondrial myopathy. Denison D, Al-Hillawi H, Turton C. 442. Cardiologia 1996;41:621–634. In the absence of a discernible plateau, the highest Vo₂ actually attained on the test is more properly termed VO₂peak. Sports Med 2000;30:171–192. Failure to obtain a unique threshold on the blood lactate concentration curve during exercise. Demand vs. 157. 251. ATS guidelines/statements/position papers/procedure manuals were likewise utilized (16–25). The impact of exercise modality (cycle exercise versus treadmill) as a function of muscle mass involved and protocol (constant work versus incremental, continuous versus discontinuous, etc.) as a reflection of differences in temporal patterns of work rate changes on interpretation is well appreciated and has been addressed previously (see Section V: Reference Values; Section III: Methodology; and Section IV: Conceptual and Physiologic Basis of Cardiopulmonary Exercise Testing Measurements). Note, however, that pulse oximetry indicated substantial exercise desaturation. Thus, fit athletes as well as those who are regular joggers or cyclists may achieve peak Vo₂ and anaerobic threshold values that are well above predicted. The American College of Sports Medicine has established a system to credential technicians in clinical exercise testing (14). An impressive number of variables are typically measured during cardiopulmonary exercise testing (Table 10) TABLE 10. Mahler DA, Faryniarz K, Lentine T, Ward J, Olmstead EM, O'Connor GT. 272. Ve/MVV (measured) is usually normal but may be increased in extreme obesity. New York: Marcel Dekker; 1991. A chest roentgenogram and high-resolution computed tomography scan of the chest were consistent with IPF. Anthropomorphic data, PFTs, and peak exercise results appear in Table 22 TABLE 22. Sullivan MJ, Higginbotham MB, Cobb FR. Likewise, this method requires validation in patients. Incremental cycle ergometry (IET) in the evaluation of airway hyperreactivity in unexplained dyspnea [abstract]. Because laminar flow is required and sputum impaction on the transducer screen can degrade performance, pneumotachographs have generally been positioned well downstream from the mouth. Br Heart J 1990;63:281–283. Johnson BD, Dempsey JA. Med Sci Sports Exerc 1986;18:344–352. Methods for cardiopulmonary exercise testing. 291. It would appear that patients with IPF (516, 517) are more likely to be circulatory limited than are those with scleroderma (478). The patient had a smoking history of more than 50 pack-years but had stopped 12 years earlier, when the diagnosis of COPD was first established. 331. The slope of the Ve–Vco₂ relationship was WNL (Figure 11D). Chronic respiratory alkalosis with a downregulated PaCO₂ set point may also be observed at rest before exercise. Chest 1989;95:218–225. 412. Corresponds to the O₂ uptake per heart beat. 227. Porszasz J, Barstow TJ, Wasserman K. Am J Respir Crit Care Med 1996;153:967–975. Physiological measurements of metabolic functions in man. Furthermore, although different interpretative algorithms are available, none has been clinically validated (3, 348, 448, 449). J Appl Physiol 1986;61:1749–1757. Furthermore, in contrast to normal subjects, in whom physiologic limitation to O₂ transport may be evident, patients are often symptom limited, and may stop exercise before reaching physiologic limits of metabolic or gas transport capacity.

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