THE PEAK VERSUS MAXIMUM OXYGEN UPTAKE ISSUE

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The terms peak and maximum oxygen uptake (V'O_2 peak and V'O_2 max, respectively) are often used as though they are synonymous. But there are important distinctions to be made between them. While the V'O_2 peak is the easier to define and determine, its relevance to physiological and patho-physiological functioning is less secure. It is, simply, the highest value of V'O_2 attained on the particular test, most commonly an incremental or other high-intensity test, designed to bring the subject to the limit of tolerance – neglecting, for the moment, considerations of what time, or breath-number, frame of reference is chosen for the determination. Unfortunately, it is the highest value achieved regardless of the subject's effort. And so while it defines the highest V'O_2 that was *attained* during the test it does not necessarily define the highest value *attainable* by the subject. This value is the V'O_2 max: a term introduced by Hill and Lupton in 1923 as *''the oxygen intake during an exercise intensity at which actual oxygen intake reaches a maximum beyond which no increase in effort can raise it''* (1); its rigorous determination depends on a particular criterion having being met. This being the demonstration that V'O_2 does not continue to increase, or only to increase by a trivially-small amount, despite further increases in WR "involving a large proportion of the muscle mass" i.e. a V'O_2 "plateau" results when V'O_2 is plotted as a function of work rate.

As originally designed in the 1950's (2, 3) the determination of the V'O_2 max utilised a series of non-continuous, progressively-increasing, constant work rate tests performed on separate days, or at different times of the day. Naturally the range of work rates that can be utilised by the investigator, and their consequent O_2 demands, is greater than the body's ability to transport and utilise the necessary oxygen. And so, when the tests are performed with this format, a plateau becomes apparent in *every* subject, as schematised in Figure 1 and demonstrated experimentally in Figs 2 and 3.

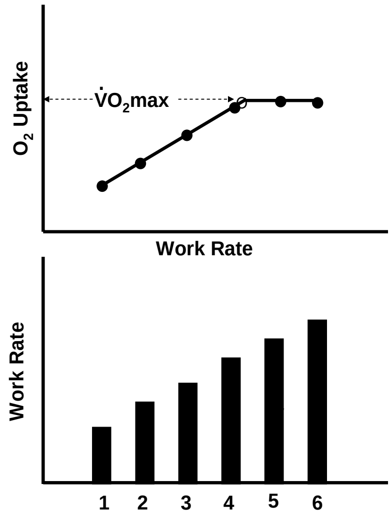

Figure 1. Schematic (and idealized) representation of the end-bout oxygen uptake to a series of constant work rate tests performed to the steady state or to the limit of tolerance.

While the demonstrable plateauing of the V'O_2 justifies the use of the term V'O_2 max. it should be noted that were the subject in Fig 1 to have ended the test at the work rate and V'O_2 depicted by the open symbol then the value should only be characterized as the V'O_2 peak – despite, in this case, actually being the subjects V'O_2 max. But of course the investigator doesn't know that this is the case without the subsequent supporting criterion of the plateau.

As stated above, the presence of a V'O_2 "plateau" requires a demonstration that the V'O_2 *not* continue to increase, or only to increase by *a trivially-small amount*, despite further increases in WR. But what constitutes an appropriate criterion of a "trivially-small amount" for V'O_2? Naturally this depends on the expected increase over the work rate increment. As originally proposed by Taylor et al., (2) in order to meet the criterion of a V'O_2 max the V'O_2 was stipulated not to increase by more than 2.1 ml/kg/min, or approximately 150 ml/min for a "typical" subject. But this was for an increment of 2.5% on the treadmill at a speed of 7 mph – clearly not relevant for clinical, and possibly other, exercise testing. This "trivially-small" value was slightly different in the subsequent study of Mitchell et al., (3) but these authors used the lower speed of 6 mph. In both cases, however, the "trivially-small" criterion amounted to approximately 50% of the *expected* increase in V'O_2 for that work rate increment. Unfortunately, the 150 ml/min criterion somehow became commonplace as a criterion of adequacy for justifying that a V'O_2 max had been obtained, independent of the work rate increment over which it was determined – even, in many instances, when that work rate increment actually required a V'O_2 of less than 150 ml/min. The original, and importantly experimentally determined, value of less than 50% of the expected increase in V'O_2 for that work rate increment can therefore be considered to be an appropriate criterion that a V'O_2 max has been obtained. But while this can apparently be justified independent of the work-rate profile it is most appropriately applied to incremental testing. To meet that criterion for a single constant-load test the investigator would have to discriminate the 50% discrepancy in the expected kinetic profile of the V'O_2 response in the final period of the test; there is, to date, no general agreement of what that is for different subjects performing very heavy exercise to the limit of tolerance (see ref 4 for several perspectives).

The issue can be resolved with a series of additional tests (e.g. Figs 2 and 3 (left panels)), where the plateau criterion for establishing the subject's V'O_2 max is met *between* tests - whether or not there was a demonstrable plateau *within* a test (it is important to note that there was no requirement for this in the original V'O_2 max proposals). But, as shown in the right panel of Fig 2, the same limiting value of V'O_2 resulting from the single ramp-incremental protocol should only be reported as the subject's V'O_2 peak.

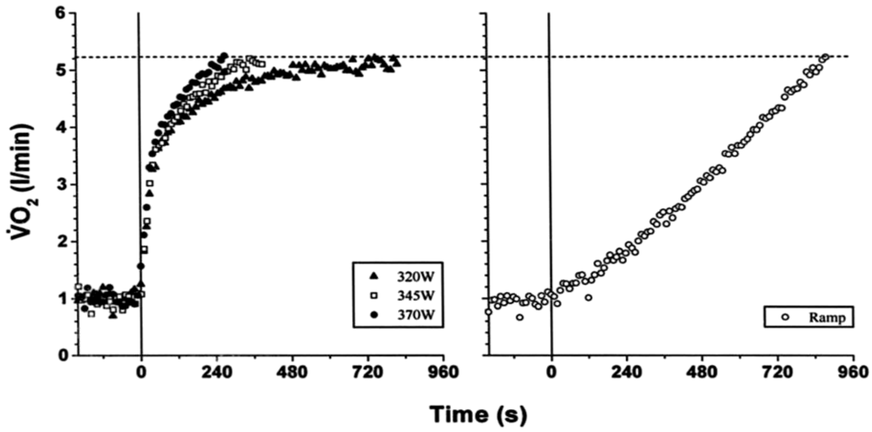

Figure 2. Time course of the oxygen uptake response the three constant work rate and one ramp-incremental exercise tests performed to the limit of tolerance in a healthy young same subject (Used with permission, from Day et al., 2003 (6)).

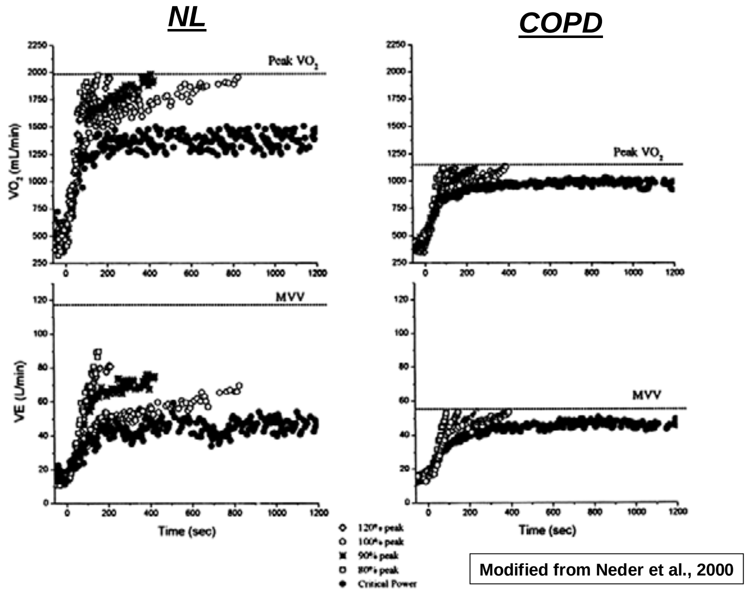

Figure 3. Time course of the oxygen uptake and ventilatory responses to four constant work rate tests performed to the limit of tolerance in a normal subject and one with chronic obstructive pulmonary disease. The results of a test performed at the upper limit of sustainable oxygen uptake are also shown. (Used with permission, from Neder J.A et al. Am. J. Respir. Crit. Care Med. 162:497-504, 2000).

The issue of “involving a large proportion of the muscle mass” also justifies consideration. Using the multi constant work rate format, described above, the $V'O_2$ plateau achieved for arm exercise will be appreciably less than for leg exercise and will be less using conventional cycle ergometry compared with treadmill ergometry. And if arm exercise is added to leg exercise the $V'O_2$ max can be even greater – as demonstrated in the classic 1955 study of Taylor et al. (2). And so, even with a demonstrable plateau of $V'O_2$ the consequent $V'O_2$ max may not be that of “the body” but rather of the muscle mass recruited to perform the task – unless, of course adding the additional arm work does not further increase the maximum value obtained in the limiting leg test, as can be the case fit young subjects (5).

During the more clinically relevant ramp-type cycle ergometer exercise, it has been reported that plateaus of $V'O_2$ are evident in only a small fraction of normal subjects (6) as shown in Fig 4.

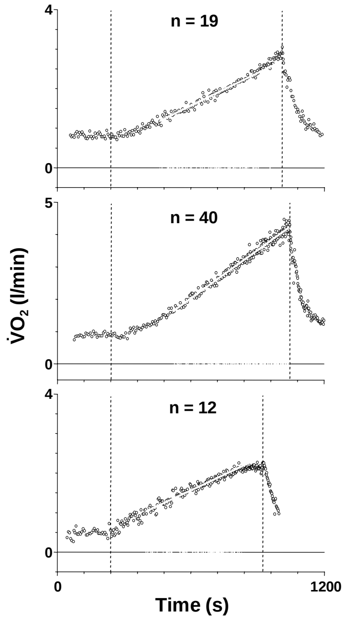

Figure 4. Examples of the three oxygen uptake response patterns to ramp-incremental exercise near to the limit of tolerance in normal subjects: concave upwards; maintained linearity; and convex upwards, i.e. evidencing a V'O_2 max pattern (Used with permission, from Day et al., 2003 (6)).

But with sufficiently good effort the final V'O_2 value attained on the ramp, even without plateauing, does not differ significantly from that attained with the demonstrable plateau criterion from a series of high intensity constant load tests (see, for example, Figs 2 and 3). This has recently supported in a large group of subjects by Snell et al. (7) – although in this instance the authors did report a consistent plateauing of V'O_2 in their subjects. These, however, were highly trained distance runners undergoing a treadmill exercise protocol that utilized 2.5% increases in grade each 2 mins at running speeds of 9 mph for men and 8 mph.

In those instances in which the investigator has chosen the ramp protocol (for the wide range of additional physiologically-relevant information it provides (8, 9, 10)) and there is concern that a sufficiently-discernable plateau of V'O_2 is evident at the limit of tolerance then performing a subsequent constant work rate test, after a short recovery period e.g. 5 mins or so, at a work rate slightly higher than that attained on the ramp (11) can provide incontrovertible evidence of the V'O_2 max, as shown in Fig. 5. This, however, has been shown to be the case in normal subjects; whether this physically challenging protocol is appropriate to patient populations is another matter.

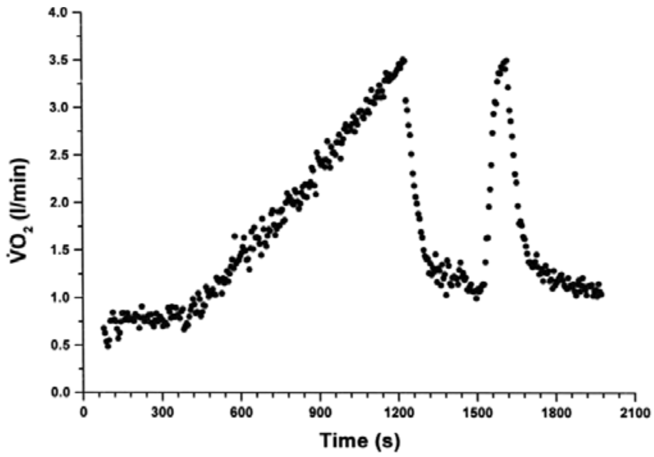

Figure 5. The oxygen uptake response to a ramp-incremental exercise test followed by a constant work rate test (performed to the limit of tolerance). The latter test was imposed at a work rate that was 5% higher than that achieved on the constant work rate test. Note that the same peak V'O_2 was attained on each individual test despite no evidence of a plateau in either; the combination of the tests, however, provide the required V'O_2 max criterion (Used with permission, from Rossiter et al., 2006 (11)).

The V'O_2 "plateau" value that is achieved is taken to reflect the attainment of a limitation at some point(s) in the O_2 conductance pathway from the lungs to the site of the mitochondrial O_2 consumption - the convective flows of O_2 into the lungs and through the vasculature, and the diffusive O_2 flows across the pulmonary and muscle capillary beds (12, 13. In normal subjects this is thought to be determined by a limit being reached in the cardiac output (14) – at least for *large* muscle group dynamic exercise. But, of course, this is not necessarily the case in patients with impaired systemic functioning i.e. where "premature" termination of the test is a consequence of unusually potent perceptual influences, such as dyspnea, angina or claudicating pain. This may, therefore, reflect as good an effort as that given by subject who does attain a V'O_2 "plateau"; just that the source of the limiting perception differs. But again, without wishing to belabor the point, the investigator doesn't (in fact cannot) know that this is the case without supporting criteria.

In an effort to circumvent the problem of whether the subject gave a "sufficiently-good" effort, other, presumably corroborative, indices of have been utilized. These include: a maximum heart rate of more than 90% predicted; a respiratory exchange ratio greater than 1.15; and a peak post-exercise lactate of greater than 8mM. Clearly, none of these provide adequate assurance that the subject actually gave a maximum effort, even in normal subjects, because:

in the first instance the predicted maximum heart rate has a standard deviation of approximately 10 beats per minute (9); in the second the maximum respiratory exchange ratio (R) is highly work-rate profile dependent (15): and in the third many subjects achieve peak post-exercise lactates that are appreciably greater than 8mM, invalidating it as an index of adequate effort (e.g. see ref 9). Furthermore, in those subjects with chronic obstructive lung disease none of these criteria typically are approached even when the subject gives his/her maximum effort. For example, the clear evidence of the $V'O_2$ plateau, associated with the constant (and limiting?) maximum V'E, exemplified by the patient with chronic obstructive lung disease in the right panel of Fig. 3 is consistent with a pulmonary-mechanical determinant of $V'O_2$ max rather than a cardiovascular, and particularly cardiac output, limitation. The peak heart rate is typically low at the limit of tolerance (as is peak lactate and R); the normal-to-high heart rate at a given sub-maximal $V'O_2$ being inconsistent with chronotropic incompetence being the cause. As in normal subjects, a plateau in the $V'O_2$ response to ramp-type incremental test is not consistently seen in patients with pulmonary-mechanical abnormalities; it is much more common in patients with cardio-vascular disease (see Fig 6).

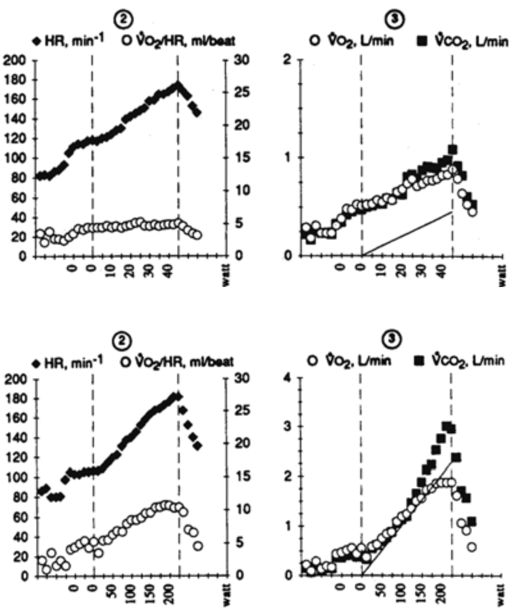

Figure 6. Examples of the oxygen uptake (and associated CO_2 output, heart rate and oxygen pulse) responses to a ramp-incremental exercise test as a function of work rate: the upper case is for a patient with idiopathic interstitial lung disease and the lower case is for a patient with coronary artery disease. Note the plateauing of oxygen uptake at, and near, the limit of tolerance in the latter case but not in the former (Used with permission, from Wasserman et al., 2005 (9); cases 49 and 18, respectively).

It was noted above that maximum respiratory exchange ratio (R) is a poor index of subject effort as it is, unlike V'O_2) highly work-rate profile dependent (see Fig. 7).

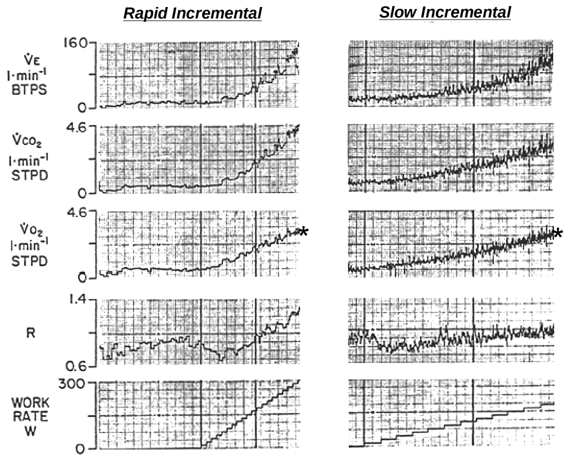

Figure 7. Ventilatory and pulmonary gas exchange responses to a rapidly-incrementing and a slowly-incrementing work rate test, each performed to the limit of tolerance in the same subject. Note that, while there is little-or-no difference in the peak O_2 uptake the maximal values of ventilation, CO_2 output, respiratory exchange ratio and work rate are all appreciably greater in the rapidly-incremental test. See text for further discussion.

This is because the *rate* at which CO_2 is produced from the bicarbonate-linked proton buffering (associated with the increased lactate ions) is a function of the *rate* of the bicarbonate decrease i.e. molecules of CO_2 per unit time being the yield from molecules of bicarbonate change per unit time. And as the bicarbonate decreases more rapidly during faster incremental tests the CO_2 yield is greater. But not only is maximum R highly work-rate profile dependent but so is maximum work rate (Fig. 7). The consequence is that care should be taken in assigning a constant work rate test as a fraction of the maximum work rate attained on a ramp test.

It is not the purpose of this note to consider “what is done” with the peak or maximum value of V'O_2 once it is determined e.g. a) whether it is then normalized with respect to: whole-body body mass; to mass$^{0.67}$ (as the mass-specific V'O_2 max is higher in small than in large subjects); whole-body, or leg(s), fat-free mass; or, in some situations, to the subjects height, b) whether the value is considered to be “normal” or not for the subject’s age, gender, height, body mass and, importantly, level of physical activity, or c) as a discriminator of the appropriateness of a subject to undergo cardiac transplantation and other major surgery.

In conclusion, therefore, unless there is demonstrable evidence that the "plateau criterion" for a $V'O_2$ max has been met in response to the exercise test then the value maximally attained should be reported as the subject's $V'O_2$ peak. When this is the case, as most typical, one is necessarily left with the concern as to whether the value achieved really is indicative of maximum effort - either given by the subject or demanded by the investigator. But, even then perhaps, this $V'O_2$ peak value may be useful in the sense that the "real" peak $V'O_2$ is "at least that" determined on the test. The lactate threshold in contrast, either determined from appropriate blood sampling or estimated from pulmonary gas exchange indices, is not effort dependent in this sense. It may therefore prove to be a "firmer" index of the functional status of the subject**.**

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