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Limitation of Maximal Oxygen Consumption: The Holy Grail of Exercise Physiology or Fool's Gold?

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Introduction

Maximal oxygen uptake (VO2 max) or maximum aerobic capacity, as it is known by exercise physiologists, is not a new topic by any means. The idea that the human body cannot survive without oxygen has been known for millennia. However, the notion that oxygen and its delivery and subsequent metabolism by exercising muscles is crucial to prolonged activity is relatively new, having first gained attention in the 1920s with the work of the English physiologist A. V. Hill. Although Archibald Vivian Hill may be most remembered by the general scientific community for his Nobel Prize winning work with the physiology of frog muscle and energy metabolism, his contributions to the initial theories and experiments relating to oxygen uptake in the exercising human make him a pioneer in the field of exercise physiology. Hill did not do all of the work, however. Credit should be given to the numerous colleagues and peers that worked with Hill, as well as those who worked independently, in designing ingenious experiments and proposing radical (at the time) theories about oxygen's role in energy metabolism, muscle contraction, and the undertaking of prolonged exercise. Over the past eighty years or so, the collective work has been accepted by essentially all exercise physiologists that oxygen uptake is intimately related to muscle contraction and aerobic exercise. This discussion seeks to focus on the topic of oxygen uptake, particularly at maximum exercise. This article will review the history of the physiological parameter of VO2 max, the theories that have been accepted or rejected over the past eighty years, the current ideas on maximal oxygen uptake and its limitations, the relevance of VO2 max, and the methods used for assessing maximal oxygen consumption.

It should be noted that this discussion looks at aerobic-type exercise and not anaerobic work. Anaerobic exercise is representative of activities of high intensity and short duration lasting anywhere from a few seconds to a minute or two depending on a person's unique physiology and the activity being performed. It is important to understand that the three primary energy systems (ATP-phosphocreatine (PC), glycolytic, and oxidative) are interconnected to such a great degree that no one system provides the entire source of energy (ATP) to working muscles at any one time, regardless of the activity, duration, or intensity. The current theory is that during certain activities of particular durations and intensities, one energy system provides the majority of ATP to the working muscles. Since it is commonly accepted that the ATP-PC and glycolytic systems are responsible for

providing the majority of ATP during exercise durations of less than three minutes or so, these types of activities will not be discussed. For the purpose of this discussion it will be assumed that anaerobic metabolism plays an inconsequential role in ATP production during prolonged, low intensity exercise and that the oxidative system is the only efficient means to provide energy to muscles.

History of Maximal Oxygen Consumption

The term "maximal oxygen uptake" was first coined by Hill and Herbst in the1920s. They postulated that there is an upper limit to oxygen uptake and that there are inter- individual differences in VO2 max. Also, they theorized that a high VO2 max was required for success in distance running and that the VO2 max is limited by the ability of the cardiorespiratory system to transport oxygen to the working muscles [1]. The early work of Hill and his colleagues was performed mostly on subjects running on a track for various distances and at different speeds. Measurements of oxygen uptake were taken while the subjects performed the activities and the primary conclusion was that once a certain speed and intensity (workload) was achieved, oxygen uptake peaks and will not rise any further despite an increase in workload. Hill was not the only investigator doing research on exercise-related physiology in the 1920s and 1930s.

Christensen [2] noted that there was a large variation in the heart rate response to exercise between subjects and that those subjects who performed regular physical activity typically had lower heart rates at a fixed workload as compared to their untrained counterparts. This led Christensen to perform a study that looked at the effects of training on three critical cardiovascular parameters: heart rate, stroke volume, and cardiac output. The study revealed that aerobic training led to a decrease in submaximal heart rate without a change in cardiac output. Since cardiac output is the product of heart rate and stroke volume, Christensen concluded that stroke volume necessarily had to increase to maintain cardiac output in the face of a decreased heart rate. These observations were made during submaximal exercise. When exercise approached maximum levels, the relationship changed a little. It was noted that maximum heart rate values were not dependent on training status and that improved performance at near-maximum levels was the result of an increased stroke volume. The stroke volume response increased cardiac output since heart rate values were essentially the same for trained and untrained individuals at maximum [2]. This increase in stroke volume might very well have explained why Henschen noticed in 1897 that cross-country skiers with larger hearts typically performed better than those with smaller hearts. The larger hearts were attributable to hypertrophy of the left ventricle, which was a result of chronic aerobic training [2].

As the twentieth century approached its midpoint, the science of exercise physiology grew rapidly in large part due to advances in medical technology which allowed for more detailed and intrusive studies to be performed. Whereas studies performed in the 1920s and 30s relied heavily on assumptions and estimations of such variables as cardiac output, stroke volume and arterio-venous oxygen difference (a-vo2 diff), experiments carried out in the 1950s and 60s actually measured such variables through intrusive, surgical means. While early studies concluded that the size of a person's heart was largely dependent on training status and subsequently was an accurate determinant of aerobic

performance, these conclusions lacked substantial concrete evidence. The advent of imaging technology, like X-rays, and later ultra sound allowed for a much more accurate determination of heart size in addition to heart weight measurements and enabled exercise physiologists to further theorize that larger hearts in non-pathologic individuals were the result of adaptive processes related to aerobic exercise.

Advances in science also allowed for the first measures of a-vO2 diff, which was one of the primary factors influencing oxygen consumption. Procedures now allowed for the measurement of oxygen content in the arterial blood as well as oxygen content in the venous blood which could be used to extrapolate how much oxygen was extracted by the working muscles at the cellular level. As procedures for placing catheters in various areas of the cardiovascular system became more practiced and accepted, detailed information about systemic flow and distribution, perfusion pressures in the tissues, and filling time of the ventricles of the heart became was published. Studies using intrusive or surgical means to analyze various hemodynamic factors dispelled many commonly held beliefs about the heart and cardiovascular system. One of the more accepted theories of the early days of exercise physiology was that stroke volume had to decrease as the frequency of heart beats approached maximum owing to a filling time not long enough to maximally fill the ventricles with blood. Studies performed in the 1960s demonstrated that the large end-diastolic volume needed to produce a large stroke volume was achieved without an elevation in filling pressure and that at high heart rates, the majority of the end-diastolic volume (80-90%) was attained within the first third of diastole [2]. This evidence contradicted the earlier theory that stroke volume must necessarily decrease with the attainment of maximal or near-maximal heart rates.

As new and revolutionary methods for measuring and analyzing the microscopic components of the cardiovascular system emerged, the focus of oxygen uptake shifted from central aspects to the periphery. By this time it was well established that the heart responds to chronic aerobic stress by a variety of adaptive mechanisms including ventricular hypertrophy, increased stroke volume at rest and exercise, decreased resting and submaximal exercise heart rates, and an increase in cardiac output during increasing workload. Although the previous parameters are listed as separate variables, they are all intertwined and act in concert with one another to reduce the work of the heart at rest and low intensity work, and they increase the heart's ability to pump blood out into the system during higher intensity and maximal work. These adaptations to chronic aerobic stressors are known as central factors and do not take into account mechanisms of the periphery, namely oxygen extraction at the cellular level.

Oxygen extraction deals with a host of issues from perfusion pressures to enzyme activity within the cells to the transport and storage of oxygen within the blood cells via hemoglobin and myoglobin, respectively. Analysis of such variables was impossible by the technological standards of the 1920s and 30s in addition to the relative lack of scientific knowledge relating to medicine in general and human physiology in particular. The progression of knowledge from the 1920s to the present day as it relates to the cardiovascular system and oxygen uptake should not have been unexpected. The past eighty years has seen a general trend that began with the basic central factors, namely

the heart and lungs, and migrated to peripheral mechanisms like the muscle cells for explaining oxygen consumption. While much is known and defined about the topic of oxygen consumption, the debate that has raged on from the beginning still exists: what is the limiting factor in maximal oxygen consumption? Is it a central factor or a peripheral mechanism? While the purpose of this discussion is not to definitively answer that question, this article does serve to review what is currently known about oxygen consumption and look at some key arguments from both sides of the debate.

VO2 Max and Possible Limitations

In describing oxygen consumption, it is appropriate to first break it down into its simplest form. As mentioned at the beginning of this article, oxygen is required for life to exist and, more specific to this discussion, it is required for muscle contraction. It can be said that oxygen equals energy and that energy equals muscle contraction. The beginning point in the illustration of oxygen consumption is the air in the atmosphere and the end point is muscle contraction. The air is inspired by the lungs at which point the oxygen from the atmosphere is taken in and the waste product of respiration, carbon dioxide, is released. This exchange of gases takes place at the alveoli, small sacs responsible for the diffusion of oxygen from atmospheric air into the pulmonary blood. The oxygen is transported in the blood by red blood cells which contain hemoglobin, the actual carrier of oxygen within the blood. The newly oxygenated blood is transported from the lungs to the heart which then pumps the oxygen-rich blood out into the system via the left ventricle. The great arteries exiting the heart branch off into smaller arteries which branch into even smaller arterioles which further increase in number but decrease in size as they become capillaries. The capillaries reach all tissues within the body, including skeletal muscle, and are the site for the diffusion of oxygen from the blood to the tissues and the diffusion of carbon dioxide from the tissues to the venules to be carried away to the lungs where it is finally expired as a waste product. This process of diffusion occurs as the result of pressure gradients. These differences in pressures between the gases in the plasma and those in the tissues establish the gradients for diffusion. The oxygen is then transported into the cell and finally from the cytosol to the mitochondria which can be viewed as the "power plant' of the cell. Oxygen within the mitochondria is then transformed into the usable form of energy, adenosine triphosphate (ATP), for immediate use by the working muscles or for storage. This rudimentary outline of the transport of oxygen from the atmosphere to the working muscles may seem simple at first glance but is composed of many complex variables that interact with each other to facilitate the transpor1 of oxygen to the tissues. The question then is: which of those variables is the rate limiting factor in VO2 max? Different authorities cite different factors for the limitation of VO2 max. About the only thing that everyone agrees on is the fact that there does seem to be an upper limit to oxygen uptake for each person, even though that upper limit can vary dramatically from one individual to the next. The following is a review of some of the more notable components of oxygen uptake and the possible limitations to VO2 max.

Pulmonary Factors and Oxygen Carrying Capacity

The pulmonary system, namely the lungs, is where atmospheric oxygen makes its entrance into the circulation. It should go without saying that if there is a problem with the diffusion of oxygen from atmospheric air to the hemoglobin within the blood at the site of

the alveoli, there will certainly be a reduced amount of oxygen being carried by the blood and reduced amounts of oxygen downstream in the mitochondria which would certainly limit various metabolic processes and therefore performance. The extreme manifestation of this can be seen with pathologic individuals suffering from obstructive or restrictive lung diseases that often times lead to death. Since this discussion deals with non-pathologic individuals, the topic of lung disease and its effects on oxygen consumption will be mentioned no further. It has been proposed that highly trained individuals with very high cardiac outputs may be operating with less than fully oxygen-saturated blood. It is thought that this arterial oxygen desaturation in elite athletes is caused by the decreased transit time of the red blood cells in the pulmonary capillaries which results from a high cardiac output [1]. In other words, the diameters of the pulmonary capillaries are relatively constant (although they are distensible to a degree) which means an increase in the volume of flow through those conduits will result in an increase in the flow rate. If the flow rate is too great, as is proposed in the systems of elite aerobic athletes, the red blood cells will pass by the oxygen too quickly and the time will not be sufficient to allow full oxygen saturation of the hemoglobin. This process will result in less available oxygen to the exercising muscles; a decease in available oxygen (energy) means a decrease in muscle contraction.

The presence of a pulmonary limitation is indicated because studies have been performed that looked at the effects of introducing high concentration oxygen mixtures to subjects performing maximal-type exercise. The untrained subjects did not appear to gain any increases in VO2 max or oxygen saturation as a result of the hyperoxic gas. The trained subjects, on the other hand, did see increases in both VO2 max and oxygen saturation values when breathing a 26% oxygen gas mixture to the tune of 70.1 to 74.7 mL/kg/min and 90.6% to 95.9%, respectively [1]. While pulmonary factors may be limiting in only the most elite aerobic athletes under normal environmental and atmospheric conditions, the limitations are quite apparent in all people at altitudes of 3000-5000 m and higher. The limitation is especially noticeable when exercising at altitude and results in symptoms similar to those caused by obstructive and restrictive pulmonary diseases. The main factor at altitude (or in certain pulmonary diseases) is a reduction in arterial PO2 which decreases the driving force for oxygen diffusion into the blood and results in less oxygen being transported to the tissues. It has been demonstrated that exercise ability can be increased at altitude by the use of supplemental oxygen which increases the driving force of oxygen diffusion into the blood and subsequently increases exercise capacity [1]. The results of such experiments reveal that there is indeed some degree of pulmonary limitation to VO2 max. Other authors, however, report that such interpretation is incorrect and is the result of poor experimental design, methodological limitations, and a lack of randomization of testing [3]. According to Hawley et al. [3], "arterial oxygen content cannot be the limiting factor for VO2 max." Hawley also discounts the conclusions made from blood doping studies citing incorrect interpretation and a disregard for certain accepted research practices. The proponents of blood doping claim that when a substantial amount (0.9-1.35 L) of blood is removed from the body and stored elsewhere, the body naturally regenerates more blood (and more red blood cells) to replace what has been lost. After a period of a few days to a couple of weeks it is assumed that the body has regained a normal amount of blood, including red blood cells and hemoglobin. The blood that was

taken out is then reintroduced into the body and results in a higher-than-normal concentration of hemoglobin. It is theorized that this high concentration of hemoglobin results in the ability of the blood to transport more oxygen and more oxygen translates to more ATP (energy). That additional energy results in more muscle contraction and higher levels of performance. That is, of course, assuming that the extraction ability at the cellular level increases also. It serves little functional benefit to double the amount of oxygen in the blood if the cell can only extract half that much at maximum. Contrary to the opinions of Hawley et al., studies have reported increases in VO2 max. of 4-9% as the result of blood doping with no increases seen in those subjects receiving a placebo of saline [1]. At the present time there does not appear to be a clear-cut resolution to the debate surrounding the ideas of a pulmonary limitation to maximal oxygen consumption and the efficacy of blood doping.

Cardiac Output

The concept of cardiac output and its limitations on VO2 max traces its roots back to Hill's pioneering work in the 1920s. Although the methods of Hill and other researchers of the time were rudimentary and relied heavily on estimations and unproven theories, their general conclusions have been shown to be accurate. One of the more important contributions of the time was the idea that trained athletes had larger hearts and the size was attributable to adaptive processes within the heart that caused ventricular hypertrophy. This hypertrophy of the main pump allows for more powerful contractions of the left ventricle which, in turn, causes more blood to be pumped per beat of the heart. It goes without saying that the more blood that can be pumped out into the arteries per beat, the more oxygen that is available to working muscles. If the average, untrained individual has a maximum cardiac output of 20 l/min. and the elite, aerobic athlete has a maximum cardiac output of 40 l/min., it can be assumed that if oxygen saturations are the same, twice as much oxygen is being transported within the arteries per minute in the elite athlete and this increased amount of oxygen results in greater muscle contraction and increased performance. One should be careful, however, not to assume that this doubling of cardiac output results in an actual uptake at the muscle equal to a factor of two as compared with the untrained individual. As noted previously, pulmonary factors may limit the amount of oxygen that actually diffuses into the blood and, as will be discussed later, peripheral limitations to oxygen extraction at the cellular level may also exist which limit the amount of oxygen taken up by the active cell.

Oxygen consumption can be defined as the product of heart rate and stroke volume and a-vO2 diff which then is multiplied by 0.01. If the limitation of VO2 max is indeed the result of a central component, then the answer must lie within one of the three previously mentioned variables. Since maximum heart rate appears to be regulated not by training but by genetic predisposition, it can be discounted as a limiting factor. Additionally, a large body of evidence points to arterio-venous oxygen difference as a variable that changes little with training and most likely is also the result of genetics [1]. While changes have been reported with maximum heart rate values in response to aerobic training, the overwhelming factor in increases in cardiac output (and VO2 max) seems to be reflective of increases in stroke volume. Take, for example, the previous comparison of an untrained individual with a cardiac output of 20 L/min. at maximum and an elite athlete with a cardiac

output of 40 L/min at maximum. Both individuals may very well have similar maximum heart rate values, therefore the dramatic difference in the two cardiac outputs must then be the result of stroke volume. The untrained individual who puts very little stress on his/her heart would not expect any adaptive changes to take place whereas the elite athlete puts chronic aerobic stress on his/her system which warrants severe changes within the muscle of the heart to accommodate the high aerobic workloads.

Although many characteristics of the muscle tissue of the myocardium is unique to the heart, it is nonetheless muscle and reacts in much the same way that skeletal muscle does to stress. Just as the biceps brachii react to chronic bouts of heavy barbell curls by growing larger in cross-sectional area to accommodate the increased tension on the muscle fibers, so to does the heart muscle react to increased levels of aerobic exercise by growing larger (hypertrophy) and being able to handle increased levels of aerobic work. This hypertrophy is most evident in the left ventricle as this is the primary "pumper" of blood out into the system. The cavity increases in size to accommodate larger volumes of blood and the muscle increases in cross-sectional area which allows for greater contractility and more forceful contractions. This combination of adaptive mechanisms leads to increased stroke volumes which can vary from minimal in recreationally trained individuals to extreme in the most elite endurance athletes. This argument is the basic premise upon which the cardiac output explanation for a limitation to maximal oxygen consumption is based. It is a fact that aerobically trained athletes have higher VO2 max values than their untrained counterparts (with the exception of extreme cases of genetic predisposition which can never be ruled out). It is also a fact that endurance-type athletes have higher cardiac outputs than sedentary individuals. It can then be postulated that the higher VO2 max values are the result of greater oxygen delivery which is a result of increased cardiac outputs. If the heart rate and a-vO2 diff components of the oxygen consumption equation are disregarded owing to idea that they are unaffected by training and are similar in trained and untrained individuals (maybe a correct assumption and maybe not), then the only remaining factor is stroke volume. It can then be reasoned that cardiac output and, more specifically, stroke volume, is the limiting factor of VO2 max and is the cause of the vast difference.

Peripheral Factors

The previous three topics of limitations to VO2 max have dealt with pulmonary factors, oxygen carrying capacity of the blood, and cardiac output. Collectively, these are know as central factors and were the foundation of early theories about what influenced maximal oxygen consumption. As medical technology improved and new methods for intrusive and microscopic measurement and analysis evolved, there was a shift in thinking by many exercise physiologists from a central to a peripheral mechanism that ultimately regulated oxygen consumption at maximum. The primary limiting peripheral mechanism appears to be oxygen extraction at the cellular level. Oxygen extraction, which is commonly associated with the physiological variable of a-vO2 diff, is most likely not determined solely by one factor, but by numerous variables interacting with each other. While a physiologist may indicate the number of variables influencing oxygen extraction by the exercising muscle cell is the result of dozens of factors, exercise physiologists have narrowed them down to a few that are most likely the main limitations to increased

amounts of oxygen extraction. Some of the more major peripheral factors at the cellular level are capillary density, number and size of mitochondria, and partial pressures of gases and their resultant gradients. The extraction of oxygen from the blood by the working muscles can be broken down and simplified into three steps: 1) the dissociation of oxygen from hemoglobin, 2) diffusion from the red blood cells into the muscle cells, and 3) diffusion and transport within the muscle cells to the mitochondria [3].

The first step in the mechanism of oxygen extraction is the dissociation from hemoglobin. An obvious question is: if the mechanism of oxygen's transport within the blood from the alveoli to the muscle cells is hemoglobin and its great affinity for oxygen, what causes this attractive force between oxygen and hemoglobin to be broken? The answer is that some greater force must overcome the attraction between oxygen and hemoglobin. That greater force is provided by myoglobin which is contained within the muscle cell. It is estimated that myoglobin's affinity for oxygen is approximately five times greater than that of hemoglobin [3]. Myoglobin's great affinity for oxygen does not fully account for the transport of oxygen from the capillary to the mitochondria, however. The transport of oxygen is largely dependent on the pressure gradient between the capillary and the mitochondria. To illustrate the concept of pressure gradients, an analogy can be made the weather people experience every day, and more specifically, the wind. Wind is the result of air being transported from areas of high atmospheric pressure to areas of low pressure within the atmosphere. The greater the differences in pressure between those two areas and the closer they are to one another, the steeper the pressure gradient and the stronger the winds will be in that atmospheric zone. This can be exemplified by a hurricane and the ferocious winds associated with it. The center of a hurricane has the lowest atmospheric pressures recorded on earth, therefore the pressure gradients are extremely large and the resultant winds are incredible. This same phenomenon takes place on a much smaller scale within the human body at many different sites. Specific to this discussion is the site of the capillary-muscle cell boundary and the extraction of oxygen from the blood. Since the final destination of oxygen is the mitochondria, it should be concluded that the partial pressure of oxygen is lowest at that site. In combination with myoglobin, the transport of oxygen is facilitated by the relatively higher partial pressure of oxygen within the capillaries as compared to that within the mitochondria. Maximal exercise causes the pressure gradient to increase and thus results in the transport of more oxygen to the working muscles. It should be noted that in even the most highly trained athletes, oxygen extraction is never one-hundred percent. One possible explanation of this is the fact that the partial pressure of oxygen decreases distally which results in a greatly reduced pressure gradient and therefore less oxygen diffusion [3].

Another theory surrounding the debate of oxygen extraction capabilities as being a limiting factor in maximal oxygen consumption is flow rate. This idea was visited earlier in the discussion as it related to the lungs and pulmonary function. As exercise increases, cardiac output is necessarily augmented to supply the working muscles with adequate amounts of oxygen. If the rate of flow of the blood is increased disproportionately to the vessels' ability to dilate, the result will be increased flow within the vessels. As the exercise approaches maximum, the flow rate also increases. It has been speculated that in highly trained athletes the flow rate is so great (as a result of such a high cardiac

output) that the blood passes by the muscle too rapidly to allow for optimal diffusion of oxygen. This has been proposed as yet another possible limitation to maximal oxygen consumption. Opponents of this theory cite the adaptive processes, namely increased capillary density, within aerobically trained individuals as evidence that flow rate does not limit VO2 max. Their argument is that increased capillary density is the body's way of decreasing the flow rate of blood past the muscle cells in response to chronic aerobic training. The idea is that increased capillary density necessarily increases the overall surface area (or volume) of the capillaries. If the capillaries can be seen as conduits of blood, and if the surface area of those conduits increases but the overall volume of blood (cardiac output) remains constant, the rate of flow will be decreased. This proposed adaptation of aerobically trained individuals allows for increased oxygen extraction at the capillary-muscle cell boundary and therefore increased performance in the form of oxygen consumption. Acting in synergy with this decreased flow rate in individuals with greater capillary density is the fact that increased density means increased surface area. If the capillary wall is the site for oxygen exchange, then it can be concluded that an increase in capillary wall area means a concomitant increase in transport capabilities.

Just as the final destination of gasoline is an engine, so to is the final destination of oxygen within the exercising person, only the engine is the mitochondria contained within the cells. Within the muscle fibers, the mitochondria act as "power plants" and represent the sites where oxygen is consumed in the final step of the electron transport chain. It has been noted that an adaptation to aerobic training is an increase in mitochondrial number and size. An obvious conclusion is that doubling the number of mitochondria will double the sites for oxygen uptake and metabolism. However, Bassett and Howley [3] report that a 2.2-fold increase in mitochondrial enzymes only resulted in a modest 20-40% increase in VO2 max. These findings further support the notion that mitochondrial size and number do not limit maximal oxygen consumption, but that the delivery of oxygen is the limiting factor. An unresolved question surrounding the mitochondrial debate is: why do adaptive processes cause increases in mitochondrial numbers if a percentage of those new mitochondria will go "unused"? As reported by Bassett and Howley [3], a paper presented by Holloszy and Coyle in 1984 attempted to answer this question. Their main argument was that the increase in mitochondria and mitochondrial enzymes effected submaximal oxygen consumption to a much greater degree than at maximum. The mechanism is that the increase in mitochondria caused exercise at given workloads and rates to elicit smaller disturbances in homeostasis in the trained muscles [3]. Thus, there are two main metabolic effects of an increase in mitochondrial enzymes: 1) muscles adapted to endurance exercise will oxidize fat at a higher rate (sparing muscle glycogen and blood glucose) and 2) there is decreased lactate production during exercise [3]. It is very possible that these are the major adaptations to endurance training which result in the improvements manifested by chronic aerobic training. The idea that mitochondrial numbers appear to playa minor role in VO2 max is illustrated by the fact that studies have revealed that individuals who have nearly identical VO2 max values can have up to a two-fold difference in mitochondrial enzymes indicating that the limiting mechanism of maximal oxygen consumption lies somewhere other than within the mitochondria [3]. However, even the proponents of this theory concede that mitochondrial number most likely plays some role, even if a minor one, in increases in VO2 max and its limitation.

What is the Limiting Factor?

After a review of past and current ideas surrounding the debate about VO2 max and its limitation, the question still remains: what is the limiting factor? Wagner [4] responds to this by saying the question appears to be "incorrectly framed". A review of the literature dating back to the early work of Hill and others indicates that many theories have been proposed but no one has been definitively and unequivocally proven and accepted by all exercise physiologists. To answer the previous question: no one single factor appears to be the limiting factor in VO2 max. Rather, all of the factors mentioned up to this point, and many of the ones not mentioned, seem to be interconnected and interact in such an intimate fashion that it is impossible to accurately determine which one variable ultimately limits VO2 max. Impossible, at least, by present technology and the current understanding of human physiology, particularly as it relates to exercise. Many exercise physiologists respond to that $10,000 question with a question of their own: does it really matter? The next section looks at the practicality of VO2 max and its usefulness in predicting such factors as athletic performance, overall health and fitness, and risk-factors relating to pathologic disease.

The Practical Value of VO2 Max

Sutton [5] refers to VO2 max as "the gold standard whereby the capacity of humans to perform prolonged exercise is judged." At first glance, this statement, the view of which is shared by many exercise physiologists as well as non- exercise physiologists, appears to be directed towards athletes and more specifically, endurance-type athletes. After all, the ability to perform prolonged exercise is of seemingly little importance to the person who chooses not to exercise and just does not care about athletics. To the athlete, on the other hand, the ability to perform at high levels in an athletic event is paramount to success. Through years and years of training, the endurance athlete slowly improves his or her ability to go longer and faster. The initial adaptation may be of a neuromuscular type followed by increased muscular endurance and/or size. However, it is difficult to argue against VO2 max as being the ultimate "trainable" factor affecting performance in endurance-type sports. An educated and well-coached athlete understands early on that their inherent genetics will be the final predictor of proficiency and success in a given sport or athletic event and not dedication or resolve. A person with a high predominance of type-2 muscle fibers in the leg musculature will never be a world class marathon runner just as a person with unfavorable upper-body tendon insertions will never be able to bench press world record weights. This is just a given and to attempt to change such factors is futile. To the athlete who does aspire to endurance-type sports and does have favorable genetics for aerobic activities, the emphasis changes from things that can not be changed (genetics) to abilities that can be honed and improved like muscular endurance, neuromuscular coordination, mechanical efficiency, and cardiorespiratory fitness. All agree that improving these and other factors are prerequisite to excelling in endurance sports. However, for the purposes and scope of this discussion, cardiorespiratory fitness is the only variable that will be analyzed.

It can be assumed that the chronically trained endurance athlete will see little additional improvements after the first 6-12 months of training in general muscle structure and neuromuscular coordination with the exception of drastic changes in training routines and

such factors as mechanics directly relating to the activity (e.g., running). The long-term factor affecting performance seems to be the cardiorespiratory system, and specifically the ability of the exercising muscles to receive oxygen. As mentioned ad nauseam in the previous sections, this ability may be limited by central factors like oxygen uptake in the lungs or cardiac output in the heart or may be hindered by peripheral mechanisms such as oxygen extraction at the cellular level. Whatever the actual limitation is, with rare exception, VO2 max will be the ultimate limiting factor in endurance activities for the chronically trained athlete. It is clear that VO2 max plays an important role in athletes but what value does it have to non-athletes? Much has been talked about relating to the ability of VO2 max to assess overall fitness in the average person and perhaps predict the likelihood of disease, specifically cardiovascular disease. The general public holds a common misconception that a high VO2 max. will ensure health and prevent the onset of cardiovascular disease. This misconception is largely the result of misinformation provided by personal trainers and others in higher educational and administrative positions that rely on older schools of thought and theories on fitness and disease prevention that have since been disproven. The medical doctor or well-educated exercise physiologist knows that a high percentage of diseases (including cardiovascular) are the result of genetic predisposition and are presently unpredictable. This is illustrated by the fact that nearly half of the people that suffer a myocardial infarction have no previous medical conditions, no family history, and are not stratified as high-risk. It is indeed a scary thought to know that every year a certain percentage of athletes or athletic individuals and another percentage of normal, low-risk, healthy people die from heart attacks and get diagnosed with heart disease. It beckons the question of why should people bother to exercise and live healthy lifestyles if it doesn't change the ultimate, genetically predetermined outcome? The answer is indeed multi-faceted.

First of all, exercise and a prudent lifestyle do appear to lessen the likelihood of cardiovascular complications even in the face of genetics. Even if exercise is not, if you will pardon the expression "a get out of jail free card", it seems foolish for someone not to try their very best to stack the deck in their favor. Maybe death by cardiac means is inevitable for certain people. What then is the value of at least staving it off for ten or twenty years? Most would probably say it is priceless. For others, perhaps they are sitting on the proverbial "genetic fence" and could go either way depending on such changeable factors as environment, lifestyle, and activity levels. What is the value of exercise then? More than priceless? Perhaps. Either way, the science of molecular genetics is still in its infancy and therefore, at the present time, no one will know just what their genetics have written out for them. So what, then, is the harm in taking all possible precautions? Some might say they have more important things to do with their time or any other of a variety of excuses not to exercise which leads to the second point of why people should exercise. Exercise has been shown time after time to improve quality of life. To put it succinctly, there is clearly no guarantee as to how long anyone person is going to be here so why not guarantee that those days, however numerous, are spent living a quality life? So how does this relate to VO2 max? It should illustrate that the value of VO2 max testing in average, non-athletic individuals is not as a precise predictor of longevity or susceptibility to a disease. However, it goes without saying that any individual who would choose an average or below average VO2 max over a high one is clearly not thinking straight.

Whereas VO2 max is regarded as important to athletes owing to its potential limitations on performance, such concerns are not warranted in non-athletes as their limiting factors will most likely be everything but VO2 max. Maximal oxygen consumption clearly has differing degrees of practicality for all populations. That relevance, however, should be put in the context of other factors that relate specifically to the individual because VO2 max is not the cure-all panacea. VO2 max does have its place, however, and therefore raises the question of what is the best way to assess it? The following section addresses the issue of maximal oxygen consumption and its assessment.

Assessing VO2 Max

It seems that over the past eighty or so years the second largest debate in the oxygen consumption topic (the largest being the limiting factor(s) of course) is its measurement. What is the most accurate method by which to accurately measure oxygen consumption? Once again the answer appears unclear in both the present and past literature. It should be noted that the only way to truly measure oxygen consumption is by intrusive surgical methods. Typically this involves the insertion of a catheter into an artery and one into a vein or the right atrium. This then allows for the simple deduction of the difference in arterial oxygen content as compared to venous oxygen content. This method, however, has its limitations as well. While catheter techniques can measure overall differences in arterial and venous oxygen content, the values are not specific to certain muscles or even cells and represent oxygen uptake of exercising and non-exercising muscles, organs, and other processes requiring oxygen like digestion. Technology has only recently allowed for more direct and specific measures of oxygen consumption at the cellular level but such procedures are still in the experimental stages and are by no means mainstream. The fact that such accurate methods for measuring oxygen consumption are confined mostly to the laboratories of research scientists and the field of medicine means that the majority of people interested in oxygen consumption must settle for estimates rather than measures.

A variety of protocols have been designed to estimate maximal oxygen uptake by incorporating submaximal exercise and regression formulas. Such popular indirect estimation protocols are the Astrand-Ryhming and YMCA cycle ergometer tests. Other VO2 tests exist that seek to provide more of a "direct" estimation of VO2 max through such techniques as open-circuit spirometry which physically measures the volumes and contents of each inspired and expired breath while exercising at maximum. VO2 max can be assessed for any type of aerobic activity but typically is limited to some form of treadmill activity (walking/running) or ergometry (upper/lower body). As briefly mentioned previously, a variety of protocols exist and the selection of which one to use is dependent on a few different factors. First of all, clinical-type techniques like open-circuit spirometry are typically relegated to laboratories and should be administered by an exercise physiologist or other qualified individual. This limits such laboratory-type tests to only a few commercial health clubs owing to the expense of the metabolic and computing equipment and the unwillingness of the health club to pay qualified personnel to be on staff .The fitness centers attended by the general public usually really on cycle ergometry and the YMCA or Astrand-Ryhming protocol to assess VO2 max. The benefit of these tests is that they are easy to perform because they do not require the subject to go

beyond sub-maximal levels of exertion and they are easy to administer and interpret by individuals who do not have a strong background in exercise physiology. The disadvantage is that such tests can be quite inaccurate owing to the degree upon which the test is based on estimation of a maximal value from a submaximal effort. In the commercial setting these tests do not provide highly accurate values of VO2 max but do serve the purpose of roughly estimating whether a person is in "good", "average", or "poor" cardiorespiratory condition. For the average, non-pathologic person, such a "ballpark" estimate is quite sufficient and can provide an indication of what kind of exercise routine to perform in order to improve cardiorespiratory fitness levels. For elite athletes or pathologic individuals, however. a more accurate determination of VO2 max is usually desired and in their cases they may want to seek out research or medical settings which offer a more detailed and reliable test of VO2 max.

In the case of athletes, mode of testing is crucial. A runner is going to be metabolically and mechanically adapted for running, a cyclist for cycling, and a rower for rowing. There is little practical value of testing a cyclist's ability to perform maximal upper- body ergometry. It is to be expected that a runner will achieve their highest VO2 max on a treadmill because that is what their body will be most efficient at and therefore will elicit the highest oxygen consumption. If a runner is put on a cycle ergometer for a VO2 max test it is assumed that his or her VO2 max on that apparatus will be predictably less than that achieved on the treadmill. This would then be referred to as his or her VO2 "peak" and is reflective of the maximal oxygen consumption possible for that particular mode of testing. For the non-athlete, it is generally accepted that the highest oxygen consumption values, and therefore true VO2 max , are achieved on a treadmill due to the necessary use of a maximal number of muscle groups (both upper- and lower-body). It goes without saying that the more muscle mass used for exercise, the greater the amount of oxygen that is required to fuel those muscular contractions. Therefore the exercise that recruits the greatest amount of musculature will be most indicative of a person's true VO2 max. No one single exercise will ever recruit 100% of a person's lean muscle mass but some modes appear to come closer to that mark than others. Running is one such mode and therefore is typically the exercise of choice when assessing VO2 max. It can be speculated that, in the case of endurance athletes, they will achieve their highest oxygen consumption while performing a maximal, sport-specific test. However, some authorities suggest that even a trained cyclist may achieve a higher VO2 max on a treadmill than on a bicycle owing to the reliance on the much larger amount of muscle mass needed for running. The bottom line is that whatever the athlete's competitive background is, the mode of exercise that elicits the greatest oxygen consumption will be indicative of a VO2 max and all others will merely be "peak" values.

Putting It All Together

Clearly, VO2 max does not increase infinitely with increasing workload and therefore a limiting factor or factors is/are at work. This can not be disputed. Nor can the idea be argued against that upper-body aerobic exercise like arm ergometry or rowing will elicit a lower oxygen uptake than lower body exercise like cycling owing to the differences in percentages of total muscle mass actively involved. It has been proven that activities involving larger percentages of muscle mass, like running which uses both upper- and

lower-body musculature, require greater amounts of oxygen. The highest values for oxygen consumption have been witnessed in elite cross-country skiers due to the intense use of total body musculature. While cross-country skiing may elicit the highest, and therefore truest, values for VO2 max, the mode of exercise is not practical for general testing of oxygen consumption nor is it relative for people who don't competitively ski. The fact that running requires such large amounts of muscle mass means that treadmill testing is a relatively accurate mode for testing the average person who is not sport-specific and who does not require "easier" tests due to age, disease, or disability. As for the value of measuring or estimating VO2 max for reasons other than performance, there is a dichotomy among exercise physiologists as to the predictive value of VO2 max in determining the likelihood of disease and in predicting longevity. Some believe the regression equations and normative data related to VO2 max that have been collected over the course of many decades are accurate predictors of certain diseases in the form of risk stratification while others insist that genetic factors and other random, unexplained variables will ultimately determine whether or not someone will be afflicted with a disease. While neither school of thought has been universally accepted, it does seem logical that a fit person is more likely to avoid disease than an unfit person. The question then arises: what defines a fit person? At this particular point in time, most agree that aerobic capacity is the best indicator of overall fitness. As the field of exercise physiology evolves, this idea may change or it may remain the same. Occasional paradigm shifts are to be expected in a field as young and imperfect as exercise physiology.

The limiting factor(s) affecting VO2 max is/are not particularly important for non-athletes because their performance will be limited by other factors like muscular fatigue and pain tolerance. However, for the athlete who has trained his or her body to work at maximal levels, V02 max appears to playa large role in the ultimate limitation of performance. Arguments have been presented that state a central component ultimately determines an individual's maximum capacity for oxygen uptake and utilization. It has been estimated that 70-85% of the limitation in V02 max is linked to maximal cardiac output [1]. This idea is based on the fact that little oxygen is left to be extracted out of the blood during heavy exercise and that the dominant mechanism for the increase in V02 max with training must be an increase in blood flow which means an increase in oxygen delivery [1]. An attractive case for this argument was presented in a study which showed that two-legged bicycle training resulted in an increase in arm V02 max [1]. An equally attractive but contradictory study looked at the effect of one-Iegged cycling on V02 max. The experiment revealed that the V02 max. of the trained leg increased by 23% while that of the untrained leg only increased by 7% which leads one to speculate that a peripheral mechanism is responsible for the increase in V02 max and not a central component [1]. Wagner [6] states that "Some workers continue to conclude that V02 max is limited not by the supply of 02 but by the metabolic machinery within the muscle..." and that "...the well- known observation that venous blood from maximally exercising muscle contains considerable 02 could be taken as support for this view, arguing that if the muscles could use more 02, they would indeed extract more from the blood." Honig et al. [7] offers a possible explanation for this peripheral limitation and states "The amount of 02 extracted at a given driving force and 02 conductance varies directly with the time available for 02 release." As these examples indicate, the jury is still out as to what limits V02 max.

Still others believe the limitation to VO2 max is not oxygen at all, but some other limitation within the skeletal muscles. One argument has been presented that cites the contractile function of skeletal muscle as being the limiting factor of maximal aerobic exercise, specifically as it relates to the control of the rate and force of myofibrillar cross-bridge interaction [3]. While VO2 max has been shown to be an accurate predictor of aerobic performance, it seems logical to assume that the percentage of VO2 max that can be maintained over time is more indicative of success than the maximal value which can not be maintained for very long. Take for example two runners who have an equal VO2 max of 70 mL/kg/min. The athlete who can run a marathon at an average percentage of VO2 max of 90% (63 mL/kg/min) will certainly perform better (i.e., run faster) than the one who operates at an average of 60% of maximum (42 mL/kg/min). If one went solely based on maximal oxygen uptake values, both runners would be predicted to perform at equal levels. The percentage of VO2 max that an athlete can maintain over a period of time therefore seems more significant in predicting performance than the maximum amount of oxygen consumption that can be achieved during a short period of time as in a VO2 max test. Ideas like this one in addition to other factors like contractile function and mechanisms of fatigue unrelated to oxygen (anaerobic) may lead researchers in new directions when seeking to unravel the various components of athletic performance and limitations to aerobic capacity. Perhaps VO2 max is a good predictor of performance but not the best predictor. Could it be that VO2 max is not the gold standard after all?

Concluding Thoughts

This article has sought to briefly summarize the history of VO2 max which finds its origins in the early part of the twentieth century with initial analyses having been performed mostly on athletes. It was identified relatively early on that there was a limitation to VO2 max and that different people had different levels of capacity for aerobic-type work like running. The real race was then on: to determine what this limiting factor was. If a mechanism could be found, perhaps it could be manipulated or trained in such a way so as to further increase performance beyond what was previously possible. The purpose of this discussion has also been to look at some of the more predominant theories that have evolved over the past eighty or ninety years as the result of countless training studies and experiments. Some of these theories have been discounted outright while others have gained universal acceptance. Most, however, have not been definitively proven or disproven and the theories on a central versus peripheral limitation to VO2 max seem to have undulated over the years and decades like a seesaw. A great many exercise physiologists agree that the seesaw has come to a stop somewhere in the middle which represents a school of thought based on the idea that multiple mechanisms are at work constantly and that at anyone given time, no single mechanism limits VO2 max. Rather, VO2 max appears to be limited by multiple interacting factors on levels ranging from macroscopic to microscopic that make it virtually impossible to trace the limitation back to the original source. It is analogous to the idea that a butterfly flapping its wings in the rain forest of South America can directly cause the formation of a hurricane thousands of miles away off the west coast of Africa. There is no doubt that every system and process, biological or otherwise, has a rate-limiting step and VO2 max is no different. The question then becomes: is the limiting factor of VO2 max the most important thing? Is VO2 max

even the most important thing? Is it the Holy Grail of exercise physiology or is VO2 max the supposed "gold standard" of health and fitness, just fool's gold? Only time and the brilliant minds of present and future exercise physiologists can answer these difficult questions. In the ongoing debate of oxygen consumption, maximum values, and limitations, one thing is certain: the topic of VO2 max has not lost its luster over the years and remains the most researched and sought after variable in exercise physiology. Until definitive theories are agreed upon and conclusive answers are found, it will surely stay that way.

References

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