CHAPTER I

INTRODUCTION

Nowadays, many industrialized developed countries are confronted with the problems of a rapidly expanding geriatric population. The increasing rate of health care expenditure is a major economic issue in these societies. The important issue of any geriatric programs do not extend the life span or reduce health care costs, but rather increase the well being and quality of life of the senior citizen. Aerobic exercise have become extremely popular in the past five years. Although, Holloszy and Smith (1987) reviewed the literature relating to the effects of exercise on longevity in rats reached the conclusion that exercise could improve the survival rate by encountering the deletion effects of a sedentary life combined with overeating. However, the relationship between aging and exercise in human subjects still unsolved (Bruce, 1984; Holloszy, 1983), so it still hard some research opportunities in this field.

EXERCISE

Plenty of physiological and medical studies indicate the positive effect of regular exercise on health. Regular exercise training means the creation of work capacity well encompassing the demands of routine work (Astrand and Rodahl, 1986) or is used repeatedly to strengthen or develop a muscle or a bodily faculty (Berger, 1982).

Exercise is usually divided into the following two types :

1) Aerobic, dynamic, rhythmic, or isotonic exercise which means usual, repetitive, rhythmic contraction of muscle groups associated with continuous or nearly continuous motion of any parts of the body. For examples : walking, running, swimming, cycling and jogging.

2) Anaerobic, static or isometric exercise which consists of sustained muscle contractions in a limit of time that produce relatively little motion of the involved body part, such as squeezing a hand dynamometer, carrying a heavy suitcase, lifting and water skiing.

Aerobic exercise refers to the variety of exercises those stimulate cardiopulmonary activity for a time period sufficiently long enough to produce beneficial changes in cardiopulmonary function and some organ functions of the body (Cooper, 1970).

The word aerobic means the mechanism of the body promoting the supply of oxygen it involves and moving vigorously and steadily over a period of twenty to forty-five minutes, three to five times a week, so that the cardiovascular system work at a rate that demands large amounts of oxygen (Cooper, 1970).

Isometric contractions of sufficient power to have any training value derive their energy from anaerobic sources, since blood flow through the contracting muscle is greatly reduced or abolished entirely.

Isotonic or dynamic exercise, by subjecting the oxygen transport system to stress, may increase endurance while having little effect on the strength of the muscles involved (Morehouse and Miller, 1971).

Most training regimens may be classified as sprint or anaerobic program, and endurance or aerobic programs. In general, endurance training refers to exercise programs consisting of prolonged, usually continuous work bouts of relatively low intensity. Sprint training most often refers to programs of short, repeated work bouts of relatively high intensity (Fox, 1984).

During aerobic exercise, the oxygen uptake of the exercising muscles is increased. As a result, the cardiopulmonary unit is placed under a physiological stress. These states could be used to evaluate the integrity of the cardiopulmonary function and capacity of person.

Cardiopulmonary fitness had been defined as the ability of man to maintain the various processes in the body with a capacity to reach a higher steady state of work than the unfit, and to restore all equilibrium which were promptly disturbed after exercise (Shephard, 1977; Seals, Hagberg, Hurley, Ehsani and Holloszy, 1984).

Muscular strength, general endurance, mechanical efficiency, and body mass all had some influences on performance over the first hour of vigorous exercise, but the main factor limiting effort of this duration was the oxygen conductance in the cardiopulmonary system (Shephard, 1982).

The ability to sustain high intensity exercise is recognized to dependent on 4 aerobic parameters (Whipp, Davies, Torres and Wasserman, 1981) :

1) The maximal oxygen uptake : $\dot{V}o_{2max.}$
2) The anaerobic threshold
3) The time constant for the oxygen uptake kinetics : τ
4) The work efficiency

These 4 aerobic parameters, general endurance capacity, are the values that can express the capacity to continuous work in aerobic way of human (Shephard, 1982).

Response of Exercise.

Principles of exercise physiology offering advantage were not only confined to the world of top-class athletes and coaches. On the contrary, they also provided guidelines by which the non athlete individual could improve their health and physical fitness (Hickson, Bomze and Holloszy, 1977). The value of aerobic exercises was arisen from the fact that they provide oxygen to replenish the ATP supply. Man was exercising without building up an intolerable oxygen debt and could therefore continue the exercise for a greater length of time. Training effect could alter physiological changes in the cardiovascular system. They must engage in a prolonged exercise in order to improve cardiovascular fitness rather than physical strength and flexibility (Sharkey, 1986). The improvement of performance brought about by endurance training could be correlated with physiological change of lungs and heart. There is an increase in lung capacity as well as in the efficiency of oxygen removed from the air and diffused into the blood. The heart muscle could be strengthened and enlarged by exercise (Shepherd, 1987), endurance training produced a pronounced improvement in its efficiency (Brancozio, 1983). An increase in the size of the heart was controversy (Brancozio, 1983; Rost and Hallmann, 1983), eventhough more blood was pumped in every stroke (Poliner, Dehmer, Lewis, Parkey, Blomquist and Willern, 1980). The high stroke volume was accompanied by a sizable decrease in the resting pulse rate (Berger, 1982) and maximal heart rate (Yoshida, Suda and Takeuchi, 1982; Pollock, Broica, Kendrick, Miller, Janeway and Linnerud, 1972). The net effect was that the heart actually increase cardiac output with fewer beats (Astrand and Rodahl, 1986).

The effects of endurance training tended to create some major changes in muscle aerobic and metabolic capacity (Morehouse and Miller 1971), which meant the

increasing in mitochondrial volume (Howald, 1985), numbers (Brancosio, 1983) and in activity of enzymes regulating pyruvate and free fatty acid oxidation, particularly in oxidative fibers (Gollnic, Armstrong and Saltin, 1973) or skeletal muscle (Beyer, Starnes, Edington, Lipton, Compton and Kwasman, 1984), to produce ATP. Muscle stores of glycogen and fat increased (Howald, 1985) and the rate of adipose tissue and fat mobilization were also increased (Gohil, Henderson, Turblanche, Brooks and Packer, 1984). The overall effect of these changes were that more oxygen delivered to the muscle cell which could cover a greater part of the energy turnover through combustion fat (Jansson and Kajjser, 1987). It brought about the advantage of fewer carbohydrate combustion. So the endurance training could be tolerated for a longer period of time (fewer lactic acid accumulation) these greater endurance had been achieved (Klausen, IbHemmingse and Rasmussen, 1982). The total of the changes were expressed in a higher $\dot{V}o_{2max.}$ (Jones, 1988), or anaerobic threshold (Rotstein, Dotan, Bar and Tenenbaum, 1986), or a greater capacity to utilize the oxygen for energy production (Brancozio, 1983). The selective utilization of fuel was related to the percentage of one's $\dot{V}o_{2max.}$ Carbohydrate utilization increased as a function of $\dot{V}o_{2max.}$ (Greenhalf, Gleeson, Whiting and Maughan, 1987), while free fatty acids remained a significant fuel source during mild-to-moderate exercise, which encountered below 60 percentage of $\dot{V}o_{2max.}$ intensity in steady-state exercise (Barry, Seymour and Gerald, 1989).

AGING

Human aging is a complex and still mysterious process. Attempts to push back the clock have existed since biblical times. While we do not yet have a universally accepted definition of aging (Harman, 1981), we do have increasing scientific information which makes the study of gerontology interesting and exciting.

Definitions.

Though there are still no universally accepted definition of aging, two conflicting views are held today. One considers aging as an involuntary process which operates cumulatively with the passage of time and is revealed in different organ systems as inevitable modifications of cells, tissues and fluids. The other views interpret the changes found in aged organs as structural alterations due to infections, toxins, trauma, nutritional disturbances or inadequacies giving rise to what are called degenerative changes and impairments (Steffl, 1984).

Senescence is a change in the behavior of the organism with age, which leads to a decrease power of survival and adjustment (Harris, 1983).

Aging is the deterioration of a mature organism resulting from time dependent, irreversible changes intrinsically to all members of a species, and with the passage of time, they become increasingly unable to cope with the stress of environment, thereby increasing the probability of death (Handler, 1960).

Aging refers to the regular changes that occur in mature genetically representative organisms living under representative environmental conditions as they advance in chronological age (Birrin and Renner, 1977).

Cardiovascular Effects.

The most common pathologic abnormality of the aging heart, other than those caused by atherosclerosis (Kahn, 1953) was a brown pigmentation of the myocardium. Its appearance was not related to sex, race, or vascular disease, and it was not found in young or middle-age individuals. The pigmentation was due to an accumulation of lipofuscin granules at the poles of the myofiber nuclei (Strehler, Mark, Meldvocn and Gee, 1959).

Other age-related changes of heart and blood vessels were due to an alteration of collagen. With advanced years, collagen become less soluble and less elastic, probably the result of increased interfibril cross-linking. The aged heart, with its cardiac muscle fibers encased in this more rigid collagen matrix would find effective cardiac contraction and physiological dilatation progressively more difficulty (Kohn, 1971). Frequently, superimposed on this basic change in collagen matrix was the accumulation of hydroxyproline, a constituent of collagen in the subendocardial layers of the left ventricle and in the papillary muscles (Ito, Yamagiwa and Yasake, 1980). Assessment by angiocardiography in aged person showed decrease in left ventricular contractile performance characterized by a decrease its ejection (Schocken, Blumenthal, Port, Hindle and Coleman, 1983; Kuikka and Lansimies, 1982).

Kohn had clearly shown that there were major changes in the composition of vessel wall as a function of age (Kohn, 1971). Not only was there gradual accretion of intimal connective tissue but there was also fragmentation and loss of lamination in the elastic media and basic changes in the solubility and flexibility of collagen fibrils. As a result, the vessel wall was less resilient and less able to accommodate the wide changes in arterial pressure. As a consequence, major vessels; such as the aorta and its branches, tended to dilate and become tortuous. Systolic blood pressure tended to rise and, since peripheral vascular resistance was not materially altered, diastolic blood pressure tended to remain constant or to fall (Fleg, 1986). The coronary arteries,

intimal thickening and accretion of connective tissue elements represented an aging process that probable occurs at birth, developed remove rapidly during middle age in male and after menopause in female, and almost exclusively affects the epicardial coronary arteries, located on the surface of the heart (Fleg, 1986). Coronary atherosclerosis, a disease of civilization is shown to be involved by genetic, dietary, aged and probably a number of environmental factors. Rapid development of atherosclerosis probably placed a limitation on the extent of collateral circulation that could be established between major coronary artery trunks. Sudden reduction in major vessel blood flow might result in widespread myocardial injury or infraction (Fleg, 1986).

During submaximal exercise the heart rate of aging individual was raised to the same extent as it did in younger. However, the oxygen pulse, the ratio of oxygen consumption to heart rate, at submaximal work loads, and did not change with advancing years (Hanson, Tabakin and Levy, 1978). The maximal attainable heart rate, however, declined with age in a linear fashion. Roughly it equaled 220 minus the age. Shephard postulated that a decrease sympathetic drive to the pacemaker might be the possible cause of declining (Shephard, 1978). Decrease in $\dot{V}o_{2max.}$ is parallel with a decline of maximal work capacity. It was indicated that a decrease of $\dot{V}o_{2max.}$ of 0.56 ml/min/kg per year of life for active men, while of 1.62 ml/min/kg per year of life for inactive men (Dehn and Bruce, 1972).

Respiratory Effects.

Aging was accompanied by morphologic change of the thorax and lungs. The total number of alveoli remains unchanged, while the internal alveolar surface area decreases from adolescence to old age. At the same time the alveolar ducts and small bronchioles enlarges (Thurlbeck, 1967). Pulmonary arterial wall thickness with age, both in the intimal and the medial layers (Steinberg, 1983). The elastic recoil of the lungs declines with aging. This decline had been estimated to about 0.25 mm H_2O per

year of life (at 50% of total lung capacity) in nonsmoking normal adults. So the pressure needed to distend the lung to a given volume was increased (Turner, Mead and Wohl, 1968; Knudson, Clark, Kennedy and Knudson, 1977). The compliance of respiratory system was reduced with age. The work needed to overcome the elastic forces of chest wall and lungs were 20% greater in 60 year-old than in 20 year-old man (Steinberg, 1983).

There was probably no change in total lung content of collagen or elastic tissue with age. Some reduction in the number and thickness of elastic fibers around the alveolar ducts and the mouths of the alveoli had been observed (Wright, 1961), and might contribute to the dilatation of these structures. An electron microscopy study (Adamson, 1968) did not find any age related quantitative differences in elastic tissue or collagen and there was no calcification, disruption or increasing in fragmentation of elastic fibers. Elastin is the major component of elastic tissue has been shown some increase with age and confined in the pleura and septa (Pierce and Ebert, 1965). As a result, the lung volume at which airway collapse during expiration becomes larger with advancing years (LeBlanc, Ruff and Milic- Emill, 1970; Begin, Renzetti, Bilger and Watanabe, 1975).

The increase in alveolar-arterial oxygen difference with age (Aunola and Rusko, 1984) is entirely due to a decrement of the arterial oxygen pressure, since the alveolar oxygen tension remain unchanged. The decline in alveolar oxygen pressure might be at least partly caused by a decrease of diffusion of oxygen from the alveoli to the blood (Brischetto, Millman, Peterson, Silage and Pack, 1984). Another factor might be a mismatch of ventilation and perfusion. As pointed out before, closing volume increases with age and as a result the dependent portions of lung might remain underventilate especially during quiet breathing. Since the rate of perfusion remains normal, inadequately oxygenated blood might flow from poorly ventilated segments of the lung (Steinberg, 1983).

PHYSICAL EXERCISE AND AGING

The decreasing in strenuous activity with age might account for the large reduction in $\dot{V}o_{2max.}$ (Cunningham and his friends, 1985). Regular aerobic exercise could improve and maintain an individual's general health regardless of the fitness level at the onset of the exercise regimen, such as daily activity in middle aged women (Zauner, Notelovitz, Field, Clair, Clair and Vogel, 1984) or training approximately 50 percentage of the individual's $\dot{V}o_{2max.}$ for 30 minutes three times a week (Nilsson, 1982). Several literatures noted that age did not significantly reduce the trainability attained from exercise (Young, Chen and Hollosz, 1983; Gardner, Poehlman, Sedlock, Corrigan and Siconolfi, 1988), however, it appeared that a prolonged sedentary lifestyle would diminish the fitness level that could be achieved (Laerun and Laerum, 1982; Raven and Smith, 1984; Ho., 1984). Cardiovascular and respiratory ability or endurance capacity was primarily a function of the oxygen transport system and therefore, were monitored by determining maximal aerobic capacity (Larson, 1974; Mazzeo, Brooks and Horvath, 1984). The $\dot{V}o_{2max.}$ had been a highly reproducible parameter related to cardiac output and the arteriovenous oxygen difference (Walsh, 1987). Exercise conditioning could improve the maximal aerobic power by augmenting both the cardiac output (Miyazawa and Yamaguchi, 1984) and the oxygen extraction with in capillaries (Jacobs, Bell and McClements, 1984; Noble, 1986). The increasing of oxygen extraction was found to be correlated with the increasing in oxyhemoglobin binding activity at rest (Szydlowski and Pawlak, 1983). Resting stroke volume was increased by a conditioning effect and resting bradycardia was common (Musch, Haidet, Ordway, Longhurst and Mitchell, 1985).

Maximal Oxygen Uptake : $\dot{V}o_{2max.}$

The best approach to the assessment of cardiopulmonary fitness was the direct measurement of $\dot{V}o_{2max.}$ during exhausting work such as uphill treadmill running, stepping or pedaling a bicycle ergometer (Bucher, 1983; Jenson and Fisher, 1979).

The rate of maximal oxygen uptake was abbreviated as $\dot{V}o_{2max.}$, where the Vo_2 represented the volume of oxygen consume, usually in liters or milliliters, and the dot over the V was a notation that this volume was expressed per unit of time usually per minute (Lamb, 1984).

1. Definition.

Because oxygen was used by all body tissues, a larger individual had a greater oxygen uptake than a smaller one both at rest and during exercise. Accordingly, it was better for comparative purposes to record oxygen uptake values on the basis of body weight, ordinarily in terms of milliliters of oxygen per kilogram of body weight. Expressing in term of lean body mass or fat-free body weight was not usually advisable because such an expression unjustifiably penalizes those who are less fat (Lamb, 1984).

The term $\dot{V}o_{2max.}$ was synonymous with the term maximal oxygen consumption, maximal oxygen intake or maximal aerobic power and represented the greatest difference between the rate at which inspired oxygen entered the lungs and the rate that expired oxygen leaves the lung (Lamb, 1984) or the maximal amount of oxygen in the body that could process during exhausting work (Jones, 1988). It involved an increase in the oxygen uptake to the highest level of activity, which the ability of the individual to utilize the greatest amount of oxygen was reached (Astrand and Rodahl, 1986).

2. Factors Affecting $\dot{V}o_{2max.}$

The function reserve capacity of the cardiovascular and respiratory systems, largely reflected by $\dot{V}o_{2max.}$, was adversely affected by aging, disuse and disease.

Differences in body size, muscle mass, age, sex, habitual level of activity, physical conditioning, and athletic training also accounted for much of the physiological variation in $\dot{V}o_{2max.}$ (Astrand and Rodahl, 1986).

2.1. Influence of Body Size and Muscle Mass.

The maximal oxygen consumption could be augmented by increasing the mass of muscle employed in performing the task used to elicit the $\dot{V}o_{2max.}$ For example, the classical study that simultaneous running and arm cranking produced a significantly higher $\dot{V}o_{2max.}$ than running alone (Taylor, Bushirk and Henschel, 1955), while lower level $\dot{V}o_{2max.}$ by cycling ergometer than running on a treadmill (Astrand and Rodahl, 1986).

2.2. Influence of Age and Sex.

Although, there was little difference in $\dot{V}o_{2max.}$ among boys and girls between 6 and 12 years old. Considerable difference were apparent between the sexes following the adolescence (Astrand, 1960; Cooper, Ravell, Whipp and Wasserman, 1984). A change in the habitual level of physical activity at the time of puberty was most likely an important cultural and social factor. On the other hand, woman had more body fat than man. The average concentration of hemoglobin was also lower among woman, resulting in a reduced oxygen-carrying capacity of arterial blood.

Cross-sectional and longitudinal studies had revealed that there was an average annual decrement in $\dot{V}o_{2max.}$ of 0.28 ml/min/kg per year (Dehn and Bruce, 1972). Part of this declining was the inevitable result of biological aging, association with decreases in pulmonary and tissue gas exchange, partly was probably also a consequence of increase sedentary living (Barry, et al., 1989).

2.3. Influence of Prolonged Bed Rest.

Study in five young men before and after 3 weeks of bed rest have demonstrated a significant 27% decrease in $\dot{V}o_{2max.}$ from 3.3 l/min to 2.4 l/min while

heart rate remained essentially unchanged (Convertino, Goldwater and Sandler, 1986; Saltin, Blomquist and Mitchell, 1968).

2.4. Influence of Physical Conditioning : Training.

Both exercise intensity and duration must be great enough to elicit a near maximal response of the cardiovascular system if $\dot{V}o_{2max.}$ was attained (Nagle, 1973). The intensity of the work load was increased progressively in test of $\dot{V}o_{2max.}$, so that eventually the intensity must reach a level sufficient to bring about a maximal response (Lamb, 1984). Moderate endurance-typed exercise training generally augmented the $\dot{V}o_{2max.}$ 28% (Musch, et al., 1985). The extent of exercise induced improvement in aerobic capacity generally showed an inverse relationship with age, habitual physical activity and initial $\dot{V}o_{2max.}$ (McDonough, 1970). Improvement in $\dot{V}o_{2max.}$ with exercise training also showed a positive correlation with the conditioning frequency, intensity and duration (Franklin, Gordon and Timmis, 1989) but not in sprint train (Aitken, Bennet and Thompson, 1989).

3. $\dot{V}o_{2max.}$ Determination.

The direct measurement of $\dot{V}o_{2max.}$ was determined by the remaining subjects during graded treadmill walking or jogging or during bicycling. Expired gas was collected and analyzed by using gas analyzer. $\dot{V}o_{2max.}$ had been determined from the graph of oxygen uptake against work load or time where there was no change of oxygen uptake with an increasing in work load as showed in figure 1 (Yerg, Seals, Hagberg and Hollosy, 1985).

Another indirect method, $\dot{V}o_{2max.}$ was determined by measurement of heart rate at submaximal test (Astrand and Rodahl, 1986) or running/cycling exercise test and detected capacity from time (Cooper, 1970).

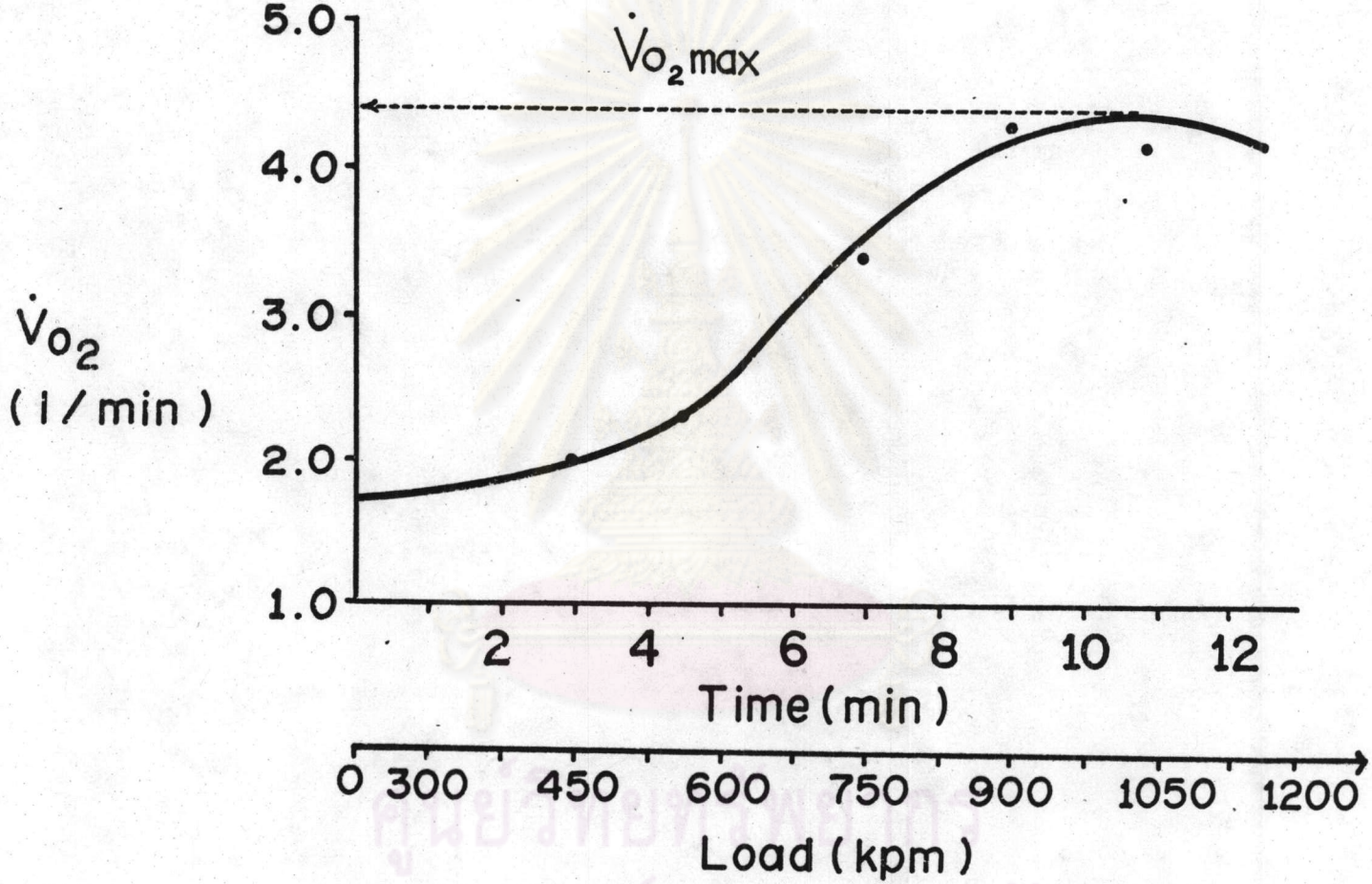

Figure 1. The direct measurement of $\dot{V}o_{2max.}$ was obtained from the graph of oxygen uptake against time.

$\dot{V}o_{2max.}$: the point where there was no change of oxygen uptake with an increasing in work load.

Anaerobic Threshold.

The anaerobic threshold has become a valuable measurement in the assessment of cardiovascular and pulmonary functions, signifying the peak work load or oxygen consumption at which oxygen demands exceed the circulation's ability to sustain aerobic metabolism that effect from endurance training (Jacob, 1986; Wasserman, 1986; Kumagai, Nishizumi and Tananka, 1987).

For a long time we have known that the endurance athlete will have a far superior maximal aerobic power than a sedentary individual or difference of athletes according to sport (Saltin and Astrand, 1967). The same year, in elite per pubertal cross-country runners, $\dot{V}o_{2max.}$ and time were reported to have a correlation of r = 0.06 (Mayer and Gutin, 1979). From a record, the great marathoner had a $\dot{V}o_{2max.}$ of 71 ml/min/kg. This was similar to the $\dot{V}o_{2max.}$ of the world report that was 69.7 ml/ min/kg (Costill, 1970). So $\dot{V}o_{2max.}$ could not use as a sensitive predictor of endurance performance within a population of elite athletes (Burk, 1980).

Potentially more valuable than maximal aerobic power may be an analysis of the time an athlete could work at varying percentage of his/her $\dot{V}o_{2max.}$ Both Astrand (1960) and Costill and co-workers (1973) had reported that analysis of submaximal work anaerobic threshold was highly correlated to $\dot{V}o_{2max.}$ and endurance performance (Yoshida, Chida, Ichioka, Soda, 1987).

Aerobic capacity had long been recognized as an important determinant of performance in endurance events (Vago, Mercier, Ramonatxo and Frefaut, 1987). So another characteristic of endurance athletes was that they can exercise at high percentages of their $\dot{V}o_{2max.}$ for longer periods without accumulating large amounts of lactic acid in their blood (Rusko, Rahkila and Karvinen, 1980). Numerous studies on anaerobic threshold in fields of exercise physiology, sports medicine and clinical medicine had been documented that anaerobic threshold correlated well with $\dot{V}o_{2max.}$, endurance performance, oxidative enzyme activity in skeletal muscle (Chance, Leigh,

Kent and McCully, 1986) and exercise tolerance in patients (Chida, Ichioka, Makiqcchi, Miyuzato, Suda and Yoshida, 1987).

1. Definition.

Wasserman and McIlroy introduced the concept of anaerobic threshold by using the respiratory gas exchange ratio to detect the onset of anaerobic metabolism for determining the work load or level of oxygen uptake at which the cardiovascular system failed to supply the oxygen requirements of active muscle (Wasserman and McIlroy, 1964). The basis of this point was that the metabolic acidosis caused by lactate accumulation. Determination could get by gas exchange parameters which were oxygen uptake, carbon dioxide output and expired ventilation (non-invasive method). Example include the detection of carbon dioxide released from buffering during an incremental exercise test (Wasserman, Van Kessel and Burton, 1967; Beaver, Wasserman and Whipp, 1986). The definition of anaerobic threshold was the level of work or oxygen uptake just below the point of metabolic acidosis and the associated changes in gas exchange occur (Wasserman, Whipp, Koyal and Beaver, 1973; Orr, Green, Hughson and Bennett, 1982; Wasserman, 1986; Yeh, Gardner, Adam, Yonowitz and Grapo, 1983).

2. Anaerobic Threshold Hypothesis.

Anaerobic threshold has been defined as the level of oxygen uptake above aerobic energy production which supplemented by anaerobic metabolism (Wasserman, 1984; Stremel, 1984). The hypothesis requires :

2.1. The O_2 requirement by the metabolically active muscle could exceed the O_2 supply to the mitochondria when the work load become sufficiently high.

2.2. The imbalance between the O_2 supply and O_2 requirement (O_2 requirement greater than O_2 supply) brought about a net increase in anaerobic oxidation in the cytosol of the cell with pyruvate conversion to lactate (Figure 2).

2.3. Lactate was buffered in the cell primarily by HCO_3^- (Figure 3).

2.4. The CO_2 generated from buffering increased CO_2 output while HCO_3^- exchanged for lactate across the muscle cell membrane according to the new electrochemical gradients; and

2.5. The buffering and acid-base disturbances produced predictable changed in gas exchange (Mader and Heck, 1986; Wasserman, William and Whipp, 1986; Yoshitake, Zaiki, Shoji, 1987).

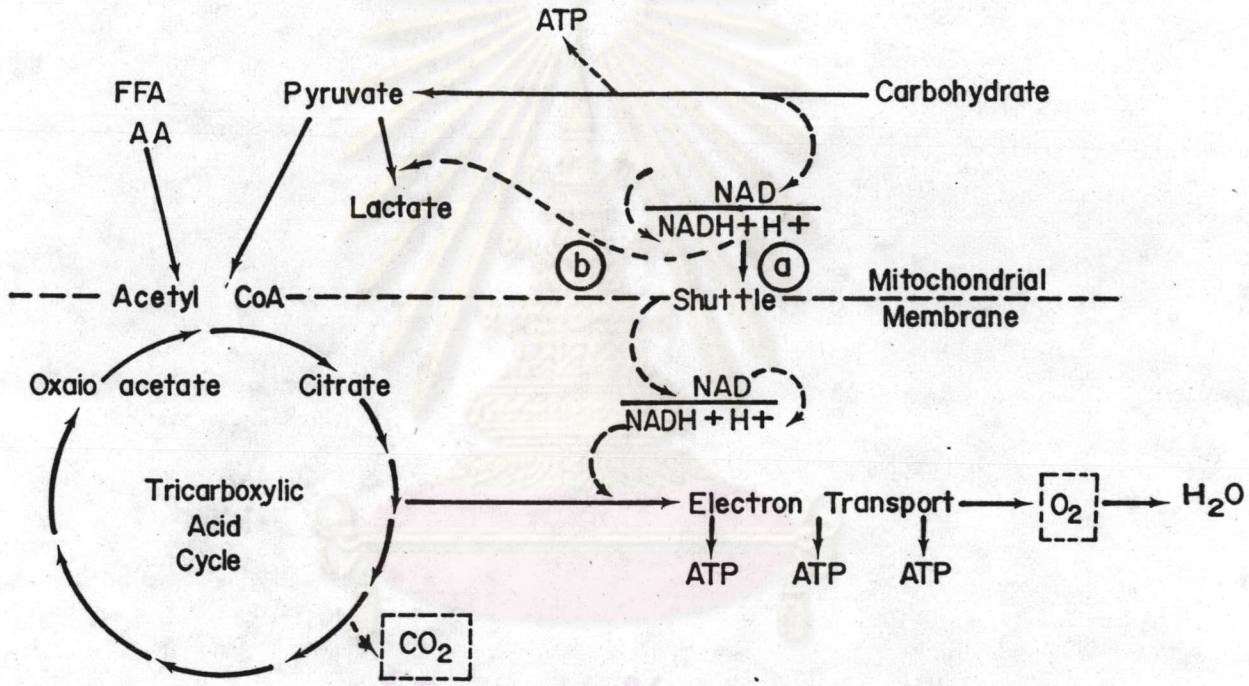

Figure 2. Metabolic pathways leading to production of ATP. Increased celluar production of lactate depends on the mechanism of reoxidation of cytosolic NADH.

(a) : when the O_2 supply to the mitochondrion is sufficient, NADH is reoxidized through the proton shuttle to the mitochondrial membrane.

(b) : when the O_2 supply to the mitochondrion is inadequate for reoxidation by the proton shuttle, pyruvate reoxidizes NADH, resulting in an accumulation of lactate and change in cytosol redoxing state (Modified from Wasserman, 1986).

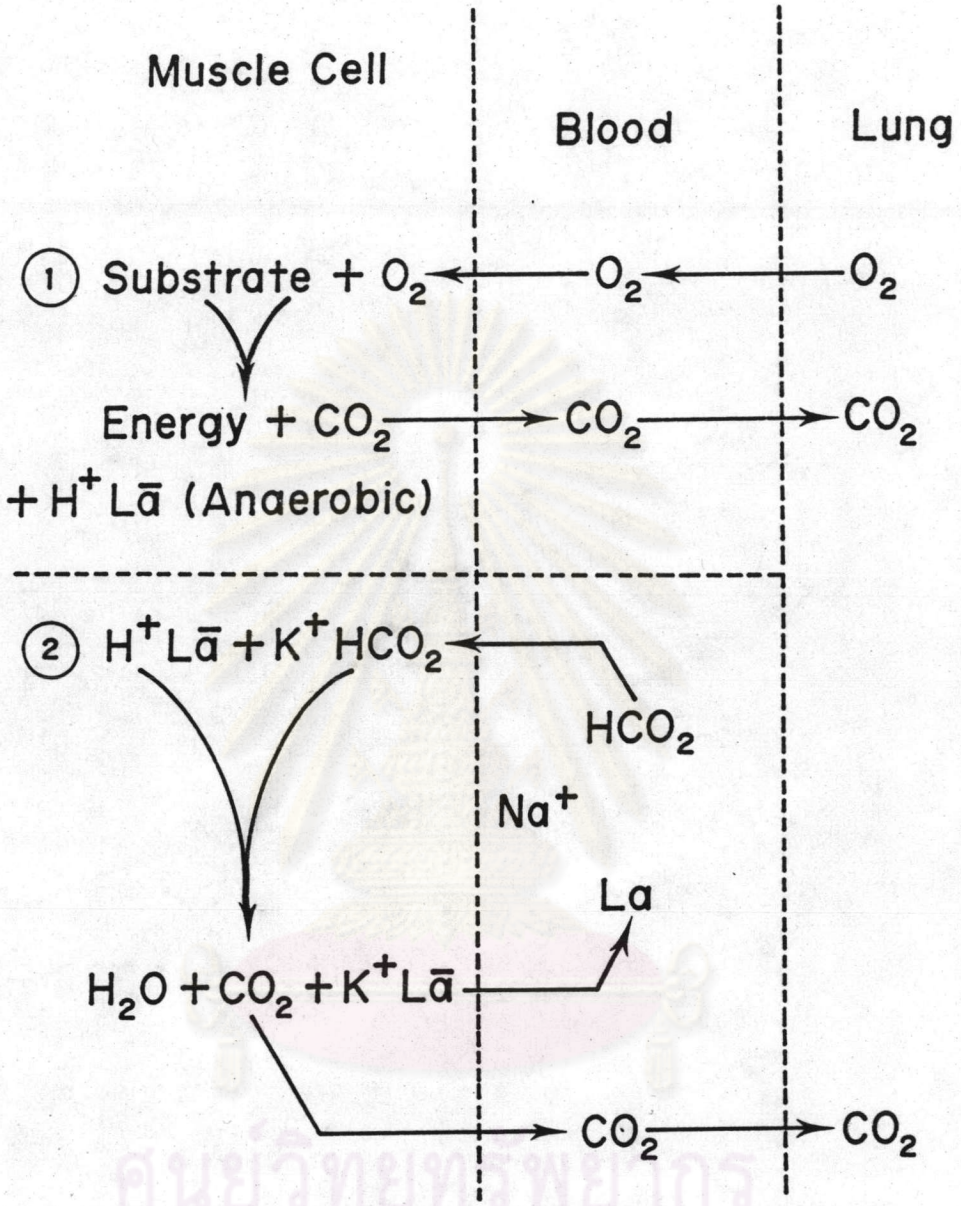

Figure 3. Mechanism of blood bicarbonate buffering.
①: aerobic metabolism results in CO_2 production with a proportionality to O_2consumption.
②: cellular buffering of increased lactic acid production, associated with an increase in anaerobic glycolysis, has an immediate by-product of CO_2 The cellular increase in lactate and decrease in HCO^-_3 stimulates anion exchange between cellar and extracellular water, causing blood lactate to increase and HCO^-_3 to decrease (Modified from Wasserman, 1986).

3. Lactate Production and Removal During Exercise.

It had long been recognized that when the O_2 supply was inadequate to reach the O_2 requirement, lactate increase. The reduction cytosol nicotinic adenine dinucleotide (NADH) can not be reoxidized rapidly enough by the mitochondrial membrane H^+ shuttle for ultimate combination of cytosol H^+ with mitochondrial oxygen. Consequently, pyruvate becomes the H^+ receptor and is converted to lactate while simultaneously reoxidizing the cytosol NADH, allow the glycolysis to proceed. The production of lactate from pyruvate had been recognized as an oxygen-conserving mechanism that allowed oxidation to continue even in a relative oxygen-deficient environment (Wasserman, 1984). The contribution of lactate to remove during exercise was mostly converted to water and carbon dioxide. Some of the lactate could undergo gluconeogenesis in active, inactive muscles and in the liver (Katz and Sahlin, 1988). Several investigators had emphasized that blood lactate concentration resulted from an imbalance between lactate production and removal (Figure 2). The endurance training induced adaptation in the muscle cell which result in a reduction of lactate production during heavy exercise (Hurly, Hagberg, Allen, Seals, Young, Cuddihee and Hollzy, 1984; Favier, Constable, Chen and Holloszy, 1986). Consequently, contradicting has reported that the effect of endurance training did not correlate with lactate production but clearance rate when studied by radiolabelled (Brooks, 1986; Donovan and Brooks, 1983; Stanley, Gertz, Wisneski Morris, Neese and Brooks, 1985).

4. Factor Affecting Anaerobic Threshold.

The anaerobic threshold is influenced by many factors such as individual difference which dependent on heredity, body size, sex, age and types of training.

4.1. Influence of Heredity. It was demonstrated in 1986 that among untrained man represented distinctly either the slow twitch or the fast twitch type groups, anaerobic exercise seemed to be dependent on the fiber type majority in exercising muscle (Aunola and Rusko, 1986).

4.2. Influence of Body Size.

Report from the cross-sectional study in children demonstrated that anaerobic threshold and $\dot{V}o_{2max.}$ increased in order with increasing size and as judged by anaerobic threshold/$\dot{V}o_{2max.}$ Therefore, they concluded that the cardiopulmonary responses to exercise in children were regulated at optimized values despite overall changes in body size during growth (Cooper, Weiler, Whipp and Wasserman, 1984).

4.3. Influence of Sex. Astrand and Rodahl, (1986) determined the anaerobic threshold from the non-linear increase in $\dot{V}_E$. They found that the anaerobic threshold in the female group was only 57.3% compared with the male group during arm exercise and 60.8% during leg exercise.

4.4. Influence of Age.

Study of Iwaoka and co-workers in 34 male runners (aged 21 to 69 year-old) performed an incremental treadmill running test showed that the mean oxygen uptake corresponding to 4 mM. of blood lactate was the same among the groups (Iwaoka, Fuchi, Higuchi and Kobayash, 1988). Copper reported that ratio of anaerobic threshold to $\dot{V}o_{2max.}$ has been decreased slightly with age (Copper, Ravell, Whipp and Wasserman, 1984). These reports suggested that there was an increase in anaerobic capacity during growth.

4.5. Influence of Training.

Davis and co-workers (1979) showed that after 9 weeks of endurance training an anaerobic threshold improved 44% interms of absolute oxygen uptake and 15% relative to $\dot{V}o_{2max.}$ in sedentary middle age male. Similarly the 36 weeks endurance training anaerobic threshold increased 32.3% interms of absolute value and 17% relative to $\dot{V}o_{2max.}$ within 12 weeks. Moreover, Tanaka, Nakadomo, Kumagai and Nishizomi, (1987) showed that the anaerobic threshold could be increased by training, eventhough there was no improvement in $\dot{V}o_{2max.}$ Possible mechanisms that account for an increase anaerobic threshold after endurance training including an improve

distribution of blood flow by an increase in capillary density, with more rapid remove of lactic acid from within the exercising muscle fiber and/or increased oxidative capacity at the cellular level (Seals, Hurley, Schultz and Hagberg, 1984). An alteration in the muscle fiber recruitment pattern resulting in a delayed activity of fast twitch muscle fibers during incremental exercise (Clavsen, 1976), which related to the initial muscle glycogen storages.

4.6. Influence of Glycogen Storage.

The recent study had designed to reduce muscle glycogen stores by did not cause a dissociation between the ventilation and lactate threshold during an incremental exercise test (McLellan and Gass, 1989). When the muscle glycogen store was increased by over eating, the endurance time decreased (Maassen and Busse, 1989). While non-carbohydrate diet and starvation remarkable reduced the capacity for prolonged work with regard to work load as well as work duration (Pernow and Karlsson, 1971; Yoshida, 1986; Elia, Lammert, Zed and Neale, 1984). When the glycogen storage was depleted, the subject was no longer able to work at a high relative work load. During a prolong high relative work load exercise such as endurance test, the higher anaerobic threshold was aerobic per anaerobic ratio was greater, the speed of muscle glycogen depletion was smaller and the tolerance of exercise was better (Davis et al., 1979; Hughes, Turmer and Brooks, 1989). Minor source of energy might due to depletion of glycogen associated with greater oxygen extraction from arterial blood (Vage et al., 1987). Indeed, as for a same ATP production, glycogen was burnt 15 to 20 times faster anaerobically than aerobically pathway (Davis, 1985). The speed of depletion of glycogen were more suitably correlate with endurance than the storage (Cartee and Farrar, 1987). They had challenged the concept of the anaerobic threshold based upon data were obtained from an exercise protocol which was designed to reduce muscle glycogen stores (Neary, MacDougall, Bachus and Wenger, 1985).

5. Anaerobic Threshold Determination.

At the point of anaerobic threshold, energy release from anaerobic metabolism was increased and lactic acidemia resulted. Thus the occurrence of the anaerobic threshold during a progressive exercise bout signifies insufficient oxygen delivery to active muscle (Hollmann, 1985). Many researchers stated that lactate concentration was reached 4 mM in peripheral blood, that was acceptable meaning of blood lactate level at anaerobic threshold point by invasive method (Whipp, Ward and Wasserman, 1986; Heck, Mader, Hees, Muckes, Muller and Hollmann, 1985; Stegmann and Kinderman, 1982).

Although the onset of metabolic acidosis during exercise had been determined by serial measurements of blood lactate. The abrupt increase in arterial lactate might now be determined by non-invasive methods as gas exchange (Davis, 1985). This method correlates well with the lactate level and obviates the need to measure lactate in repeated blood samples (Arkarapanthu, 1988).

The physiology underlying an anaerobic threshold involves a temporary metabolic acidosis was compensated by a respiratory alkalosis. Lactic acid was produced and buffered by bicarbonate in blood (Wasserman, 1986). Carbon dioxide was released excessively by energy metabolism. As a result of an increase carbon dioxide production ($\dot{V}co_2$), the lower pH of the blood, and/or volume of expired gas ($\dot{V}_E$) exhibited a break point in linearity. At an anaerobic threshold point, the $\dot{V}_E$ and $\dot{V}co_2$ increased out of proportion to the work load performed, that they increased more abruptly than expected (Wasserman, 1973; Fukuba and Munaka, 1987). This non-linear regression was difficult to identify an aerobic threshold. Recently, a new approach for detecting anaerobic threshold name V-slope method, which was calculated from $\dot{V}o_2$ against $\dot{V}co_2$ was exhibited (Beaver, Wasserman and Whipp, 1986). This new method was combined in our study for determining of anaerobic threshold (Figure 4 and 5).

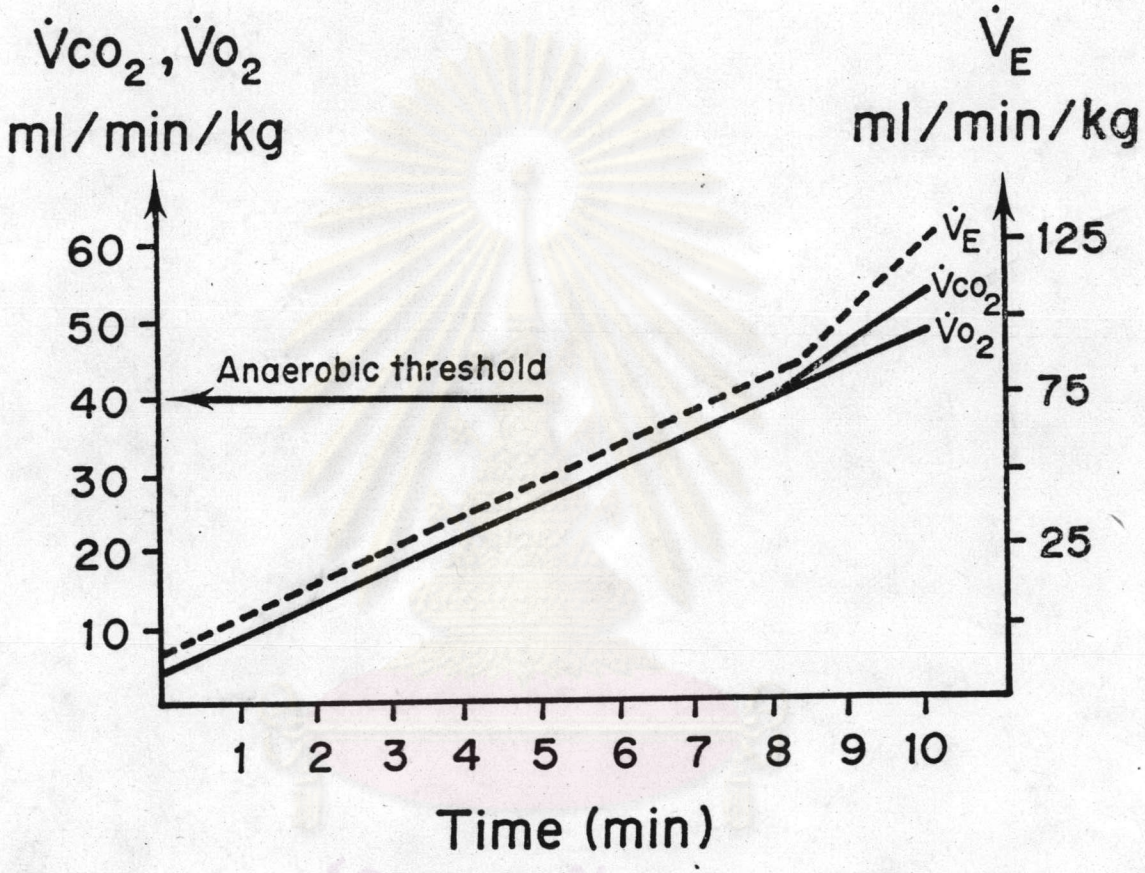

Figure 4. The first criteria used to determine anaerobic threshold was defined as the point that $\dot{V}_{CO_2}$ and $\dot{V}_E$ started to non-proportional to the work load, while $\dot{V}_{O_2}$ graph still had a linear increase (Modified from Chick and Somet, 1988).

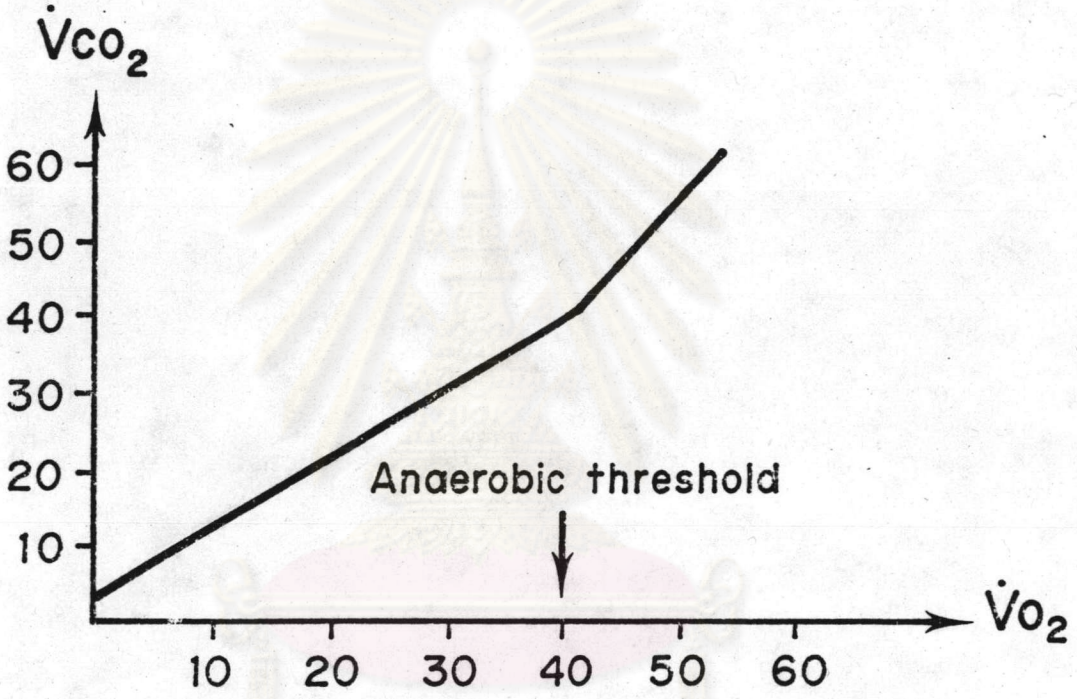

Figure 5. The second criteria used to determine anaerobic threshold was called V-slope method. Anaerobic threshold was determined at the point that the slope of $\dot{V}_{O_2}$ against $\dot{V}_{CO_2}$ graph started to change (Modified from Beaver, Wasserman and Whipp, 1986).

Oxygen Uptake Kinetics.

From the physiological point of view, let us assume that adequate oxygen transport was the most important function that enables all the body cells to work in unique toward the common goal of total performance. The components of the integrated system contributing to this function (blood, circulation, and respiration) could not be triggered on a moment's notice to meet such immediate adjustment as were necessary for sudden change in metabolic demands. So mechanisms had been provided in the active cell or tissue to release energy on an "anaerobic" basis for a limited period of time. Thus an oxygen deficient phase of energy exchange was initially involved in every work situation even one of minimal intensity. This energy turnover which proceeding on a partly anaerobic basis disturbed the existing homeostasis and activated a feedback loop by homeostatic conditions in the tissue were restored at a higher metabolic level. If the work demands were so high that they exceeded the maximal possible oxygen transport functions. However work could only go on until all the energy stores available for anaerobic energy exchanges were exhausted (Larson, 1974).

1. Definition.

The inadequacy of aerobic energy production to meet the total energy need of the body, especially at the beginning of exercise period, was known as the oxygen deficit (Lamb, 1984).

The concept of oxygen deficit was first introduced in 1920 by Krogh and Lindhard as the difference between the curve of the actual oxygen uptake at the beginning of exercise and the steady-state level of the oxygen uptake. Hermansen reintroduced the principle in 1969 and calculated the accumulated oxygen deficit as the area between the curve of the oxygen demand and the curve of the actual oxygen uptake.

The oxygen deficit was defined as the difference between the total energy cost of work (expressed as units of oxygen) and the portion of total energy cost that was met during the exercise period by aerobic energy production, that was measured by oxygen consumption during the exercise period (Lamb, 1984).

Oxygen uptake kinetics at constant work load during submaximal exercise in this test means the value of oxygen uptake that increased from the starting point to the steady state. In this study, time constant "τ" was used to define this increment of oxygen uptake kinetics.

2. Control of Oxygen Uptake Kinetics

During continued submaximal exercise was shown in figure 6. The curve illustrated the oxygen consumption during each minute of a relatively constant work load that below anaerobic threshold. Oxygen consumption raised rapidly during a few minutes of exercise (phase I and II). By the second to the third minute (Wessel, Stoul, Bastanio and Paul, 1979; Beaver, Wasserman and Whipp; 1973), the third minute (Whipp, 1987), or the sixth minute (Whipp and Wasserman, 1972) a plateau was reached and then oxygen consumption remained stable. After phase I (about 15-20 seconds) a more gradual increase (phase II) toward the exercise steady state (phase III) was seen (Sietsema, Daly and Wasserman, 1989). In this region, oxygen consumption curve was considered to be the steady state. This steady state reflected a balance between the energy required by the working muscle and the rate of ATP production via aerobic metabolism (Bason, Billings, Fox and Gerke, 1973). In this region, oxygen supply for the working muscle was adequate. Whereby lactic acid produced either oxidized or glycolysis, lactic acid accumulation, was minimal (McArdle, Katch and Katch, 1986).

The initial readjustment of the cardiovascular and pulmonary systems after the onset of dynamic muscular exercise were inadequate to allow the oxidative requirements of the exercising muscles to be met entirely by oxygen from the

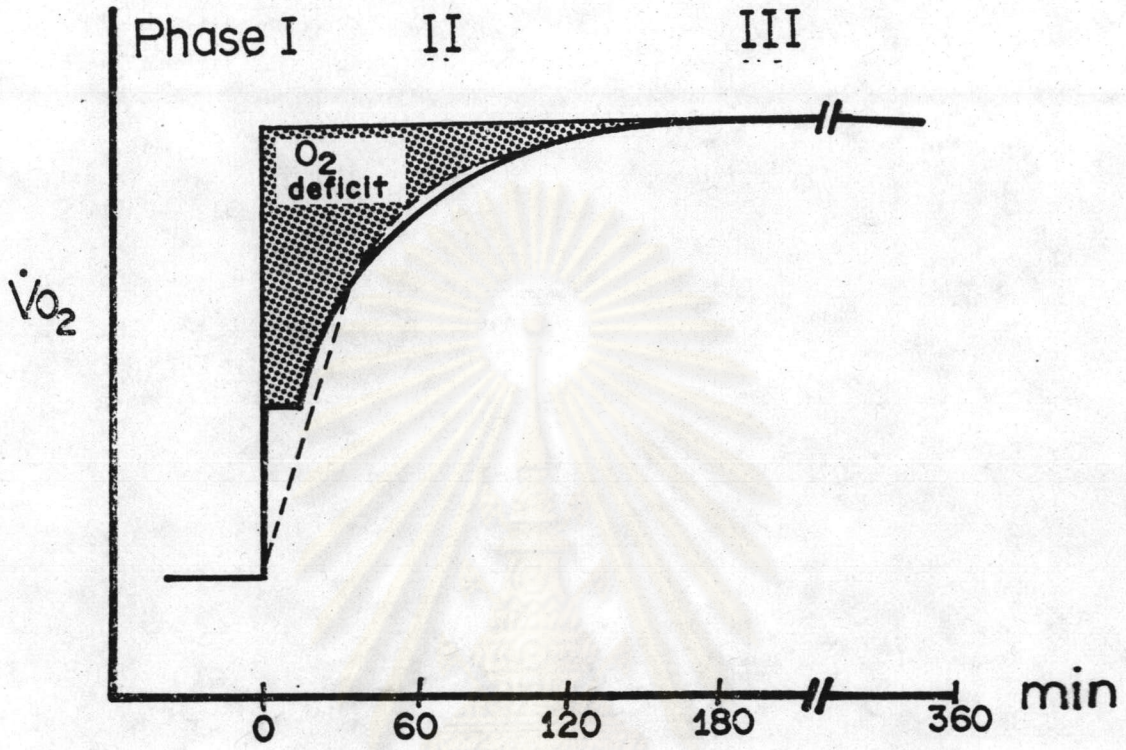

Figure 6. Idealized representation of kinetics of oxygen uptake after onset of moderate intensity and constant work rate exercise. The broken line of $\dot{V}O_2$ values in phase I and II was best fitted by a single exponential function. Time constant (τ), was determined from this fitted function (Modified form Sietsema, Daly and Wasserman, 1989).

atmosphere. During this nonsteady- state phase (phase I and II), the muscles could utilize an increase amounts of oxygen delivered to them. The mitochondrial respiration must increase sufficiently to lower muscle oxygen tension and create an oxygen gradient which permits first a partial desaturation of myoglobin followed by an increase oxygen extraction from the blood (Hickson, Bomze and Holloszy, 1978). In keeping with the finding that anticipate cardiac function (Inman, Hughson, Weisiger and Swanson, 1987) tended to rise cardiac output (Casaburi, Whipp, Wasserman, Beaver

and Koyal, 1977; Gussoni, Veicsteinas and Sloan, 1982). Rapid increase in venous return with little or no change in arteriovenous oxygen difference had been proposed to account for the sudden increase in oxygen uptake kinetics (Linnarsson, 1974; Whipp, et al., 1982). The widening of arteriovenous oxygen difference was equivalent to a reduction in the oxygen stores of the venous blood. Heart rate responses which showed very rapid increasing. So one possible limiting factor for oxygen uptake kinetics at the onset of exercise was the transport of oxygen (Hughson and Morrissey, 1982).

The breakdown of energy-rich phosphate compounds, ATP and phosphocreatine was certainly anaerobic and essential (Connett, Gayeski, Honig, 1985), but their quantitative role was limited (Casaburi, Barstow, Robinson and Wasserman, 1989). Therefore the anaerobic breakdown of glycogen (glycogenolysis) and glucose (glycolysis) to lactic acid played an important role to support the aerobic processes when they could not provide enough energy for ATP production (Hughson, 1984). Actually, in exercise that engaged large muscle group, such as running, which demands oxygen uptake higher than 50 percentage of the individual's maximum and which was performed for some minutes, lactate production in the activated muscle escaped and appeared in the blood. The heavier the exercise went on, the more important the anaerobic energy yield in the exercising muscle and the blood-lactate concentration was increase. As the exercise become more strenuous, a decrease in the body's pH affected muscular tissues, respiration, and other functions.

Lactic acid was produced by the exercising muscles at high work load. It was buffered mainly by sodium bicarbonate, leading to additional generation of carbon dioxide. This extra carbon dioxide was produced only when lactate levels were increased (Whipp, 1987). The accelerate rate of blood lactate was generally highest during the first few minutes of high intensity exercise (Roston, whipp, Davis, Cunningham, Effros and Wasserman, 1987), this superimposed component would be

expected to supplement aerobic carbon dioxide production early in exercise (tending to speed carbon dioxide relative to oxygen uptake kinetics). The ventilatory response to the lactic acidosis of high intensity exercise was a hyperventilation in correlation to carbon dioxide production that tend to drive down arterial carbon dioxide, thus washing out body carbon dioxide stores (Casaburi, et al., 1989).

The cause of the rising in oxygen uptake kinetics during constant work load has been unknown. Some researcher theorized that it was due to an oxidative removal of lactic acid from the blood. Further stydy showed that oxygen uptake kinetics were slower as work load increased for exercise intensities. This increasing was not associated with lactic acidosis (Casaburi et al., 1989). They indicated that the causes of the slow increase in volume oxygen was primarily a temperature effect, both directly and indirectly; by causing a slight hyperventilation which increases the oxygen to the respiratory muscles (Hagberg, Mullin and Nagle, 1978).

Two opposing mechanisms could account for the rate of increasing in oxygen uptake at the onset of light to moderate intensity exercise (Hughson, Sherrill and Swanson, 1988).

1. A limitation in the ability to transport oxygen to the metabolic site of working muscles (Hughson and Morrissey, 1983).

2. A limitation in the ability of the muscle to use the oxygen (Lynch and Paul, 1984).

The slow increase in oxygen uptake at the beginning of exercise was explained by the sluggish adjustment of respiration and circulation : phase I (Hughson and Morrissey, 1982; Miyomoto, Nakazono, Hiura and Abe, 1983) and/or removal of the buffer effect : phase II (Connett, 1987).

Generally, glucose transport is rate limiting step for glycolysis in unstimulated vascular smooth muscle. Further study by Lynch and Paul (1984) demonstrated by hypothesis of active Na^+ - K^+ transport and couple in the aerobic glycolysis. They

indicated that the decreasing in aerobic glycolysis associated with the inhibition of active Na^+ - K^+ transport is not due to a decreasing in glycolysis transport but rather to an inhibition of glucose utilization (Lynch and Paul, 1984). However, the immediate effect of vigorous exercise is a small increase or decrease of blood glucose (Shephard, 1982).

The control of cellular respiration had brought to considerable attention (Bason, et al., 1973). In general, it was believed that intracellular respiration was regulated by intracellular levels of ATP, ADP and inorganic phosphate (Chance, et al., 1986; Karlsson, 1971). Analysis using a model of phosphofructokinase kinetics indicated that an initial alkalinization was a major regulatory factor in red muscle (Connett, 1987), mediated via the carotid body (Oren, Whipp, and Wasserman, 1982).

Above the anaerobic threshold, the graph showed slower component of oxygen uptake became evident that delayed the steady state. The excess oxygen uptake in this state is uncertain. Some parameters were in high correlated with : 1; the increment of arterial blood lactate (Whipp and Wasserman, 1986). 2; the increment of temperature, and 3; other mediators that change with a similar time course, such as catecholamines (Dodd, Power, Malley, Brook and Sommer, 1988; Manhen, Lecerof and Hokfelf, 1978).

3. Factors Affecting Oxygen Uptake Kinetics.

3.1. Influence of Work Intensity.

A number of studies on the effect of work intensity to the time course of the increasing in oxygen uptake following the onset of constant work load had shown that the time required to attain steady-state oxygen uptake was longer in the heavier work (Linnarsson, 1974; Whipp and Wasserman, 1972). The same exercise test represent a lower relative work load when the subject's $\dot{V}o_{2max.}$ was higher than the other one. It was, therefore not too surprising that oxygen uptake kinetics increases more rapidly in response to the same absolute work load in individuals with a high $\dot{V}o_{2max.}$ than in

those with a low $\dot{V}o_{2max.}$ (Whipp and Wasserman, 1972; Booth, 1988), or in the same individual in the exercise as compared to the non exercise state (Swanson and Hughson, 1988). Above anaerobic threshold, oxygen uptake kinetics were slower than below anaerobic threshold (Sietsema et al., 1989).

3.2. Influence of Transition at Start Test.

The conclusions reached by different investigators with regard to this possibility were in sharp contrast. On one side diPrampero, Davies, Cerretelli and Margaria (1970), Davies and his team (1972) and diPrampero, Boutellier and Pietsch (1983) had claimed that a base line of light exercise, allowed a more rapid readjustment of oxygen uptake at the onset of a heavier rectangular stepping or cycling load; on the other side Diamond, Casaburi, Wasserman, Whipper (1977), Casaburi and co-workers (1977) and particularly Hughson and Morrissey (1982) confirmed that in the transition from a base line of light cycle ergometer exercise to heavier loads equal or longer oxygen uptake time constants were found as compared with those recorded when starting from rest. Some of these indicated that the difference in the observations grouped by races of subjects and/or duration of the experiment (Whipp and Wasserman, 1972), corrected by model of calculation (Hughson and Morrissey, 1982). Recently, an interesting in groups of exercising muscle and accumulation in blood lactic acid that could explain in term of energy requirement (diPrampero, Mahler, Giezendanner and Cerretelli, 1989).

3.3. Influence of Position.

$\dot{V}o_2$ during upright cycle ergometer was greater (0.30 litters) than during supine exercise. And oxygen deficit in the upright position was 0.64 litters as compared to the supine test (Convertino, Goldwater and Sandler, 1984), because of changing in cardiac volume (Longhurst, Musch and Ordway, 1986).

3.4. Influence of Sex and Age.

The female teen-agers (15-18 years) had slower kinetics than kinetics of children (7-10 years) and boys (15-18 years) in phase I but not significant (Cooper,

Berry, Lamarra and Wasserman, 1985).

3.5. Influence of Muscle Type.

Arm exercise, characterized by a relatively greater involvement of type IIA fiber and therefore by a large lactic acid component for any given greater τ values (diPrampers et al., 1989).

3.6. Influence of Training Effect.

Endurance athletes could be expected to be decreasing τ levels. This finding could be explained for the former case with an almost exclusive involvement of slow-twitch fibers and for the latter, with a shift toward heavier loads of the individual anaerobic threshold (diprampero et al., 1989).

Endurance exercise by increasing the muscle content of mitochondria should result in a more rapid adjustment of respiration to energy need. With more mitochondria the oxygen uptake had to lower to some extent in order to attain the same total submaximal oxygen uptake. Exercise had been shown to increase muscle myoglobin concentration. If an increase in muscle myoglobin occurred in the trained subject (Hickson, Bomze and Holloszy, 1978), increased oxygen extraction from the blood might be delayed. Despite a more rapid adjustment of muscle respiration (Casaburi, Storer, Ben-Dov and Wasserman, 1987), the exercise muscles could attenuate oxymyoglobin stores. Thus, an increased oxymyoglobin content could mask a more rapid adjustment of aerobic metabolism to energy demand earlier than the rising in $\dot{V}o_2$ at the beginning of exercise in the trained state.

3.7. Influence of Disease.

A pathological blockage of anaerobic glycolysis as in McArdle syndrome is characterized by very rapid changes of oxygen uptake kinetics (diPrampero et al., 1989).

4. Oxygen Uptake Kinetics Determination.

The time course of oxygen uptake kinetics following changes in exercise intensity had been shown to depend on aerobic capacity (Ebfefd, Hoffmann and Stegemann, 1987; Hagberg, Hichson, Ehsani and Holloszy, 1980).

In most cases the data thus obtained were additionally fitted by explicit mathematical models (Wessel, et al., 1979). The dilemma of these approaches was that some physiological and mathematical modelings were necessary for a quantitative analysis of the oxygen uptake kinetics step transients. (Bates, Prisk, Tanner and McKinnon, 1983). For mild and moderate intensity of exercise or for the early predominantly alactic phase of more intense exercise, the time course of the changes of oxygen consumption may be represented by a simple exponential equation (Whipp, 1971; Whipp, and co-workers, 1981; Sietsema et al., 1989) of the equation :

$$\dot{V}o_2(t) = \dot{V}o_{2(ss)}(1 - e^{-kt}) \qquad (1)$$

where $\dot{V}o_2$ (t) represented the oxygen uptake above the resting value at any time (τ) after the onset of exercise, $\dot{V}o_{2(ss)}$ was the steady-state value (above rest) for oxygen consumption, and k was the rate constant of the reaction with the dimension of $time^{-1}$.

The distribution of k values within the groups reflected the relative effectiveness of the cardiopulmonary and metabolic readjustment to the imposed task (Bates, et al., 1983). Other studies have used the half time ($t_{1/2}$), the time constant (τ) or the slope of this response. All of these parameters that below anaerobic threshold are related (Hughson and Morrissey, 1982) :

$$\tau = \frac{1}{k} = t_{1/2}/0.693 \qquad (2)$$

Above the anaerobic threshold, oxygen uptake kinetics might only be described by a more complex equation involving two exponential terms (Bason et al., 1973) thereby invalidating (Whipp, 1971).

The accurate approach of measurement was used in research. Further recommendation and stated that computerized non-linear least-squares curve-fitting function as opposed to estimations of rate constant, time constant and time half life was showed suitable calculation (Hughson and Morrissey, 1982; Hughson, et al., 1988; Beaver, Lamarra and Wasserman, 1981).

This study was undertaken in an attempt to compare the general endurance capacity by aerobic parameters of aerobic-trained and untrained Thai male and to determine the declining rate of their by aging.