EFFECT OF HYPOXIA ON AEROBIC CAPACITY IN ATHLETES WITH LOW BLOOD HEMOGLOBIN LEVEL

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Flt.Lt. CHANTANA AKARATHAM

ชื่อวิทยานิพนธ์ ผลของสภาวะขาดออกซิเจนต่อความสามารถทางแอร์โรบิคในนักกีฬาที่มีระดับฮีโมโกลบินในเลือดต่ำ

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บทคัดย่อ

ได้ทำการศึกษา อิทธิพลของระดับฮีโมโกลบินในเลือดต่อความสามารถทางแอร์โรบิคในสภาวะขาดออกซิเจนในนักกีฬาทหารอากาศชายจำนวน 11 คนอายุระหว่าง 20 - 29 ปี ความเข้มข้นของฮีโมโกลบินในเลือด 12.1-14.9 กรัมต่อเดซิลิตร ได้แบ่งนักกีฬาทั้งหมดออกเป็น 2 กลุ่ม คือกลุ่มที่มีระดับฮีโมโกลบินในเลือดน้อยกว่า 14 กรัมต่อเดซิลิตร เรียกกลุ่มที่มีเลือดจาง(anemia) และกลุ่มที่มีความเข้มข้นของฮีโมโกลบินในเลือดตั้งแต่ 14 กรัมต่อเดซิลิตรขึ้นไป เรียก กลุ่มควบคุม (control) ทำการทดสอบความสามารถในการใช้ออกซิเจนสูงสุด (VO_2max) และค่าแอนแอร์โรบิคเธรชโฮลด์ในนักกีฬาแต่ละคน โดยให้ออกกำลังกายแบบเพิ่มความหนักของงานอย่างต่อเนื่องจนกระทั่งถึงงานสูงสุดที่ผู้ถูกทดสอบสามารถทำได้ โดยใช้จักรยานวัดงาน ในสภาวะอากาศที่มีปริมาณแก๊สออกซิเจนปกติ(normoxia) และในสภาวะขาดออกซิเจน (hypoxia) ซึ่งกรณีหลังนี้กระทำโดย ให้ผู้ถูกทดสอบหายใจแก๊สผสมที่มีปริมาณออกซิเจน 14.5 % และไนโตรเจน 85.5 % ซึ่งเทียบเท่ากับการอยู่บนที่สูงประมาณ 10,000 ฟุตเหนือระดับน้ำทะเล ผลการทดสอบพบว่าค่า VO_2max ของผู้ทดสอบทั้งหมดไม่ขึ้นกับระดับฮีโมโกลบินในเลือดเมื่ออยู่ในสภาวะnormoxiaแต่จะลดลงในสภาวะhypoxia และการลดลงนี้เป็นปฏิภาคโดยตรงกับค่า VO_2max ในสภาวะ normoxia แต่เป็นปฏิภาคผกผันกับระดับฮีโมโกลบินในเลือด นอกจากนี้ยังได้ทำการวัดค่าเปอร์เซ็นต์ความอิ่มตัวของเม็ดเลือดแดงที่มีต่อออกซิเจน (SaO_2), อัตราเต้นของหัวใจ และอัตราการเคลื่อนที่ของลมหายใจออก(V_E)

ในขณะพักและขณะออกกำลังกายพร้อมทั้งวัดค่าแลคเตทในเลือดทั้งก่อนและหลังออกกำลังกาย พบว่าในสภาวะ hypoxia ค่า SaO_2 ทั้งในขณะพักและขณะออกกำลังกายมีค่าต่ำกว่า SaO_2 ในสภาวะ normoxia และในขณะออกกำลังกายสูงสุด SaO_2 ลดลงมากในนักกีฬาที่มี VO_2max ต่ำลงมากด้วย การเปลี่ยนแปลงเหล่านี้ปรากฏมากในนักกีฬาที่มีระดับฮีโมโกลบินในเลือดต่ำ จากการสำรวจกลุ่มนักกีฬาที่มีเลือดจางพบว่า อัตราเต้นของหัวใจสูงสุด(HRmax)ในสภาวะขาดออกซิเจน ต่ำกว่าค่าที่ได้ในสภาวะอากาศที่มีปริมาณออกซิเจนปกติ ในสภาวะขาดออกซิเจนพบว่า ผู้ที่มี HRmax ลดลงมากมีค่า VO_2max ลดลงมากด้วย ในขณะที่ความสัมพันธ์แบบนี้ไม่พบในนักกีฬาที่มีระดับฮีโมโกลบินปกติ ภายใต้สภาวะขาดออกซิเจนการลดลงของแลคเตทในเลือดภายหลังการออกกำลังกาย สอดคล้องกับการลดลงของงานที่ทำได้สูงสุดอย่างไรก็ตาม ในสภาวะขาดออกซิเจนนี้ ปริมาณแลคเตทในเลือดภายหลังการออกกำลังกายของกลุ่มเลือดจางมีค่าสูงกว่ากลุ่มควบคุมแม้ว่างานสูงสุดที่ทำได้ของทั้งสองกลุ่มเท่ากัน นอกจากนี้ยังพบว่า ขณะออกกำลังกายแบบเพิ่มความหนักของงานอย่างต่อเนื่องภายใต้สภาวะอากาศที่มีปริมาณออกซิเจนปกติ อัตราการเคลื่อนที่ของลมหายใจออก ณ จุดที่มีการใช้ออกซิเจนสูงสุด (V_E at VO_2max) ของผู้ถูกทดสอบทั้งสองกลุ่ม ไม่ถูกเปลี่ยนแปลงโดยสภาวะขาดออกซิเจน ในทำนองเดียวกับการเปลี่ยนแปลงของ VO_2max การลดลงของอัตราการใช้ออกซิเจน ณ ตำแหน่งของแอนแอร์โรบิคเธรชโฮลด์ (VO_2 at AT)ในเชิงสัมพัทธ์กับน้ำหนักตัว (หน่วยเป็นมิลลิลิตรต่อกิโลกรัมต่อนาที) อันเนื่องมาจากสภาวะขาดออกซิเจน มีมากในนักกีฬาที่มีค่า VO_2 at AT สูง โดยค่าที่ลดลงนี้สัมพันธ์กับค่า SaO_2 ที่ลดลง ภายใต้สภาวะอากาศที่ปริมาณออกซิเจนปกติและสภาวะขาดออกซิเจน หากเปรียบเทียบกลุ่มที่มีระดับฮีโมโกลบินปกติกับกลุ่มเลือดจาง พบว่า ระดับฮีโมโกลบินในเลือดไม่มีผลต่อ AT ตลอดจนค่าตัวแปรต่างๆ ที่เกี่ยวข้อง เช่น SaO_2, อัตราการใช้ออกซิเจนต่อการบีบตัวของหัวใจ 1 ครั้ง (O_2 pulse),ความหนักของงาน, และอัตราการเคลื่อนที่ของลมหายใจออกภายใต้สภาวะขาดออกซิเจน อัตราเต้นของหัวใจ ณ ตำแหน่งแอนแอร์โรบิคเธรชโฮลด์(HR at AT)เป็นตัวแปรตัวเดียวของกลุ่มเลือดจางที่พบว่ามีค่าต่ำกว่ากลุ่มฮีโมโกลบินปกติ ผลจากการศึกษาครั้งนี้แสดงว่า 1) ความสามารถทางแอร์โรบิคซึ่งแสดงโดย VO_2max และ VO_2 at AT ลดลงเมื่ออยู่ในสภาวะขาดออกซิเจน ซึ่ง

การลดลงนี้เป็นสัดส่วนกับความสามารถทางแอร์โรบิคในสภาวะอากาศที่มีปริมาณออกซิเจนปกติ 2) การลดลงของความสามารถทางแอร์โรบิคสืบเนื่องมาจากค่า SaO_2 ที่ลดลง 3) ระดับฮีโมโกลบินที่ต่ำในกลุ่มนักกีฬาเลือดจาง มีผลให้การลดลงของ VO_2max อันเนื่องมาจากสภาวะขาดออกซิเจนรุนแรงมากขึ้น แต่ไม่มีผลต่อการเปลี่ยนแปลงของ AT เมื่อร่างกายอยู่ในสภาวะขาดออกซิเจน ข้อมูลเหล่านี้บ่งชี้ว่าภายใต้สภาวะขาดออกซิเจน การมีเลือดจางก่อให้เกิดผลเสียต่อความสามารถในการใช้ออกซิเจนขณะออกกำลังกายสูงสุดแต่ไม่มีผลขณะออกกำลังกายปานกลางจนถึงระดับของแอนแอร์โรบิคเธรชโฮลด์ 4) ในสภาวะอากาศที่มีปริมาณออกซิเจนปกติ การมีเลือดจางไม่มีผลกระทบอัตราการใช้ออกซิเจนขณะออกกำลังกาย ณ ความหนักใด ๆ 5) ยังไม่ทราบกลไกที่แท้จริงสำหรับการที่ความสามารถในการใช้ออกซิเจนสูงสุดที่สภาวะขาดออกซิเจนในกลุ่มเลือดจางลดลงมากกว่ากลุ่มฮีโมโกลบินปกติ อย่างไรก็ตาม อาจเป็นไปได้ว่าปัจจัยที่ทำให้การขนส่งออกซิเจนในเลือดแดงลดลงน่าจะมีส่วนเกี่ยวข้องกับปรากฏการณ์นี้ ปัจจัยดังกล่าวรวมถึง ระดับฮีโมโกลบินในเลือดต่ำ , การลดลงของปริมาณออกซิเจนในเลือดแดง (CaO_2) และการลดลงของอัตราเต้นของหัวใจสูงสุด

Thesis Title Effect of Hypoxia on Aerobic Capacity in Atheltes with Low Blood Hemoglobin Level

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Abstract

The influence of blood hemoglobin concentration (Hb) on the reduction in aerobic capacity during acute exposure to hypoxia was investigated in eleven healthy male athletes of the Royal Thai Air Force (R.T.A.F.).Their ages and Hb ranged from 20-29 years and 12.1-14.9 g/dl,respectively. According to their Hb, the subjects were divided into two groups: control and anemia. For the subjects whose Hb equal or more than 14 g/dl were defined as the control and those who had Hb level less than 14 g/dl were stood for the anemia. Each subject performed an incremental exercise test until exhaustion on a bicycle ergometer at both normoxia and hypoxia. Hypoxia was induced by inspiration of 14.5 $\%O_2$ with N_2 balance (equivalent to an altitude of approximately 10,000 feet).The maximum rate of O_2 consumption (VO_2max) and anaerobic threshold (AT) of each subject were determined. The results showed that despite the differance in Hb , the normoxic VO_2max and the VO_2 at AT of the two groups of subjects were similar. It was also found that for all

subjects at normoxia the VO_2max was independent on Hb and was significantly decreased at hypoxia. The reduction in VO_2max at hypoxia from that at normoxia (Δ VO_2max) was directly correlated with the normoxic VO_2max but was inversely correlated with Hb. That is, at any Hb, the higher in normoxic VO_2max the greater Δ VO_2max occurred, and at any normoxic VO_2max , the lower in Hb the greater ΔVO_2max was observed. Hence, the athletes with high normoxic VO_2max and low Hb exhibited considerably high ΔVO_2max. Percent arterial oxygen saturation (SaO_2), heart rate (HR) and minute ventilation (V_E) at rest and during exercise were also determined.Blood lactate was measured before and immediately after the exercise test. SaO_2 was found to be decreased from normoxic values both at rest and during maximal exercise at hypoxia. The effect of hypoxia on the exercise-induced decrease in SaO_2 was more pronouced in athletes who exhibited high ΔVO_2max compared to those with low ΔVO_2max and also in the high ΔVO_2max athletes with low Hb than those with normal Hb. Only in the anemic athletes, maximal exercise heart rate (HR_{max}) at hypoxia was lower than the normoxic value.It was also found that subject who exhibited great reduction in HR_{max} at hypoxia showed high ΔVO_2max while such therelationship was not appeared in the non-anemic athletes. Under hypoxic condition, the decline in postexercise blood lactate was correspoded to the reduction in maximal work load;however,the former values in the anemia was higher than the control even though the hypoxic maximal work load was similar between the two subject groups. During

incremental exercise, V_E at the point where VO_2max was achieved in both subject groups under normoxia were not changed by hypoxic exposure. Similar to VO_2max change, the level of VO_2 at AT expressed in term of ml/kg/min was markedly decreased by hypoxia in athletes who possessed high VO_2 at AT.The decrease was correlated with the lowering in in SaO_2. Under both environmental conditions, comparison between the anemic and the control athletes showed no effect of Hb on the AT and its related parameters such as SaO_2, O_2 pulse, V_E ,and work load. Only HR at the AT showed lower in the anemia than the control under hypoxia. The results of this study indicated that: 1) aerobic capacity determined by VO_2max and VO_2 at AT, was decreased at hypoxia in proportion to its normoxic level; 2) the reduction in the aerobic capacity was attributed to the decreased SaO_2; 3) low Hb in the anemic athletes could magnify ΔVO_2max but not ΔVO_2 at AT during acute hypoxic exposure indicated that,under hypoxic condition, the anemia exerted deterioration on VO_2 during maximal exercise but not submaximal exercise at the level of AT; 4) no effect of anemiaon VO_2 at any level of exercise intensity could be found under normoxic condition; 5) the exact mechanisms responsible for the more marked reduction in VO_2max at hypoxia in the anemia than the control were unknown.However, possible contributing factors for this might be those which caused lowering in arterial O_2 transport. These might include the low Hb, the reduction in CaO_2 and HR_{max}.

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LIST OF ABBREVIATIONS

$(A-a)O_2$	=	alveolar-arterial oxygen
AT	=	anaerobic threshold
$(a-v)O_2$	=	arterio-venous oxygen
CaO_2	=	arterial oxygen content
CvO_2	=	oxygen content in mixed venous blood
CO_2	=	carbon dioxide
cu mm	=	cubic millimeter
D_L	=	diffusing capacity
F_EO_2	=	fraction of O_2 in the expired air
F_ECO_2	=	fraction of CO_2 in the expired air
fl	=	femtoliter
g%	=	gram percent
HR	=	heart rate
Hb	=	hemoglobin concentration
kg	=	kilogram
kpm/min	=	kilopond meter per minute
m	=	meter
min	=	minute
ml	=	milliliter
mmol/l	=	millimole per liter
MCH	=	mean corpuscular hemoglobin
MCHC	=	mean corpuscular hemoglobin concentration
MCV	=	mean corpuscular volume
N_2	=	nitrogen
O_2	=	oxygen

$PaCO_2$	=	partial pressure of carbon dioxide in arterial blood
$PACO_2$	=	partial pressure of carbon dioxide in alveoli
PaO_2	=	partial pressure of oxygen in arterial blood
PAO_2	=	partial pressure of oxygen in alveoli
P_IO_2	=	partial pressure of oxygen in inspired air
Q	=	cardiac output
R	=	respiratory gas exchange ratio
rpm	=	revolution per minute
SaO_2	=	arterial oxygen saturation
SD	=	standard diviation
SEM	=	standard error of mean
V_A/Q	=	ventilation-perfusion ratio
VCO_2	=	carbon dioxide production
V_E	=	minute ventilation
V_E/VCO_2	=	ventilatory equivalent for cabon dioxide
V_E/VO_2	=	ventilatory equivalent for oxygen
VO_2	=	oxygen consumption
VO_2max	=	maximum oxygen uptake
ΔVO_2max	=	normoxic VO_2max - hypoxic VO_2max
VO_2 at AT	=	oxygen uptake at anaerobic threshold
ΔVO_2 at AT	=	normoxic VO_2 at AT - hypoxic VO_2 at AT
WL	=	work load

CHAPTER I

INTRODUCTION

Previous studies illustrated that there was a closed relationship between maximal aerobic power (VO_2max) and maximal systemic oxygen transport [1,2,3,4]. Since the latter is governed by maximal cardiac output (Qmax) and arterial oxygen content (CaO_2), the VO_2max, therefore, is influenced by any factors that can cause changes in CaO_2. For examples, elevation of CaO_2 by raising the ambient air pressure [5,6] or by increasing the hemoglobin concentration of the blood can increase VO_2max [7]. On the other hand, decreasing the CaO_2 by acute exposure to high altitude [8,9,10] or reducing the oxygen carrying capacity of the blood by anemia [11] have all experimentally been shown to decrease both the VO_2max and physical performance. From these information it might be expected that highly aerobically fit athletes with large VO_2max should possess high hemoglobin concentration. But this is not always true since some top athletes, especially in endurance disciplines, possess a lower hemoglobin concentration but higher VO_2max when compare with normal healthy sedentaries [12,13]. A term 'sports anemia' was used to denote the anemia occurring in relation to intensified physical training [14] but the causes of this are not exactly known [15]. A possible contributing factor of such the low hemoglobin concentration in these alhletes is

considered to be a mismatched elevation of plasma volume and total hemoglobin [16-20].

It has been reported that at high altitude above 1,200-1,800 meters VO_2max decreases by about 3% for every 300 meters additional increase of altitude [8,21,22] and that the reduction of VO_2max at high altitude is directly varied with sea level VO_2max i.e., the more aerobically fit individuals suffered a larger decrement in maximal aerobic power at high altitude [8,10].

Since athletes with sports anemia could possess high VO_2max, a question arise whether the low blood hemoglobin concentration in these athletes which shows no deteriorative effects of anemia on VO_2max at sea level could enhance the reduction of VO_2max when they acutely expose to high altitude.

Up to now the studies of the combined effects of acute exposure to high altitude and low blood hemoglobin concentration, especially in case of sports anemia, have not been reported. It is ,therefore, of interest to investigate the effect of high altitude exposure on aerobic capacity in anemic athletes in comparison with athletes with normal blood hemoglobin level.

CHAPTER II

LITERATURE REVIEW

I. AEROBIC CAPACITY :

The Ability of humans to perform work or exercise is best esamined by determining work capacity and the total amount of oxygen that can be consumed during exercise which is called "aerobic capacity" [23]. For each liter of oxygen consumed,about twenty kilojoules (range from 19.7 to 21.2) [23] will be delivered ; hence, the higher the oxygen uptake, the higher the aerobic energy output. Since we can only estimate an aerobic capacity but not measure it, so the term "aerobic power" is used to reflects what is measured,that is,the rate of aerobic energy use [24].

I.1 Maximal Aerobic Power (VO_2max) :

Maximal aerobic power (VO_2max) is the maximal amount of oxygen that can be consumed per minute during maximal exercise [24] or is defined as the point where the oxygen consumption plateaus and shows no futher increase (or increase only slightly, not more than 150 ml) with an additional workload [25]. Like many other physiological terms, the term maximal aerobic power can be written in the other words such as maximal oxygen consumption, maximal oxygen intake, and maximal oxygen uptake. The VO_2max provides a quantitative statement of an individual's capacity for aerobic energy transfer. As such, it is one of the more important factors determining our ability to

sustain high-intensity exercise for longer than 4 to 5 minutes. Absolute value of VO_2max is expressed as liter per minute to describe the absolute power of the cardiorespiratory system [24]. It's more usual to present VO_2max in term of milliliter per kilogram body weight per minute (ml/kg/min) which express the value of VO_2max relative to the amount of tissue that must supplied. This unit is best suited for making comparison between athletic groups or between athletes and non- athletes. Those who have highest VO_2max reported so far are 94 ml/kg/min for a male and 77(ml/kg/min) for a female cross-country skier[23].

I.2 Criteria for Achievement of Maximal Oxygen Uptake

If the subject is well motivated, the oxygen uptake fails to show an increase with increasing work load [26]. Because it is known that oxygen uptake increases linearly with increasing work loads up to the maximal rate of oxygen uptake, a plateau of oxygen uptake with an increasing workload is a sure sign that the subject has achieved his maximum. In an absence of a plateau or a fall in oxygen uptake, one cannot be certain that the highest oxygen uptake is indeed the subject's VO_2max [27]. Other subsidiary criteria of a good maximum effort include [26] :

1. heart rate close to the age-related maximum (220-age) +10 [23]

2. a respiratory gas exchange ratio of 1.15 or more

3. a high blood lactate level (11-16 mmol/l).

However, the body must be driven into a substantial oxygen debt before a plateau is demonstrated,

and this may be difficult to realize in children or older subjects [28].

Test of VO_2max should follow 4 general requirements[23]:

1. the exercise test must involve large muscle group
2. the rate must be measurable and reproducible
3. the test must be tolerated by all healthy individual
4. type of exercise test should be independent of the skill.

In laboratory experiments VO_2max is usually measured by one of three types of exercise ; running on a treadmill, cycling on a bicycle ergometer, and stepping up and down from a bench [23]. There are some advantages and disadvantages to each of these procedures. Running on a tradmill produce the highest values for VO_2max, independent of the skill and is the least differences in efficiency between the subject [27] but it is quite difficult to measure respiratory and physiological changes due to body and limbs motion [28]. Cycling on a bicycle ergometer can be used to measure the quantity of work performed very accurately and is prefer able for measurement of the physiological changes, taking blood and testing of respiratory function since in cycling the upper body and limbs are relatively motionless. However, in persons who have never ridden a bicycle before, the maximal test may be undesirable. A step test is very inexpensive and portable so it may be the only realistic test alternative in field studies, but it is more difficult to perform recording such as ECG or blood collecting of exercising subjects when

compare with the 2 former methods[27].

In general, a test of VO_2max starts with a submaximal work rate which also serves as a warming-up activity. After this, the load may be increased in one of several ways: (1) the load may be immediately increased to a level that represents the predicted maximal load for the subject and is maintained for three to six minute. (2) The load may be increased stepwise every minute or every other minute until exhaustion. (3) The load may be increased stepwise with several submaximal, maximal, or supra maximal loads and maintain exercise for five to six minute at each load with or without resting periods between each step [23].

I.3 Factors Determining Maximal Aerobic Power (VO_2max)

The oxygen which is utilized during exercise is supplied by two processes, oxygen transport by the blood and oxygen extracted by the tissues. Systemic oxygen transport can be expressed mathmatically as the product of the arterial oxygen content (CaO_2) multiplied by cardiac output (Q) : [Systemic oxygen transport = CaO_2 x Q]. Hence the processes of oxygen supply may be further distributed into CaO_2, Q, and tissue extraction. These three factors are the end products of three important physiological systems : pulmonary, cardiovascular, and local circulatory systems [29] accompanying with the one important factor : tissue factors (diffusion of oxygen from the capillaries to the cell [30,23] and oxygen utilization ability of the cell [30,31]). It is sufficient to say that Vo_2max is reached when CaO_2, Q, and tissue extraction have achieved

their maximal functional state [29]. [$VO_2max = Q_{max}$ x $(a-v)O_2$ difference] Figure 1 indicates the close relationship between VO_2max and maximal systemic oxygen transport (Q_{max} x CaO_{2max}). This relationship exists over a wide range of values in the presence of normoxia [2] and hypoxia [1,3,4].

I.4 Effect of Training on Maximal Aerobic Power :

changes in VO_2max as a result of aerobic training range from no improvement to increases as great as 43 % and more [32]. The extent of any training effect depends on many factors, including physical condition prior to initiation of training, age, heredity, mode of exercise during assessment of VO_2max, and type of training programe [27]. For instant, in sedentary people, low intensity training with sessions lasting about 30 minutes repeated 3 times per week, and demanding approximately 50 % of VO_2max, can increase the maximal oxygen uptake 5 to 10 % after 6 to 12 weeks. And when training at 70 to 80 % of VO_2max, the improvement is on the average 15 % [32,33]. When expressing an improvement in percentage of the VO_2max those individuals who start with a relatively low level of fitness improve the most [32,34]. However, natural endowments set a final ceiling for the improvement [32,34]. Sex of the trainee is not an important factor in predicting improvement of VO_2max as long as other factors, since both males and females respond to aerobic training with similar increments in maximal oxygen uptake [32].

Aerobic training changes include increases in

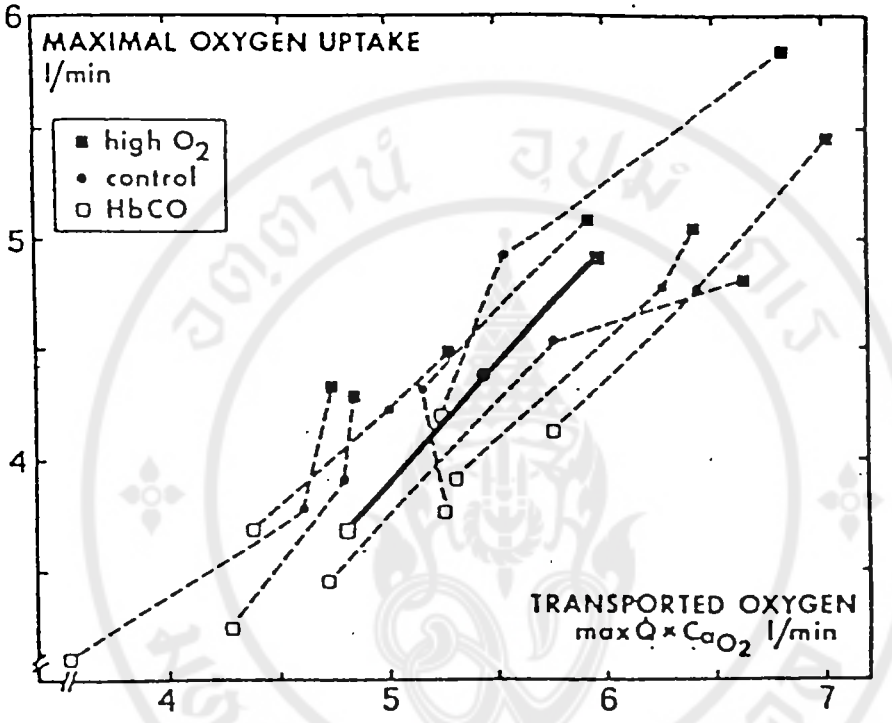


Fig 1. The relation between VO_2max and systemic oxygen transported (Modified from Astrand, 1964[2]).

mitochondrial size and number as well as the activity of aerobic enzymes, increased myoglobin and enhanced oxidation of fat and carbohydrate, These adaptation are geared to a greater aerobic production of ATP [25].

Aerobic training also brings about both functional and dimentional changes in the cardiovascular system. These include decreases in resting and submaximal exercise heart rate, enhanced stoke volume and cardiac output, and an expanded arterioalveolar oxygen difference ($(a-v)O_2$ difference) [25]. In longitudinal studies of sedentary young men, an increase in maximal cardiac output and systemic $(a-v)O_2$ difference both contribute to the increased VO_2max [23]. With prolonged training resulting in a further increase in the VO_2max, an increment in the cardiac output is the cause of the increase. There is no significant difference in the maximal $(a-v)O_2$ difference between well-trained athletes who have a very high VO_2max and trained subjects who have much lower VO_2max. The individual variations in maximal stroke volume are much larger than differences in $(a-v)O_2$ difference [23].

I.5 Hematological Indices and Maximal Aerobic Power :

It is well established that physical performance, endurance capacity, resistance to fatique, and maximal aerobic power are depend on many different factors. The important one is the oxygen carrying capacity of the blood which is mainly determined by hemoglobin concentration, number of circulating erythrocytes, and the efficiency of their functions [44]. Highly significant positive

correlations were observed between the total amount of circulating hemoglobin,hemoglobin concentration, hematocrit, number of circulating erythrocytes , and red blood cell hemoglobin content on one hand, and the VO_2max, and the duration of physical work to exhaustion on the other [7,17,35-40]. Exblom at al [7] studied the response to exercise after blood loss and reinfuse reported that there was a more or less parallel decrease following 800 ml blood loss in maximal work time and VO_2max. The latter came back to control level after 14 days, while the former did not reach prebleeding value before reinfusion. Reinfusion of packed red cells that increased total hemoglobin 16 % , increasing both red cell volume and hemoglobin concentration. This was followed by a dramatic "overnight" increase in maximal work time of 23 % and a parallel increase in VO_2max of 9 % [7].

The observed changes in VO_2max both by blood letting and by reinfusion were highly correlated with the changes in hemoglobin concentration and the total hemoglobin.

Celsing and coworkers [35] performed the experiment about effect of long term anemia and retransfusion on central circulation during exercise found that a peroid of 8 to 10 weeks of anemia, where the reduction of hemoglobin concentration was 27.9 % compare with pre-venesection period , was followed by a decrease in VO_2max, maximal heart rate and maximal cardiac output. The formor was back to normal after retransfusion of erythrocytes, whereas maximal heart rate and maximal

cardiac output were still reduced 48 hours after a retransfusion.

I.6 Other Factors Influencing Maximum Aerobic Power

a) Genetic factor :

By analyzing the genetic contribution to aerobic power, Klissouras [52] found that 93 % of aerobic power is under genetic influence although aerobic power is trainable there is a genetic ceiling on improvement.However, there is one study about physical performance and muscle fiber types in monozygous and dizigous twins revealed no significant genetic contribution to aerobic power but slow twitch fiber percentage had a high genetic influence, 99.6 % for males and 92.2 % for females [53]. Since may be this study failed to control socioeconomic, health, and physical activity factors between groups [30] it is likely that besides these factors the successful performance in aerobic sports is largely a matter of inheritance [24].

b) Sex influence :

After puberty female's VO_2max(L/min) is twenty-five to thirty percent lower than male's [37]. In women muscular strength, body weight, and maximal power capacity are also lower than those of men [33].Thus it seems obvious that the body composition differences between the sexes account for some of the sex difference in VO_2max. In addition, stroke volume, hemoglobin concentration, and mitochondrial density are likely contributing factors, since the average values of these three parameters in women are lower than those of men [24].

c) Age influence :

During childhood and adolescence the maximal aerobic power increases with increasing age because there is a growth in all tissues of importance for strength and power during this period. After the VO_2max reaches its peak between sixteen to seventeen years in females, and eihgteen to twinty years in males, there is a gradual decline [54]. The decrease in VO_2max and endurance capacity with advancing years is caused by morphological aging processes in the vascular system, respiratory organs, and skeletal musculature. Among important causative factors are the following :

1) Changing inside and between the capillaries and cells reduced oxygen permeability and oxygen utilization.

2) Progressive diminution of power reserves and maximal cardiac output caused by atrophy of myocardium and progressive sclerotic processes in the heart.

3) The reduction of oxygen saturation of the blood due to the changing of alveolar membrane and capillaries.

4) The connective tissue is increase whereas muscular mass is decreased so it is resulted with the reduction of VO_2max [28].

d) Muscular mass involved in exercise :

The size of active muscles is considered to be one factor that can varies the demand on the oxygen-transporting functions. Astrand and Saltin [30] noticed a five percent difference, VO_2max being higher during running than during cycling. To obtain maximal values when

using the cycle ergometer, motivation and stimulation may be particulary important, owing to more pronounced local fatique in the legs (Knee region) when cycling. In arm exercise, the VO_2max is about 70 % of what is attained in leg exercise. At a given work rate, the intra-arterial blood pressure and the heart rate during arm exercise are higher than in leg exercise. When combining arm and leg exercise (cranking and cycling) the highest oxygen uptake that can be attained depends upon the relative load on the arms. Evidently the organism (inclusive heart) could tolerate a prolongation of the exercise period when a larger mass of skeletal muscle were activated since the subjective feeling of strain is related more to the metabolic rate per square area of muscle than to the total metabolism. The assessment of the individual's VO_2max should be made with the subject exercising in the upright position (running or cycling) with or without arm exercise added.

e) <u>The influence of ambient temperature, humidity, barometric pressure and time of day</u> :

For all types and degree of perfarmance, there are probably physiological optima of ambient temperature, humidity, barometric pressure, and time of day. Herxheimer found that at the equal steady-state of exercise, there is a great increase in heart rate when the ambient temperature is increase [55]. Temperature and humidity above the comfort range can lead to an extra load on the organism during ergometric performance, depending on movement of the

ambient air. They cause a rise in heart rate, cardiac output, and amplitude of arterial pressure during equal powers as expressions of increased regulatory functions. During the performance, the organism generates amount of heat and that makes the increment of internal temperature. As internal temperature rises, the heart rate and cardiac output increase, accompanied by decreased arteriovenous oxygen difference, in order to distribute and dissipate the increased muscular heat. Temperatures below 20 c have a favorable effect on endurance performance whereas higher temperatures favour sprints [28]. To evaluate Vo_2max by bicycle ergometer, the data for oxygen consumption and carbon dioxide production obtained under ambient conditions must be reduced for standardization purposes to values based on 0 c and 760 mmHg (STPD). Also the increase from morning to evening in heart rate, systolic pressure, and other biological factors must be taken into account.

As barometric pressure and partial oxygen pressure fall, the VO_2max decreases. In the case of submaximal exercise intensities, the heart rate and respiratory minute-volume rise as the ambient pressure falls [28].

II HYPOXIA AND MAXIMAL AEROBIC POWER

II.1 Hypoxia

Hypoxia is the condition of oxygen deficiency at the tissue level [46]. Traditionally, hypoxia has been divided into 4 types :

a. Hypoxic hypoxia. The PO_2 of the arterial blood is

reduced.

b. Anemic hypoxia. The arterial PO_2 is normal but the amount of hemoglobin avialable to carry oxygen is reduced.

c. Stagnant or ischemic hypoxia. The blood flow to a tissue is so low that adequate oxygen is not deliverd to the tissue despite arterial PO_2 and hemoglobin concentration are normal.

d. Histotoxic hypoxia. The amount of oxygen delivered to a tissue is adequate but, because of the action of a toxic agent, the tissue cell cannot make use of the oxygen supplied to them.

II.2 The Study of Hypoxia :

Three procedures have been used to study hypoxia [24] :

a. By exposing subjects to the high altitude areas such as Pike's Pead (4,300 m or 14,108 ft), this procedure is used when the biological effects of the total altitude environment are under study.

b. By using a hypobaric (low pressure) chamber, when only the hypoxia is under study. In this case, mobility is limited but hypoxia can be closely controlled.

c. To manipulate the percentage of oxygen inspired by the subject. In this way , altitude can be simulated.

II.3 Physiological Response to Hypoxia

At an altitude 10,000 feet where PO_2 is approximately 60 mmHg there is enough hypoxic stimulation of the chemoreceptors to definitely increase ventilation [48].

II.4 Effect of Hypoxia on VO_2max :

The impact of moderate hypoxia upon maximum oxygen uptake has both practical and theoretical interest. From the practical viewpoint, sports physician wish to know the likely deterioration in endurance performance when competitions are staged at moderate altitudes [43], While from the theoretical viewpoint hypoxia seems a useful tool to distinguish a central limitation of oxygen transport from a peripheral restriction of performance [28.44.45].

It is well known that VO_2max is directly proportional to the maximal rate of systemic oxygen transport, which is the product of arterial oxygen content (CaO_2) and maximal cardiac output (Qmax). With acute (less than 24 hrs), hypoxic exposure, Qmax is unchanged from sea level, but arterial oxygen saturation, thus CaO_2, is reduced resulting in a decrement in VO_2max [1.47.48]. Apparently, a greater than 3 % drop in CaO_2 resulting from hypoxia may be required before VO_2max is measurable affected [49].

Recently, in 1988 shephard et al [9] reported that hypoxia induced by breathing 12 % oxygen in nitrogen (equivalent to an altitude of 4400 meters) caused an average 28 % decrease of VO_2max, with a somewhat small decreases in peak heart rate, peak blood pressure, peak ventilation and peak blood lactate concentration. The major part of the impairment in oxygen transport was due to a reduction of arterial oxygen saturation, with small contributions from the decrease in heart rate and the decrease of ventilation. Like many previous experiments [8.10.50.51] they found

that the more aerobically fit individuals do tend to suffered a larger decrement in VO_2max than the less aerobically fit ones. They summarized these relationships in a multiple regression equation of the type [8]:

$$\hat{} VO_2max = 0.5\ VO_2max + 0.007\ V_E + 0.009\ fh - 0.35 - 1.23$$

$(r = 0.945,\ SEE. = 0.188\ l/min)$

where $\hat{} VO_2max$ (l/min) is the hypoxic change of VO_2max (VO_2max normoxia minus VO_2max hypoxia), VO_2max (l/min) is the maximal oxygen uptake in normoxia, V_E (l/min) is the hypoxic change of respiratory minute volume, fh is the hypoxic change of the heart rate, and S is the sex (male = 1, female = 2) When VO_2max and V_E were related to body weight the relationship was :

$$\hat{} VO_2max = 0.50\ VO_2max + 0.0074\ V_E + 0.139\ fh - 2.08(S) - 14.8$$

$(r = 0.935,\ see = 2.72\ ml/kg\text{-}min)$

The primary and the most immediate function of the cardiovascular system is to supply oxygen in adequate quantity to the tissues. To perform exercise, the active muscles have a manifold increase in O_2 requirement as compared to rest. Thus, meeting the increase in O_2 requirement to do physical work requires remarkable cardiovascular and respiratory adjustments to maintain $PaCO_2$ and pH [105].

III.1 Anaeroic Threshold Hypothesis

The anaerobic threshold is defined as the level of exercise VO_2 above which aerobic energy production is supplemented by anaerobic mechanisms [108]. The hypothesis states that :

1. the O_2 required by the metabolically active muscles can exceed the O_2 supply to the mitochondria when the work rate is sufficiently high

2. the imbalance between the O_2 supply and O_2 requirement (i.e.,O_2 requirement greater than supply) brings about a net increase in anaerobic oxidation in the cytosol of the cell with pyruvate conversion to lactate (fig 2).

3. lactate is buffered in the cell primarily by HCO_3 (fig 3)

4. the CO_2 generated from buffering increases CO_2 output while HCO_3 exchanges for lactate across the muscle cell membrane according to the new electrochemical gradients

5. the buffering and acid-base disturbances produce predictable changes in gas exchange.

III.2 Noninvasive Measurements of the Anaerobic Threshold

The noninvasive detection of the AT has gone to several refinements. Initially, it was suggested that departures in the linearity of ventilation (V_E) and carbon dioxide output (VCO_2) plus and abrupt increase in the gas exchange ratio (R) could be used as markers for the onset of a metabolic acidosis [106,107]. While these are valid indices, they are not optimal, because it is often difficuly to judge the VO_2 value at which V_E, VCO_2 and R begin to increase more steeply. A better detection scheme would involve determining the AT as the breakpoint from a variable that is decreasing or is relatively

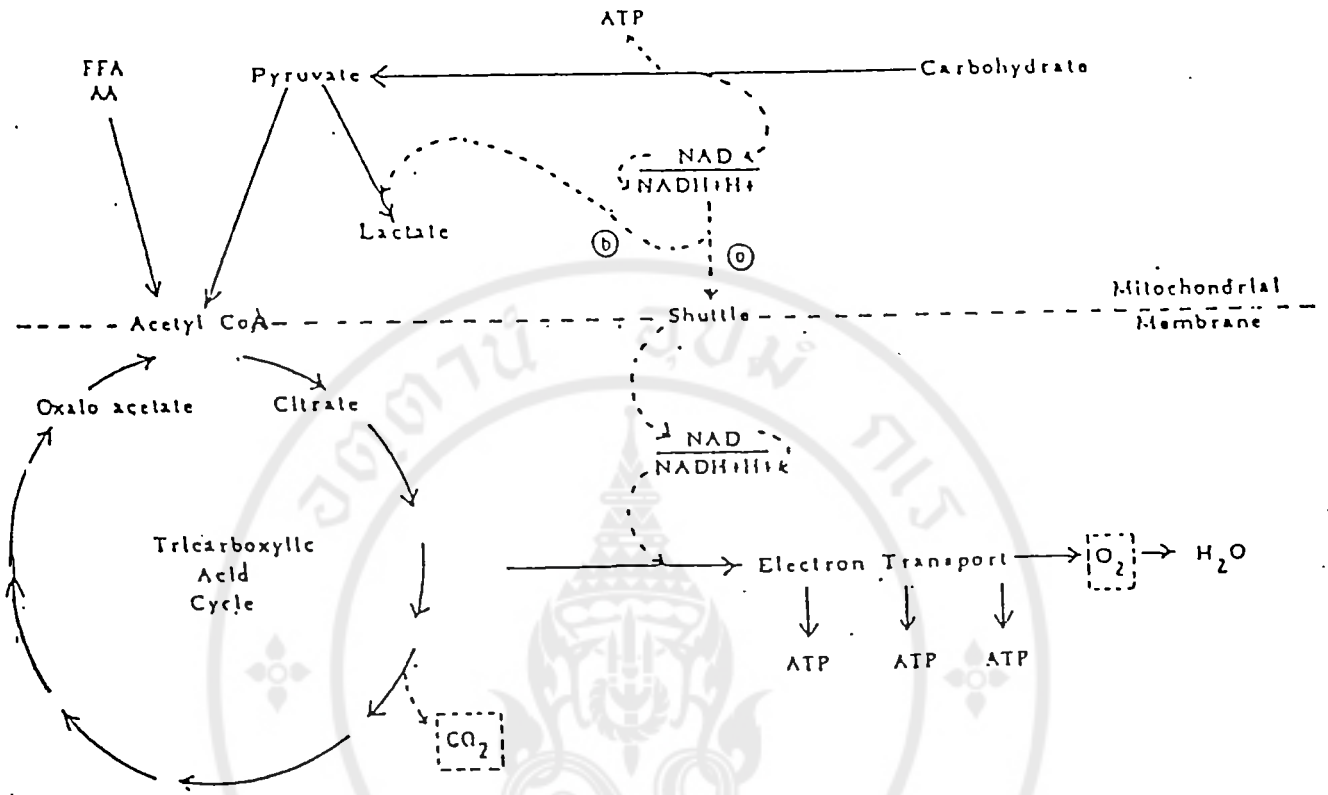


Fig 2. Schematic of metabolic pathways leading to production of adenosine triphosphate. Pathway "a" is used for low to moderate intensity work rates. Pathway "b" supplements pathway "a" at heavy and very heavy work intensities. From Wasserman, 1984[105].

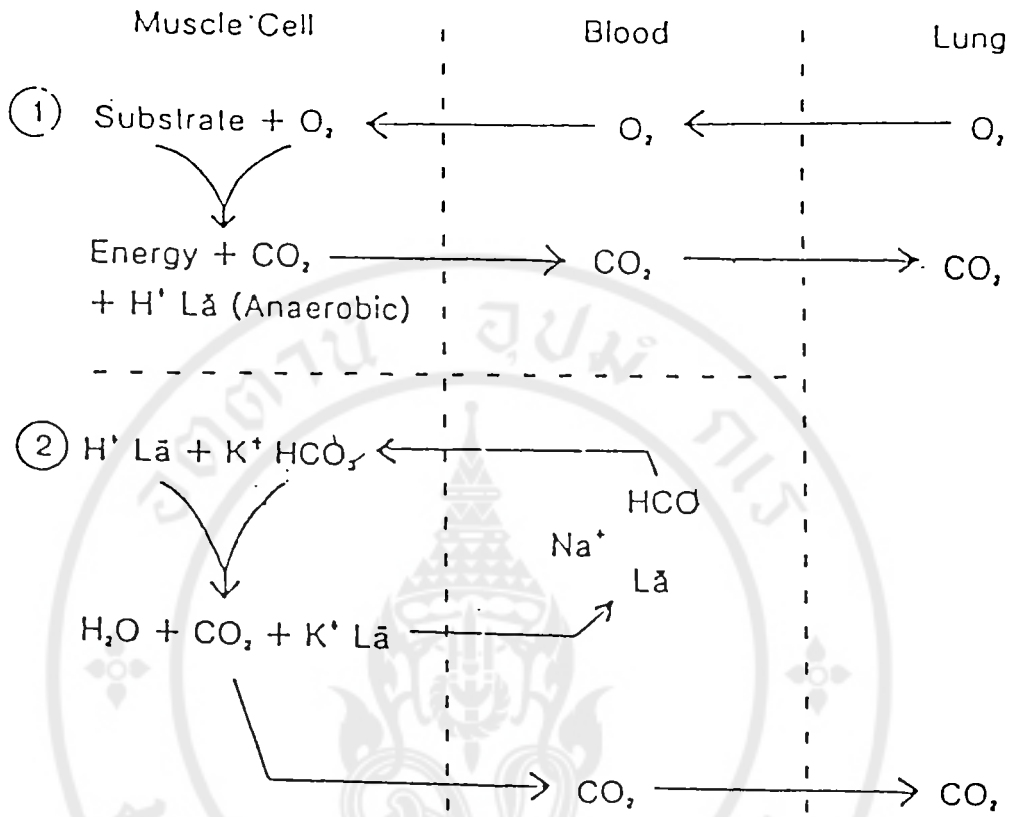


Fig 3. Cell buffering of the increase in lactic acid production when pathway "b",described in Fig.2 cotributes to the reoxidation of cytosol NADH. From Wasserman,1984[105].

unchanging over a number of work rates before it begins to increase.

Two variables have this pattern of response during incremental exercise. They are the ventilatory equivalent for VO_2 (V_E/VO_2) and end-tidal PO_2 ($P_{ET}O_2$). During the early work rates of an incremental test both variables decrease because the physiological dead space to tidal volume ratio (V_D/V_T) decreases. The decrease becomes less steep as the work rate continues to increase. At some point V_E/VO_2 and $P_{ET}O_2$ begin to systematically increase (fig 4,5). But other events can also cause these two variables to increase, e.g.,anxiety, pain, hypoxemia, and volitional hyperventilation. How then can one be sure that the increases in V_E/VO_2 and $P_{ET}O_2$ are due to an exercise-induced lactic acidosis and not to some other ventilatory stimulus ?

The answer involves the concept of "isocapnic buffering". Wasserman et al [109] have shown that for rapid incremental exercise tests, V_E and VCO_2 increase at the same rate for a few work rates beyond the AT (see fig 5). This is evident by the fact that V_E/VCO_2 does not increase at the AT but remains stable. Thus, the criterion of the systematic increase in V_E/VO_2 without a concomitant increase in V_E/VCO_2 is the most specific gas exchange method for detection of the AT [108].

However, the optimal protocol for the noninvasive detection of the AT would appear to be one that

1) maximizes the investigator's ability to observe the

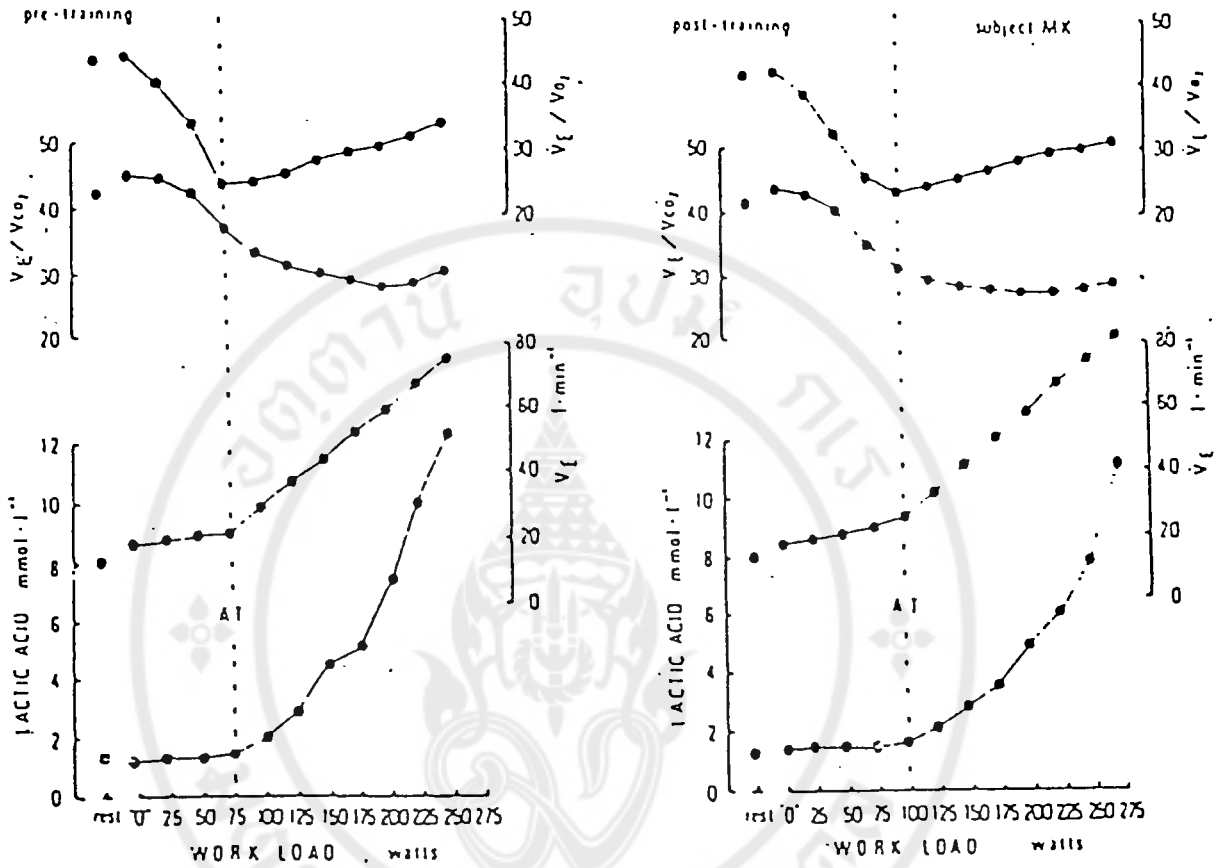


Fig.4. Comparison of the anaerobic threshold before and after endurance training. Horizontal dashed line represented anaerobic threshold. (From Yoshida,1984[112]).

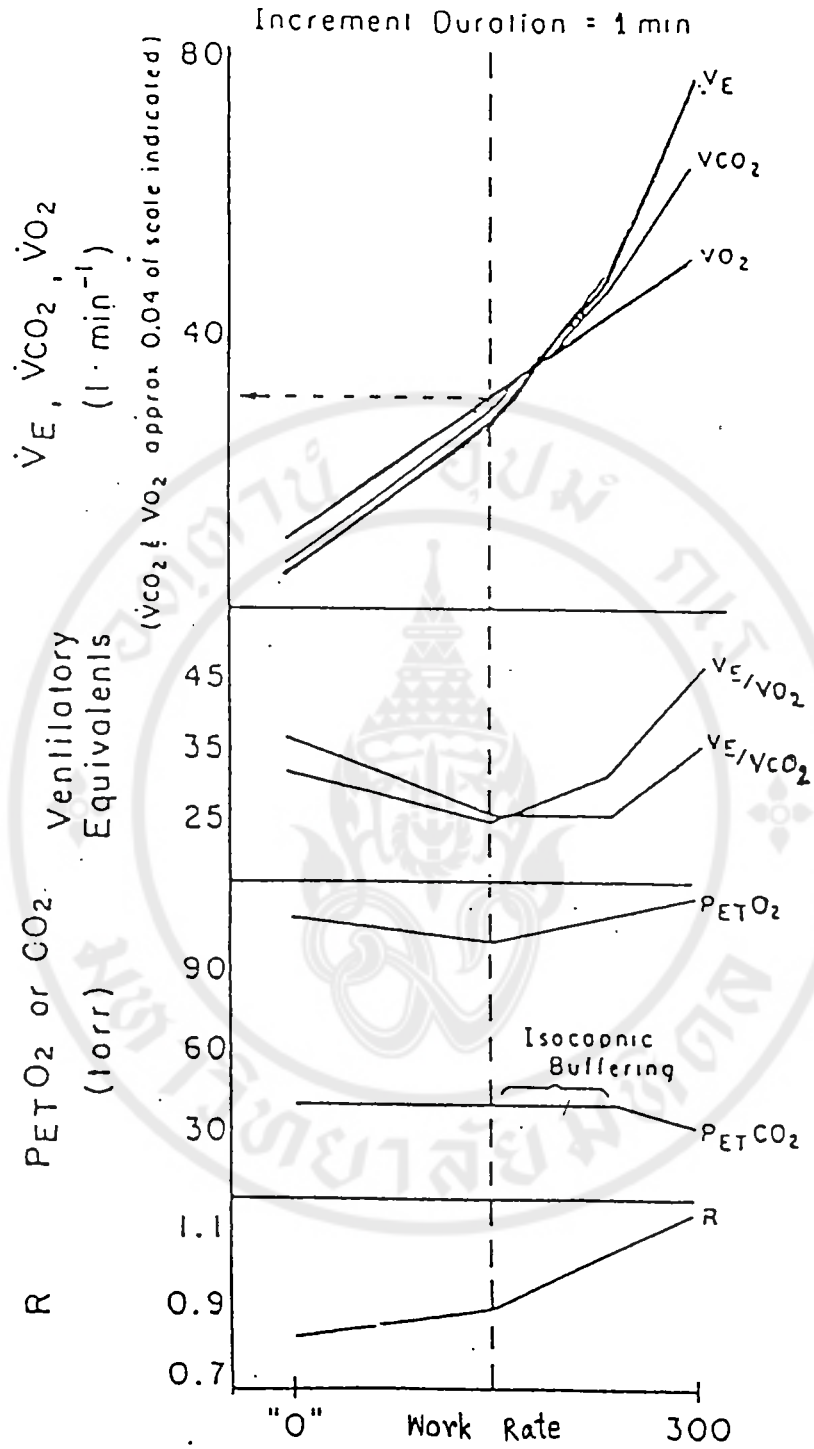


Fig 5. Diagramatic representation of ventilatory anaerobic threshold determination. The AT is indicated by the horizontal dashed line. Modified from Wasserman and Whip, 1975 (106).

isocapnic buffering region and

2) results in a clear break point in V_E/VO_2 [108].

III.3 Factors Affecting Anaerobic Threshold

The AT is influenced by many factors. Of these, the inportant appear to be mode of exercise, heredity, state of training, body size, sex, and age.

a) Mode of exercise :

In various experiments where the AT was determined on the same subjects during different forms of exercise. The AT is not the same for all types of exercise. For instance, the VO_2 at the AT is usually higher for tradmill exercise than for leg cycle ergometry [110], presumably because the work is distributed over a larger muscle mass. In different speed of pedaling, Hughet al. found that [111] the higher the frequency the lesser the work rate at AT. The duration of each work rate during incremental exercise does not affect the AT [112].

b) Heredity :

In 1986, Aunola and Rusko [113] demonstrated that among untrained men, who were grouped so that they represented distinctly either the slow twitch or the fast twitch type groups, AT seemed to be dependent on the fiber type majority in exercising muscles.The increase recruitment of fast-twitch fibers could accont for the increase in blood lactate this in turn , reduces the anaerobic threshold [117].

c) Training :

Several studies suggest that the AT be

increased after training [114,115]. Based on the study of Gibbons et al [116] they suggested that the AT was improved at training intensity levels equal to the AT, above the AT and below the AT. However, by observation, it can be deducted that the AT group showed a greater degree of improvement in AT than the other two groups. Possible mechanisms that account for an increased AT after endurance training include an improved distribution of blood flow (facilitated by an increase in capillary density) in trained muscle or increased oxidative capacity at the cellular level ,and an alteration in the muscle fiber recruitment pattern resulting in a delayed activity of fast twitch muscle fibers during incremental exercise [117].

d) Body Size :

From the cross-sectional study in children Cooper et al [118] found that AT and VO_2max increase in a highly ordered manner with increasing size, and as judged by AT/VO_2max. Therefore, they concluded that in children cardiorespiratory responses to exercise are regulated at optimized values despite overall change in body size during growth.

e) Sex :

Nicolic and Todorovic [119] found that in female group the AT was only 57.3 % compared with the male group during arm exercise and 60.8 % during leg exercise.

f) Age :

Regbranck et al.[120] found that there is a

significant decrease in AT in boys and girls with age when the AT was expressed as both absolute and relative values but Cooper et al. [118] found only slightly decresed in the ratio of AT to VO_2max with age. These suggest an increase in lactacid anaerobic capacity during growth.

III.4 Anaerobic Threshold and Performance

It is widely appreciated that a relative high level of VO_2max is necessary for high level aerobic endurance performance in competition with other athletes who also have relatively high VO_2max. Another characteristic of endurance athletesis that they can exercise at high percentages of their VO_2max for long periods without accumulating large amounts of lactic acid in their blood [121].

It has been pointed out by a number of studies that AT reflected endurance capacity [107,122-125]. Tanaka et al. [126] have demonstrated that alterations in 10,000 m. running performance are more directly accounted for by the AT changes ($r = -0.69$ to -0.92) and by the VO_2max changes ($r = -0.60$ to -0.85).

The postulated rationale for the close relationship between the AT and endurance performance relates to the rate of muscle glycogen breakdown. Because long-term, high intensity exercise results in, and is perhaps ultimately limited by, muscle glycogen depletion [127,128], exercise just below the AT would result in a much slower reduction of the muscle glycogen stores than exercise above the AT and would therefore be tolerable for much longer periods of time. This is because glycogen is

used at a rate that is 18-19 times faster during anaerobic glycolysis compare to oxidative phosphorelation for the same energy(ATP) yield. Boyd et al. [120] have demostrated that elevetions in blood lactate concentration inhibit lipolysis in exercising man and thus force obligatory carbohydrate utilization.

III.5 Application of the Anaerobic Threshold Measurement

In testing patients with the complaint of exercise intolerance we use the AT to complement our VO_2max measurement (Figure 6). If the VO_2max is normal , then we conclude that the patient is normal, limited by obesity (a common condition that reduces exercise tolerance because of the high metabolic cost but without cardiovascular or respiratory dysfunction) , or we look for evidence of mild coronary artery disease or lung disease.

If the VO_2max is low, it is valuable to know if the AT is normal or low.Our lower limit for normal AT is 40% of the predicted VO_2max wih a mean[130]. We use the same method for predicting the AT for females.

The AT is reduced when O_2 flow to the metabolically active muscles is inadequate. Therefore, conditions that limit cardiac output during exercise such as primary heart disease, pulmonary vascular occlusive disease, peripheral vascular disease,and anemia will cause AT to be reduced because of their effect of O_2 flow.

If the AT is normal but the VO_2max is low(or the patient stop the exercise before reaching its maximal level) then the cardiovascular system is probably not limiting. The

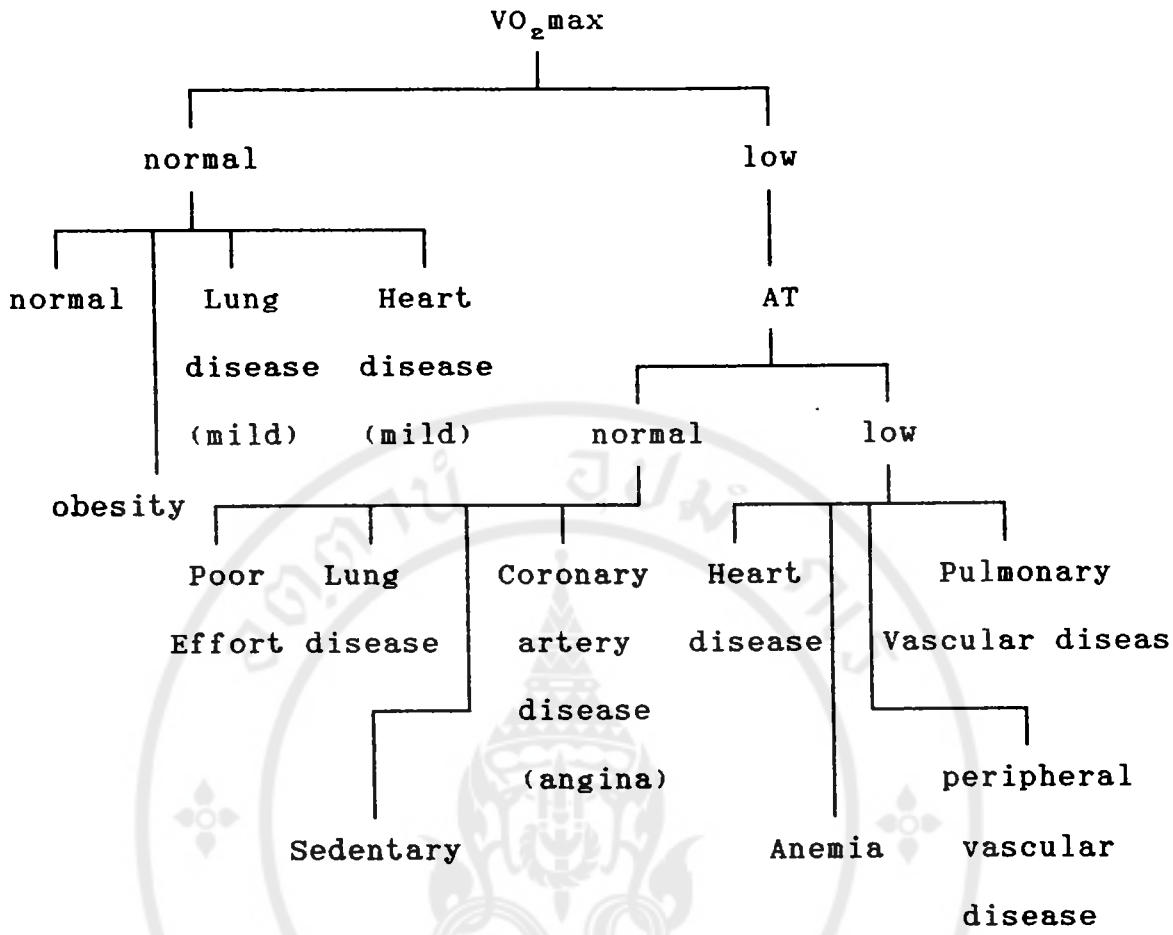


Figure 6. Use of the AT for decision making in the differential diagnosis of exertional dyspnea (From Wasserman, 1984).

combination of reduced VO_2max and normal AT generally signifies either that the patient is limited by lung disease or is not willing to put forth the effort needed to achieve a normal VO_2max (Figure 6).

Thus the AT is an aid in the differential diagnosis of disorders of cardiorespiratory coupling to cellular respiration. Combined with other measurements, the pathophysiology of exercise limitation can be further subclassified. The AT can also be used for evaluating therapy because it is sensitively affected by changes in O_2

flow to the tissues. It is relatively independent of effort, in contrast to VO_2max [105].

IV SPORTS ANEMIA

It is already known that at sea level anemia causes both VO_2max and physical work capacity to decrease [38,39,56,57] even when there is only as little as one to two gram percent decrease in hemoglobin concentration [40]. The greater severity of anemia , the greater decrease in work capacity. Post exercise lactate concentration also appears to be higher in anemic group, eventhough they work shorter and with lower work rate [57]. On the other hand, it has been reported that transfusion of packed red cells which leads to increased hematocrit and blood hemoglobin concentration resulted in enhanced VO_2max [7,35]. Since physical training can actually enhance VO_2max, logically, it might be inferred that the physical training coupled with the increase in physical fitness should bring about an elevation of oxygen carrying capacity of blood by raising the values of hematological indices such as erythrocytes count, hematocrit and hemoglobin concentration. However there are many reports showed that elite sportsmen, especially in endurance disciplines, demonstrate decreases in these three hematological indices even at rest [21,22,53]. Interestingly anemia was observed in top athlete of both sexes, including those participating in the Olympic games. Anemia also occured after prolonged intense physical effort [14,15]. These phynomenon has been referred to as "sports

anemia", "athletes' anemia", "post exercise or post effort anemia" [13,14,58,59-62]. These terms are used to denote the anemia occurring in relation to intensified physical training [15].

A definitive criterion for hemoglobin concentration that has been used in diagnosing sports anemia was set in 1983 by Pate as shown in table 1 [163]

Table 1. Suggested criteria for sports anemia and suboptimal hemoglobin concentration.

	Sports anemia	Suboptimal [Hb]
Men	<14 gm/100 ml	<16 gm/100 ml
Wemen	<12 gm/100 ml	<14 gm/100 ml

- sports anemia will be used in the traditional clinical sense to designate a subnormal hemoglobin concentration in an athlete or physically active persons.

- Suboptimal hemoglobin will designate a hemoblobin concentration that is lower than could be considered optimal for oxygen transport purposes and will be defined as a hemoglobin concentration below the mean for the normal population.

IV.1 Morphological Features of Erythocytes in Sports Anemia:

Generally, sports anemia has been observed in athletes ranging from previously sedentary individuals beginning a running programe (16), to fit individuals

performing daily submaximal exercise [61], and to individuals participating in prolonged severe exercise [62] and strenous endurance training [131]. Besides the lower hematocrit, hemoglobin concentration and erythrocyte count, development of sports anemia can also be determined by the morphological alterations of erythrocytes such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). However the reports pertaining to these indices are contradictory. For instant, Rodemski et al [57] found that, development of sports anemia in physically fit men after daily sustained submaximal exercise, had a hematological pattern, characteristic of hypochromic macrocytosis (MCH and MCHC decrease but MCV increase). They suggested that this pattern possibly reflects a promote release of young RBC from the bone marrow. Another explanation for this is that, after exercise the intracellular water content increased which in turn leads to increase in water content in erythrocyte reflected by decrease values of MCHC, mean cell density of erythrocytes (MCD) and by increase of MCV [64,65]. Anyway in the study of Hiramatsu et al [111] they reported that sports anemia is normocytic and normochromic that is caused by destruction of erythrocytes in the initial stage of physical training that involves hard muscle work.

More recently, iron deficiency has been considered as the most frequent cause of anemia in sportsmen [66] as reported by several exhaustive studies [38,56,67]. If the

hemoglobin level suggests the presence of a true anemia, the physician should look at the MCV, because the two most common contributors to true anemia in athletes-iron deficiency and footstrike hemolysis are characterized by red cells that are too small and too large, respectively. For example, if the hemoglobin level is 10 to 11 gm/100 ml and the MCV is 85 fl or below,iron deficiency anemia is probably the correct diagnosis. If the MCV is 95 fl or more (runner's macrocytosis),it's probably footstrike hemolysis[66].

IV.2 Combined Factors Causing Sports Anemia :

Sports anemia usually occurs as a combined effect of several factors acting together and the sum of each these effects which, when considered seperately may not be deemed important at all. The combined causes of sports anemia are following :

a) Post-training blood plasma expansion

It is well documented that endurance training is accompanied by increases in plasma volume and total blood hemoglobin [16,17,19,20]. But an increase in plasma volume is not matched by a proportional elevation of the red blood cell mass or total hemoglobin [16,18]. So it is not unusual for well-trained endurance athletes to have a lower hemoglobin concentration than nonathletes [56,66]. Cirtainly, an increase in total blood volume may increase stroke volume and maximal cardiac output. These increases are expected to promote blood flow and oxygen delivery to peripheral tissues during strenous exercise that in turn increase the sea level VO_2max as well [63].

b) Disturbances in erythropoiesis

Hallberg and Magnusson [68] suggested that because of adaptive changes caused by training, such an an increase in concentration of 2,3-DPG that shift the hemoglobin-oxygen dissociation curve to the right. This shifts leads to an increased delivery of oxygen to all tissues, including sensory cells of the kidney responsible for erythropoietin synthesis. Thus the increased level of 2,3-DPG would be associated with a reduction in the production of erythropoietin and there by induce a lower hemoglobin concentration and hematocrit in the peripheral blood.

Moreover the reduction of serum testosterone caused by repeated competition also leads to the disturbances in erythropoiesis[68] since it is known that serum testosterone plays a significant role in erythropoiesis at various levels of its regulation.

Another one factor that can disturb the erythropoiesis system of athletes is a reduction in the number of T_4 (helper) lymphocytes and the helper to cytotoxic suppressor (T_8) ratio in the peripheral blood after intense physical endurance efforts [68,70]. The T_4 lymphocytes play an important role in stimulating the early stages of erythropoiesis [71].

c) Iron deficiency

In the recent years several reports showed that iron deficiency is the most frequent cause of anemia in sportsmen [66,67]. The diagnostic triad is microcytosis

(MCV = 85 fl) [66], a subnormal hemoglobin concentration (lower than 14 g/dl in male and less than 12 g/dl in femele) [63], and a subnormal serum ferritin concentration (less than 12 ug/l) [66,67].

In sportsmen, iron deficiency may arise from many causes including :

1 Insufficient iron supplement in diet [56,72] especially on a strict vegetarian diet where all iron comes from nonheme groups which are difficult to absorb [73,74].

2 Reduced iron absorption from the digestive tract [56,67,72,75]. Ehn et al. found that in eight distance runners, absorption in iron in the inorganic,ferrous state was particulary depressed[76].

3 Increased demand for iron particulary in young athletes, in those just begin intense physical training periods [14,59,60,73], and in menstruating women [56,72]. Such an increased demand is connected with intensified synthesis of myoglobin and iron-containing enzymes.

4 High rates of iron loss. There are many reports show that increased loss of iron from athlete's body may result from bleeding into the digestive tract [56,67,72,77-79]. Accelerated iron loss by sweating has also been suggested. For instance, Ehn and his coworkers [76] suggested that loss of iron through heavy sweating could have been a factor for the much lower of iron hal-life in male runners than in male controls. Other factors considered to associate with the increment of iron loss in athlets are hemoglobinuria, myoglobinuria and hematuria[56,67,76,79-83].

d) Intensified hemolysis during physical effort

The appearance of hemoglobinuria have been found in both following prolonged running or marching on firm surfaces and on soft surfaces [80,84-86]. Increased hemolysis was also found in other exercise disciplines such as weight lifting [87], swimming [88], and rowing [89] where there is no traumatization of soles. Hence it seems that stressing mechanical damage to erythrocytes is not the only cause of exercise-related hemolysis but there are some other factors emerging during intense physical activity can also adversely affect red blood cells. Factors enhancing hemolysis during physical exercise are :

1 Age of erythrocytes : Aging of red blood cells causes decreases in enzymatic and metabolic activity, and changes in blood cell membranes [90,91]. These changes lead to fragmentation of cell membranes and increased hemolysis of older erythrocytes resulting from intense physical exercise [14,40,82,84,87,92-94].

2 Changes in erythrocyte shape : Changes in shape and morphology of red blood cell were observed after a 100 km run and a marathon [95-98]. These changes decrease the erythrocytes' filterability and deformability which may increase hemolysis of such altered red blood cells.

3 Mechanical trauma : Mechanical damage to erythrocytes may occur as a result of accelerating blood circulation [51] or compression of the erythrocytes in microcirculation during rapid contraction of large muscle groups [88,70,97]. The extent of the hemolysis is related

to the race distance [๘๐].

4 Dehydration and hemoconcentration : The results of post exercise such as dehydration, hemoconcentration, increase in blood viscosity and blood plasma, increase in the osmolarity of blood plasma, increase in the intraerythrocytic osmolarity, and acute postexercise acidosis can accelerate hemolysis of older erythrocytes [๕๖.๕๙.๘๘ - ๙๒.๙๔].

5 Elevation of body temperature : The elevated body temperature during exercise may also promote hemolysis of erythrocytes by lowering their osmotic and mechanical resistance [๕๖.๕๙.๙๔.๙๘].

6 Catecholamines and lysolecithin : The increase in the catecholamines levels under exercise stress increases osmotic and mechanical susceptibility of erythrocytes so the erythrocytes can break down more easily [๕๖.๑๔.๕๙.๖๒.๙๔.๙๙.๑๐๐]. There is also a hemolytic agent, lysolecithin , possibly released into blood circulation during exercise by spleenic contraction under the action of catecholamines [๑๔.๘๐].

7 Hypoglycaemia : The decrease in glucose concentration in blood during exhaustive exercise can affect the osmotic resistance of erythrocytes and thus facilitate hemolysis [๙๒].

8 Peroxidation of the erythrocyte membrane: Exercise, particulary exhaustive maximal exercise, induces the production of free radicals in large quantities [๖๒.๖๓.๑๐๑.๑๐๒]. These oxidants induce the changes in red blood cell membranes which may result in increased red

blood cell hemolysis [90,101-103].

e) Loss of erythrocytes by bleeding into the digestive and urinary systems :

Endurance running has been shown to cause gastrointestinal blood loss [94,95]. Possible causes of this blood loss included local lesions such as hemorrhoids, damage of the intraabdominal hollow organ due to repetitive impacts of a free surface against a fixed surface ,and gut ischemia due to diversion of the splanchnic circulation [104]. In a study of physically active serviceman found that profuse hematuria could occur occasionally in long distance runners from lession in the bladder due to trauma [133]. The mechanism of injury was described as repetitive impacts of the posterior bladder wall against the bladder base during each stride [133]. Even though hematuria in contact sports may be due to direct renal trauma, noncontact sports such as swimming, crew, and track were also demonstrated hematuria [134]. The possible mechanisms for hematuria in nontraumatic to the kidney are :

1) there is so much vasoconstriction of the renal blood vessels during severe exercise that may result in renal ischemia which causes hypoxic renal damage [134].

2) vasoconstriction of the renal blood vessels may result in an increased filtration pressure and stasis in the glomerular capillaries that leads to an increased filtration of protein and red blood cells through the glomerular membrane [132].

CHAPTER III

OBJECTIVE

The aim of this study was to investigate the effect of acute hypoxic exposure on maximal aerobic power (VO_2max) and anaerobic threshold (AT) and their related parameters in sports anemic athletes.

CHAPTER IV

Materials and Methods

1. Subject

All subjects were volunteer male athletes of the Royal Thai Air Force (R.T.A.F.). Screening tests were performed to identify those who exhibits either normal or under normal blood hemoglobin level by the table of sports anemia's criteria [63]. According to this table anemia was defined as an athlete or a physically active person who had blood hemoglobin less than 14 g %. Based on such definition (or criteria) the subjects could be divided into two groups, control and anemia. Attempt was made to select subjects who were physically active and had no history of any diseases, except anemia, that might limit maximum exercise performance. Attempt was also made to match the two subject groups for their average level of maximum aerobic power. No attempt was made to select subjects through physical education and sports programs.

Eleven subjects , with age range 21-29 yr, were selected to participate in this study. There were four volleyball players, four runners, two cyclists, and one triathlete participated. Five of the eleven who exhibited blood hemoglobin concentration of less than 14 g % were in the anemic group. The subjects of the control group were within the normal range for hematological indices. None of the subjects took medication at the time of the study, non

were they prolongly exposed to hypoxic air. The physiological and physical fitness characteristics of the two subject groups are shown in table 2. Prior to this study all subjects had trained for at least 1 year at the RTAF Sports Association, Bangkok. From subjects' interview, training had been performed for 3-5 hour/day, 5 days/week. Informed consent was obtained from each subject before participation in this study.

2. Equipments:

The following equipments were use to measure VO_2max , percent body fat , and blood lactate concentration.

2.1 Analysis of VO_2max and percent body fat

- Bicycle ergometer (Monark 818, Sweden)
- Polygraph (Grass Model 7, U.S.A.)
- Three-way value and mouthpiece (Collins, U.S.A.)
- Timer (Hanhart-timer, Germany)
- Pneumotachograph ((i/a) 7320, #2) and pressure transducer, Grass, U.S.A.)
- 12% O_2 standard calibration gas (Corning U.S.A.) and gas regulator (Scott model 2, U.S.A.)
- Gas mixture (14.5% O_2, balanced N_2) prepared by Thai Industrial Gas, CO.
- Expired gas mixing chamber 13.0 l
- Heart rate meter (Sport tester PE 3000, Polar electro, Finland)
- Oximeter (S-100, Simed U.S.A.) and finger probe (Simed U.S.A.)
- Weight balance with height measuring meter

(Detecto, Japan)

- Thermometer for measurement of oral temperature (SK normal glass, Safte, Japan)
- Sphygmomanometer (AIL-KIT, Japan)
- Stethoscope (3M, Germany)
- Skinfold calipers (Lange, C.S.I., U.S.A.)
- Wet and dry bulb thermometer (Japan)
- Gasometer 120 l (Warren e. collins incorporated, U.S.A.)

2.2 Blood lactate determination

- Stapple with lancet (Autoclix, Bachringer Mannheim Gmbh, W-Germany)
- Haparinized capillary tube (Vitrex, Modulohm I/S, Denmark)
- Lactate analyzer (madel 23L, YSI Inc., U.S.A.)

3. Environmental Conditions

This study both normoxic and hypoxic condition were conducted in a temperatured-control room at Sports Science Center, Bangkok. The former condition was induced by room air inspiration while the latter was induced by inspiration of 14.5% oxygen in nitrogen. The reduction between the two conditions was three to four hours apart. The average values of barometric pressure ,relative humidity , and ambient temperature in the morning and in the afternoon were 749.7 + 1.1 mmHg, 52 + 0.5%, 23.2+0.4 ˚C, and 748.8 + 1.4 mmHg, 51.8 + 0.4%,23.6 + 0.5'C,respectively.

4. General Procedure:

4.1 Screening method

Prior to their participation, each subject was screened by screeing procedures included medical history and physical examination. Exclusion from participation was indicated when any condition or illness that contraindicated performance of heavy exercise was observed.

One day before participation in this experiment, all subjects were told to have a night sleep at least 6 to 8 hours. Questionaires about daily physical activity pattern and the former highest competitive match were filled up prior to an exercising protocol. Oral temperature and heart rate were measured at rest with oral thermometer and heart rate monitoring (sport tester), respectively. The blood of 2.5 ml was collected at anticubital vein of the arm for measuring hematocrit, hemoglobin concentration, and erythrocytes count.

4.2 Anthropometric studies.

Body weight and height were measured with a mobile balance (Detecto, Japan). The body weight was measured with subject wearing minimal clothing and recorded to the nearest tenth of a kilogram. The height was measured to the nearest millimeter.

The percentage of body fat (% Body fat) and lean body mass were determined by using skinfold calipers to measure the skinfold thickness at 4 sites of the body : biceps, triceps, subscapular, and suprailiac [138]. The details of selected sites were as follows :

- Biceps : over the mid-point of the muscle belley with the arm hanging vertically and relax.

- Triceps: over the mid-point of the muscle belley, midway between the olecranon and the tip of the acromion, with the upper arm hanging vertically and loosely.
- Subscapular : just below the tip of the inferior angle of the scapular at the ankle of about 45 degree to the vertical.
- suprailiac : just above the iliac crest in the mid axillary line.

Calculations of body fat were based on the equation given by Lawrence et al.[139]:

Body fat (%) = [(4.95/body density) - 4.5)] x 100

Equations for the prediction of body density were calculated from :

body density = 1.1631 - 0.0632 log x (>20 yrs man)

= 1.1631 - 0.0630 log x (<20 yrs man)

Where x = the sum of skinfold thickness at all four sites. The lean bodymass (LBM) was calculated from the following equation :

LBM = Body weight [1-(% body fat/100)]

4.3 Continuous multistage progressive non-steady state exericse test.

4.3.1 Analysis of ventilatory gas

The subject was seated on a bicycle ergometer (Monark 818,Sweden)of which the saddle height was adjusted appropriately and breath through a three-way value assembly connected to the gasometer (Warren e. collins incorporated, U.S.A.) that supplied inspired gas. After 20-minute breath of inspired gas mixture at rest on a bicycle ergometer

(Monark 818, Sweden), the subject started pedalling the ergometer at 60 revolutions per minute (rpm) with no resistance for 4 minutes as a warm up peroid. Thereafter, the resistance was increased by 20 watts every minute until volitional exhaustion and/or the subject was unable to continue pedalling at the prescribed rate. During the test, for each minute change in work load, the time marker was activated and its signal was marked on the chart paper.

During the exercise test, respiratory gases, heart rate, and arterial oxygen saturation were continuously monitored.

4.3.2 Manipulation of inspired air

In normoxic condition room air was standed for inspired gas while in the hypoxic condition the inspired gas came from gas mixture which composed of 14.5% oxygen and balance nitrogen (approximately equivalent to an altitude of 10,000 feet ; see Appendix I for calculation of gas mixture).

The normoxic gas (room air) or the prepared hypoxic gas was filled in the 120 l gas meter (Warren e. collins incorporated, U.S.A.), saturated with water vapor, and inspired by subject via a connecting tubing and the three-way value. The rate of inflow of the gas to the gas meter was manually adjusted so that the outflow of the gas meter was continuous and adequate for ventilation both at rest and during incremental exercise.

4.3.3 Heart rate monitoring

Sport tester, PE 3000, heart rate meter which

consits of receiver, electrode belt and transmitter was used to monitor the subject's heart rate. Before having the subject monitored on the bicycle ergometer, we buckled the electrode belt around the subject's chest in the position that the transmitter was symmetrically attached with respect to the chest. Selected the time and pulse mode on the receiver and when the heart symbol appeared on the lower left of the display, the heart rate was determined and shown digitally on the display.

4.3.4 Arterial oxygen saturation measurement

In this study, noninvasive technique for determination of arterial oxygen saturation (SaO_2) was performed with the use of oxemeter (finger probe type,S-100, Simed corporation, U.S.A.). During sitting on the bicycle ergometer, the subject's right or left index finger was put firmly on the finger probe. Percent SaO_2 as well as the subject's heart rate were continuously displyed both at rest and during incremental exercise. The values at the end of each minute were recorded.

4.3.5 Measurement and analysis of expired air

A pneumotachtograph was connected to the expiratory side of the three-way value. Two air outlets of the pneumotachtograph (Fleisch i/a 7320 (#2), Instrumentation Associates Inc., U.S.A.) were connected to two arms of differential pressure transducer (PT 5 A, Grass Instrument Inc., U.S.A.). Signal from the pressure transducer was amplified with low-level DC preamplifier (7P1E, Grass Instrument Inc, U.S.A.) which was further

amplified by drover amplifier (7DAC, Grass Instrument Inc., U.S.A.). The amplified signal was then connected to integrator (7P10A, Grass Instrument Inc., U.S.A.). Both output from the low-level DC channel and the integrator output were recorded on chart paper. The former output represented the expired flow rate while the latter represented the expired volume of each breath. When there was no expired air flowing through pneumotachtograph between the end of each expiration phase and the end of its consecutive inspiration phase the signal from the integrator was automatically adjusted to zero. With expiration the integrator signal increased, reaching its maximum at the end of expiration, after which it automatically adjusted back to zero. The beginning of inspiration up to the beginning of next inspiration was the criteria for "one breath".

For analysis of gas composition of inspired and expired air, small lumen sampling lines from oxygen analyzer (OM-11, Beckman Instruments Inc.,U.S.A.) and carbon dioxide analyzer(LB-2,Beckman Instruments Inc.,U.S.A.) were inserted to the gas mixing chamber.The gas analyzer outputs were sent to multi-channel polygraph(7DAC,Grass Instruments Inc;U.S.A.) and then oxygen and carbon dioxide composition of expired air was recorded on chart paper. Paper speed was set through the exercise test at 2.5 mm/sec. Sampling flow rate for oxygen and carbon dioxide analyzer were set at 500 ml/min.

Schematic and picture of experimental set up are shown in Fig.7-9.

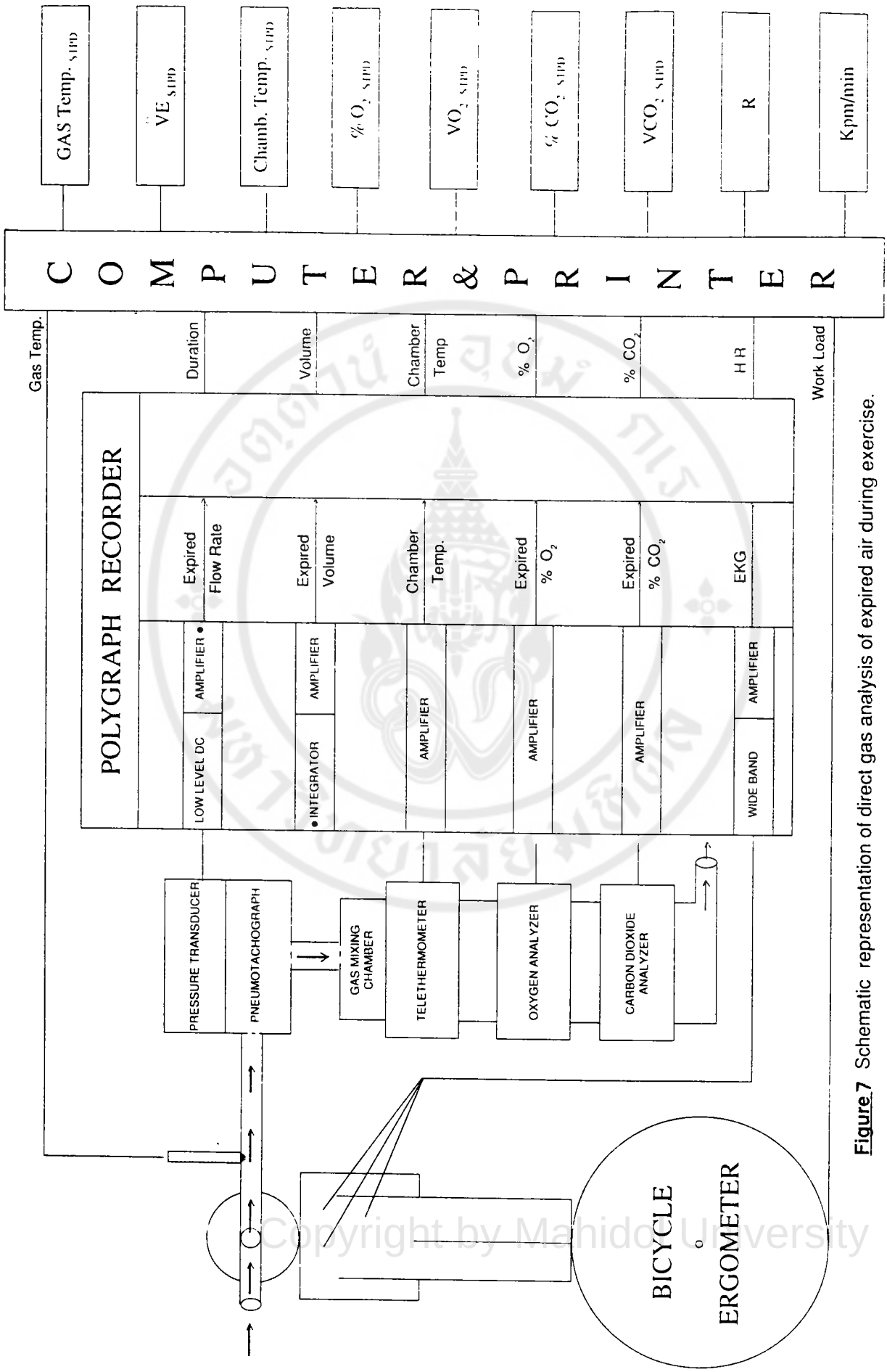


Figure 7 Schematic representation of direct gas analysis of expired air during exercise.

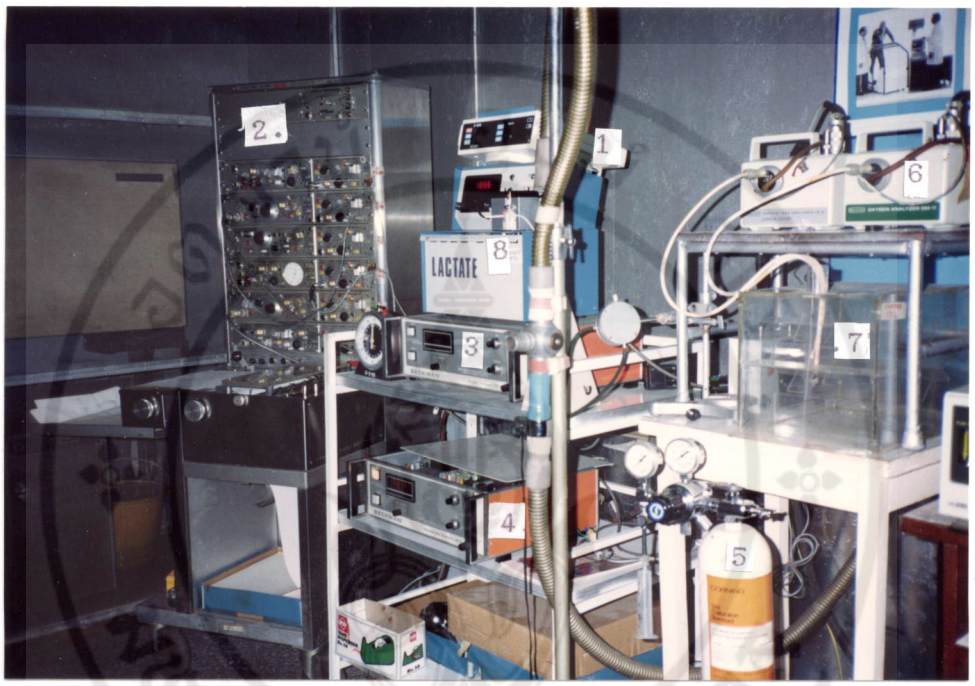


Fig 8. Experimental set up for continuous multistate non-steady state exercise test.

1. Oximeter
2. Grass model 7 polygraph
3. Oxygen analyzer
4. Carbon dioxide analyzer
5. Standard calibration gas
6. Pneumotachograph
7. Expired gas mixing chamber
8. Lactate analyzer

Fig 8-1. The other equipments for progressive exercise test.

1. Gasometer 120 l
2. Inspired gas mixture's tank (14.5% O_2 balance N_2)
3. Bicycle ergometer

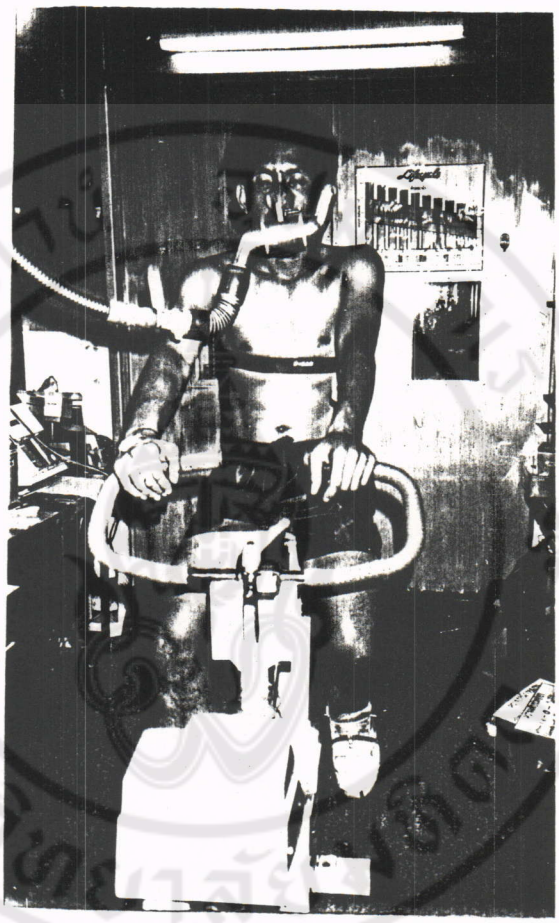


Fig 9. Resting position of the subject on bicycle ergometer just before the beginning of continuous multistate progressive non-steady state exercise test.

4.3.6 Data storage and calculation of ventilation

Minute by minute values of work rate, heart rate, and arteral oxygen saturation were transferred to computer system. Inspired and expired air oxygen and carbon dioxide content, volume of expired air and duration of each breath were also transferred to computer. A special Lotus-based spread sheet was developed for storage and calculation of VO_2, VCO_2, V_E and other variables for the determination of anaerobic threshold and VO_2max. These variables were plotted against the same time scale and graphic output were generated.

4.3.7 VO_2 max determination

Since it is known that oxygen uptake increases linearly with increasing work rate up to the maximal rate of oxygen uptake, a plateau of oxygen uptake with an increasing work rate is a criteria that the subject has achieved his maximum [28]. However, in and absence of VO_2 plateau, the other criteria of a good maximum effort include [26] :

1. heart rate close to (220-age) + 10 [23]
2. respiratory gas exchange ratio (R) of 1.15 or more
3. a high blood lactate level (11-16 mmol/l)
4. an increase in VO_2 with a further step increase of work load not more than 150 ml [10].

The subject was well motivated during the test expecially one to two minutes before exhaustion.

4.3.8 Anaerobic threshold determination

The ventilatory anaerobic thushold (AT) could

be identified by the point of :

1. An increase in end-tidal O_2 without a corresponding decrease in end-tidal CO_2 (Fig.5.) [105]
2. A decrease or remain unchanged of ventilatory equivalent for O_2 (V_E/VO_2) starts to increase without and increase in V_E/VCO_2 [105]
3. Departures in the linearity of ventilation (V_E) and carbon dioxide output (VCO_2) plus and abrupt increase in the gas exchange ratio (R) [106,107].

4.3.9 Hematological determination

The levels of hematocrit , hemoglobin concentration, erythrocyte count and red cell morphology of each subject were determined before performing the exercise test. These parameters were determined by the hematological laboratory staffs at Bhumibol Adulyadej Hospital, Directorate of Medical Survices, Royal Thai Air Force.

Then mean corpuscular volume (MCV),mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were calculated from the known parameters mentioned above by the following equations [106]:

$$MCV(fl) = \frac{\text{Hematocrit (\%) x 10}}{\text{erythrocyte count (million/cu mm)}}$$

$$MCH(pg) = \frac{\text{Hemoglobin concentration (g\%) x 10}}{\text{erythrocyte count (million/cu mm)}}$$

$$MCHC(\%) = \frac{\text{Hemoglobin concentration (g\%) x 100}}{\text{Hematocrit (\%)}}$$

4.3.10 Blood lactate determination

Blood samples of approximately 25 microliter each were collected from finger tip into haparinized microcapillary tubes at rest and at 1 and 3 minute after the end of exercise. The samples were then analyzed for blood lactate concentration by the YSI 23L lactate analyzer (see Appendix II).

5. Experimental Protocol

Each subject was informed of the perposes, experimental protocol,and procedures of the experiment,as well as risk from participation,and then signed a statement of informed consent.

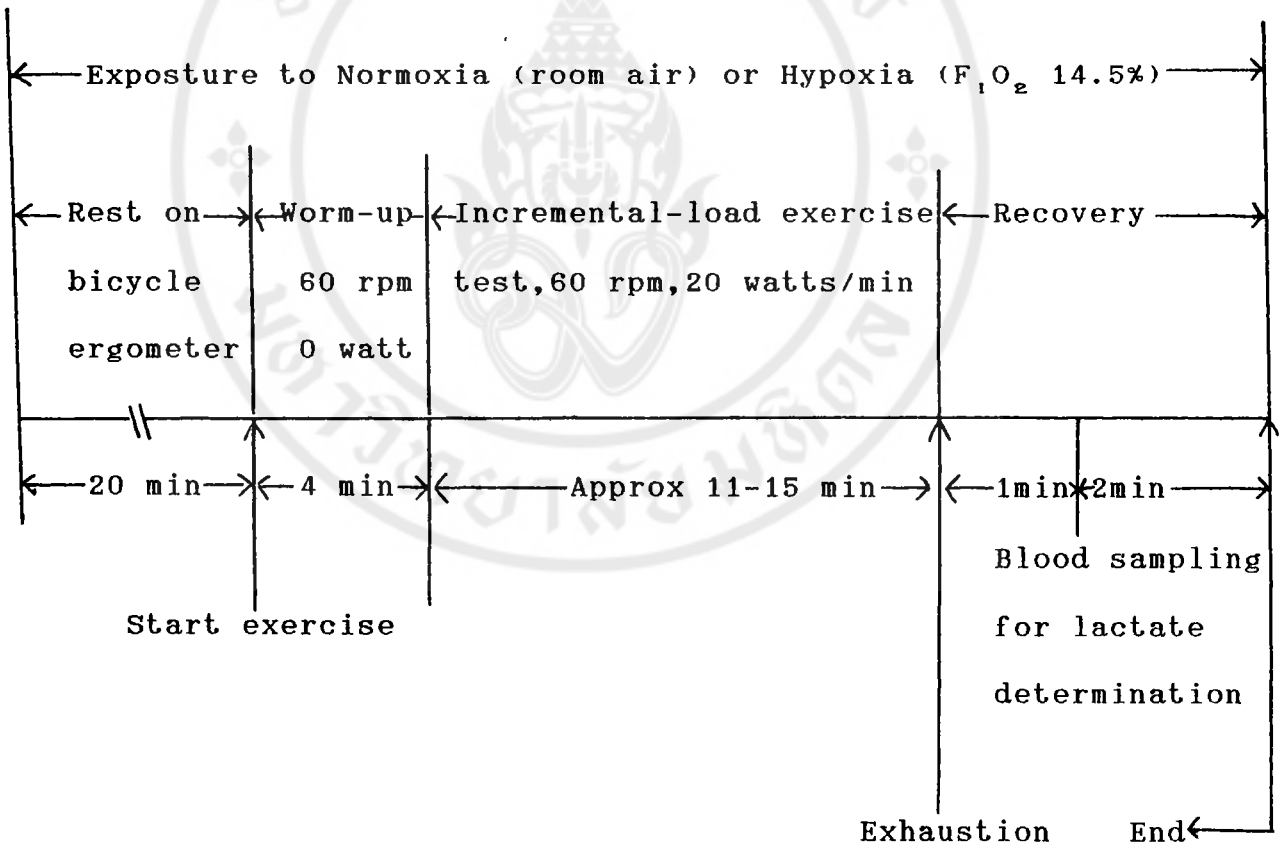
The subjects were divided into two groups based on their Hb concentration, namely control and anemia. The level of Hb concentration of 14 g/dl was used as a criterion for the justment of anemia[83].

The experimental design was managed so that the average VO_2max of the control and the anemic groups of subjects were comparable. The physiological characteristics of the two subject groups were presented in Table 3.

Two exercise tests under the normoxic and hypoxic exposures were conducted on the same day about three to four hours apart in randomized order.The reason for this is that since the presence of sports anemia may be transient which could be disappeared after a peroid of less than one week[42,81],so to keep the hematological indices of each subject the same at both normoxia and hypoxia the two exercise tests were performed on the same day.

To avoid the effect of diurnal variation and the ordering effect on the VO_2max testing , randomized normoxic and hypoxic exposures were performed.Similar to the present study , two exhaustive exercise tests on the same day have been performed previously by other investigations and no effect of such the tests on work performance have been reported[140,172].

Exercise Testing Protocol



6. Data Analysis

Student's paired t-test was used to examine the effect of hypoxia on work performance and all physiological paramenters measured in each group of subject.

An unpaired t-test was used to test for

statistical significant differences in all measured variables between the control and the sports anemic groups.

Correlation and simple linear regression were also employed to see whether any intercorrelations existed among the measured parameters in question.

The level of statistical significance was considered at the probability (p-value) of 0.05. Results are reported as means $\pm$ SEM.

CHAPTER V

RESULTS

1 Physical and Hematological Characteristics.

The physical and hematolocical characteristics of the control and the anemic groups are presented in table 3. Both had statistically the same physical fitness level at normoxic condition , but had significant differences in all hematological paramiters except the mean corpuscular hemoglobin concentration (MCHC) which was statistically the same in control and anemia.

Table 2. Physical and hematological characteristics of overall subjects.

Parameter	Control	Anemia
Age(year)	23.0 ± 1.2	14.7 ± 1.8
Height(cm)	171.75± 2.82	171.30± 4.52
Weight(kg)	61.18± 4.96	62.72± 3.45
% Body fat	12.37± 0.40	13.22± 0.53
Fat free mass(kg)	53.67± 4.49	54.44± 2.80
RHR(beats/min)	57.3 ± 1.3	56.6 ± 1.8
VO_2 at rest(ml/kg/min)	5.33± 0.38	6.10± 0.59
Hb(g/dl)	14.62± 0.14	12.86± 0.24
Hct(%)	42.23± 0.71	37.66± 0.86^{+++}
RBC($x10^6$)	4.77± 0.08	5.20± 0.24^{+}
MCV(fl)	88.61± 0 55	72.94± 3.62^{+++}
MCH(pg)	30.72± 0.5	24.92± 0.94^{+++}
MCHC(g/dl)	34.65± 0.59	34.21± 0.41

Values are means ± SEM.

Significantly different from control; $^{+}p<0.05$, $^{+++}p<0.001$.

2 Maximum Oxygen Uptake ($VO_{2\ max}$)

In Fig 10 ,the absolute decrement in VO_2max at hypoxia is plotted as a function of the normoxic VO_2max. The linear regression equation of the control subjects was Y = 0.24X - 6.8,where Y is the absolute decrement of VO_2max, X is the normoxic VO_2max. The correlation coefficient (r) between these two variables was 0.81($p<0.05$) ,indicating that regression of ΔVO_2max on normoxic VO_2max was significantly correlated. There was also a linear correlation between VO_2max and ΔVO_2max for the anemic subjects: Y = 0.68X - 26.15, r=0.88 ($p<0.05$).

In Fig 11 ,the hypoxic VO_2max was plotted against the normoxic VO_2max showing the distribution of hypoxic VO_2max under the influence of normoxic VO_2max and hemoglobin concentration. The hypoxic VO_2max of every tested subject was lower than the normoxic VO_2max. Moreover,when the control and anemic groups were considered seperately ,the rate of hypoxic VO_2max over normoxic VO_2max was lower in the later group.

When ΔVO_2max , was expressed as either ml/kg/min or a percentage of normoxic VO_2max , was plotted against hemoglobin concentration negative correlation was found in both cases but only the later case showed significant correlation (Fig 12a and b).

Fig 13 the distribution of SaO_2 in relation to hemoglobin concentration at rest and at VO_2max at both normoxia and hypoxia. Only significant correlation

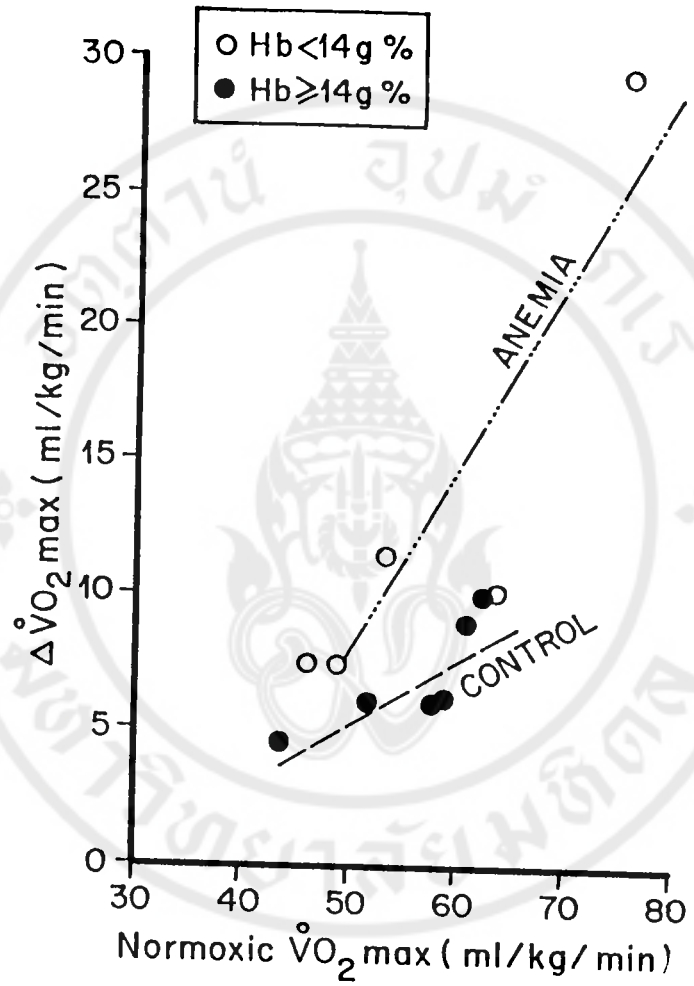


Fig 10. The absolute decrement in VO_2max at hypoxia(ΔVO_2max) plotted as a function of normoxic VO_2max in control and anemic subjects :

-----The regression line is Y = 0.2X - 6.8 ; r=0.81($p<0.05$).

-.-.- The regression line is Y = 0.7X - 26.6; r=0.88($p<0.05$).

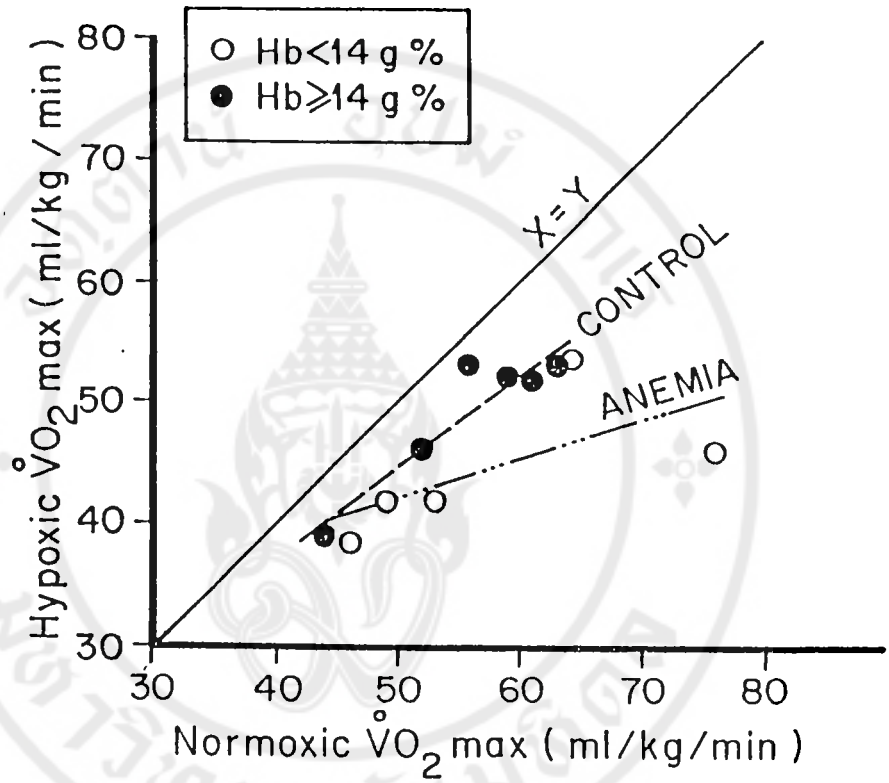


Fig 11. The hypoxic VO_2max plotted as a function of normoxic VO_2max.

_____ denotes the line where the value of hypoxic VO_2max is equal to normoxic VO_2max

----- the regression line is Y = 6.8 + 0.8X ; r=0.97

_._._ the regression line is Y = 26.2 + 0.3X; r=0.66.

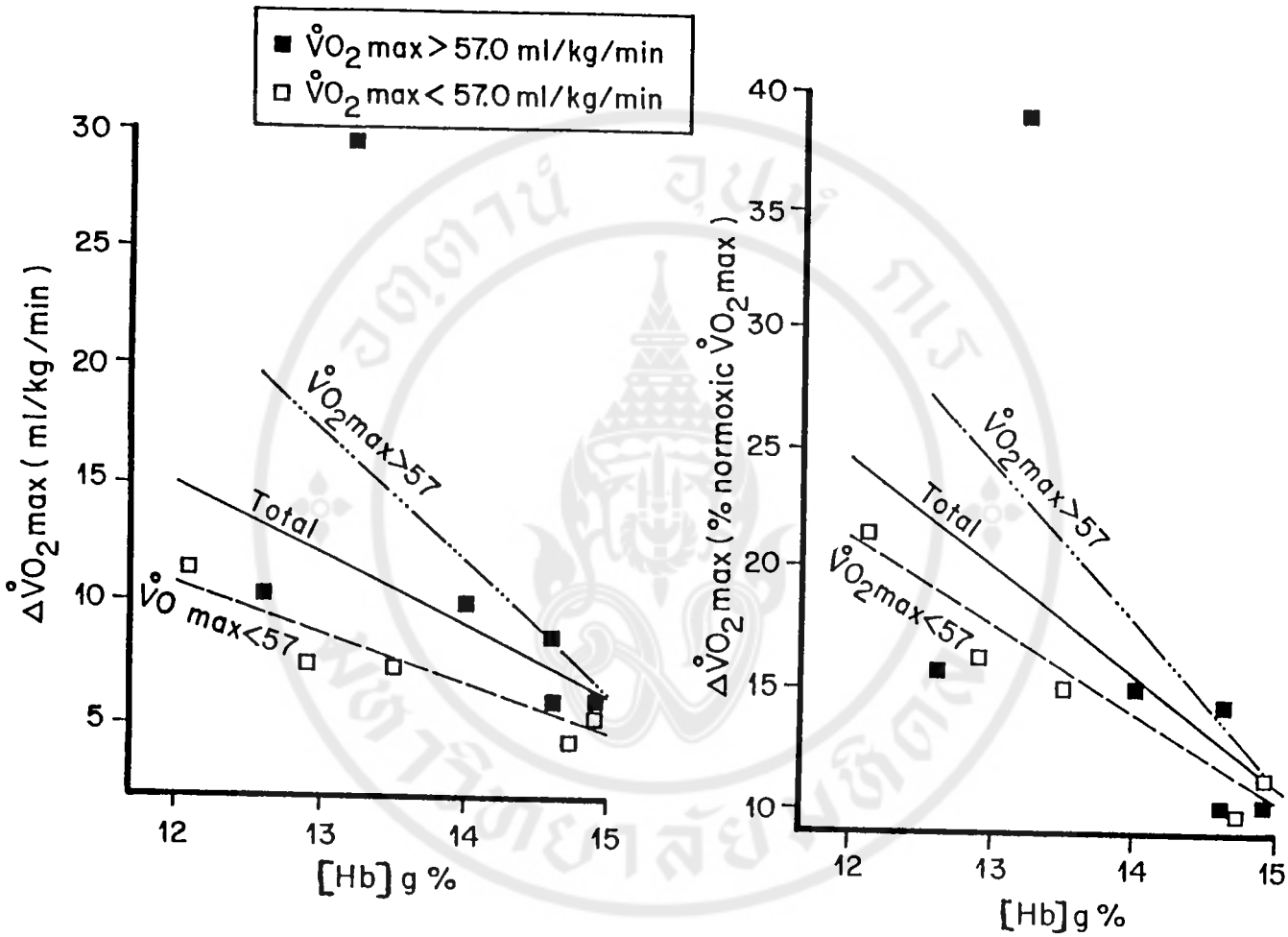


Fig 12. (a) The absolute value of Δ VO_2max is plotted against hemoglobin concentration, (b) The ΔVO_2max expressed as a percent chage from normoxic VO_2max is plotted against hemoglobin concentration.

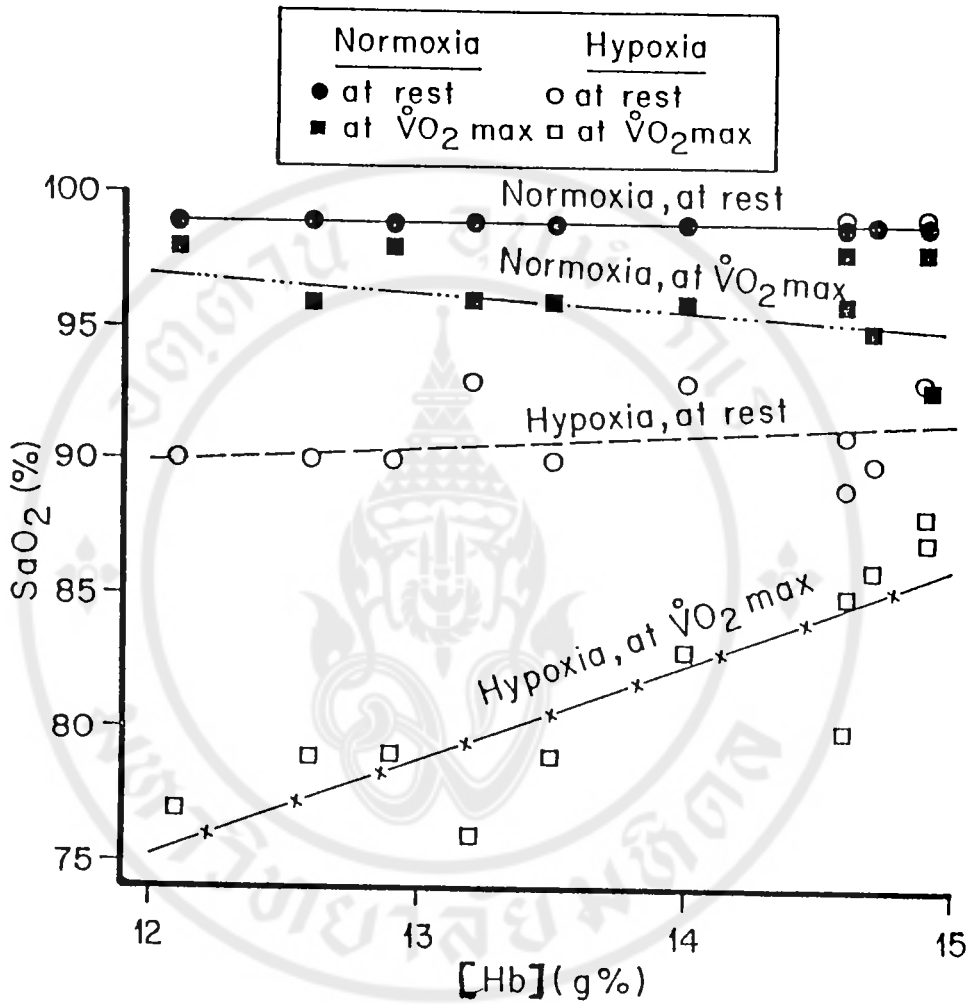


Fig 13. The individual values of arterial oxygen saturation (SaO_2) of overall subjects plotted against hemoglobin concentration.

($p<0.001$) between these two parameters was observed in subjects during exercise at the point of VO_2max under acute hypoxia. Under this condition , subjects with lower hemoglobin concentration exhibited more reduction in SaO_2.

The relationship between the reduction in SaO_2 from resting value at VO_2max (that is , SaO_2 at rest - SaO_2 at VO_2max or ΔSaO_2) and hemoglobin concentration was shown in Fig 14. Significantly negative correlation was found in hypoxic ($p<0.01$) but not in normoxic condition. It's linear regression equation was $Y = 51.7-3.1X$, where Y represented ΔSaO_2 and X represented hemoglobin concentration. The fitness of the equation was statistically significant ($p<0.01$).

When the decrement of VO_2max at hypoxia (ΔVO_2max) and hypoxic ΔSaO_2 (SaO_2 at rest - SaO_2 at VO_2max) were plotted against each other (Fig 15a,b), significantly positive correlation and regression were found in both control and anemia: $Y = 0.8X+1.5; r=0.92$ ($p<0.01$) and $Y=3.5X-30.5; r=0.97$ ($p<0.01$),respectively, where Y represented ΔVO_2max(ml/kg/min) and X represented hypoxic ΔSaO_2 (%). However,when the rate of reduction in VO_2max (ΔVO_2max) over hypoxic ΔSaO_2 was considered it showed greater in the anemic subjects. In addition, when the VO_2max was accounted at any magnitude of hypoxic ΔSaO_2 the subjects with high VO_2max of greater than 57 ml/kg/min exhibited ΔVO_2max greater than those with lower VO_2max.

Fig 16 shows the relationship between the

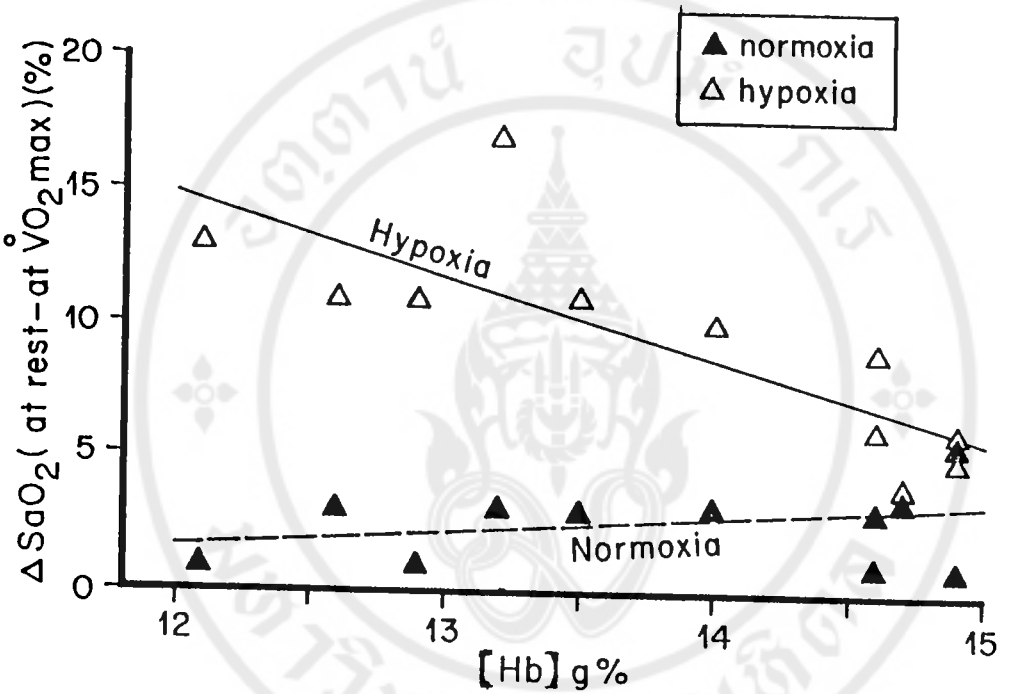


Fig 14. The reduction in SaO_2 at VO_2max (i.e. SaO_2 at rest minus SaO_2 at VO_2max; ΔSaO_2) is plotted against hemoglobin concentration of individual subjects at normoxia and hypoxia.

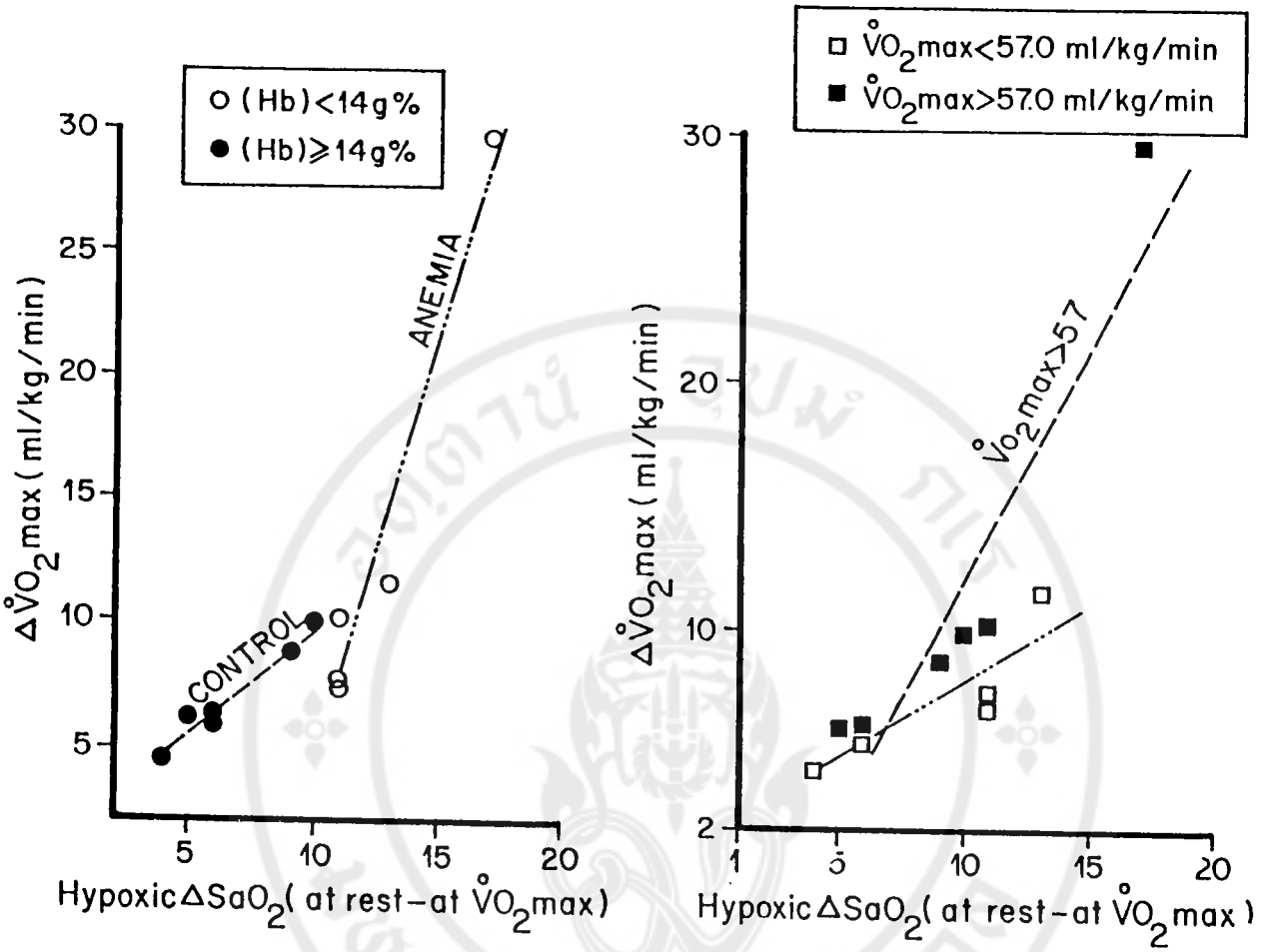


Fig 15. The reduction in VO_2max at hypoxia (Δ VO_2max) is plotted as a function of ΔSaO_2 at hypoxia in two subject groups with different a) blood hemoglobin level [Hb] and b) maximal rate of oxygen uptake (VO_2max).

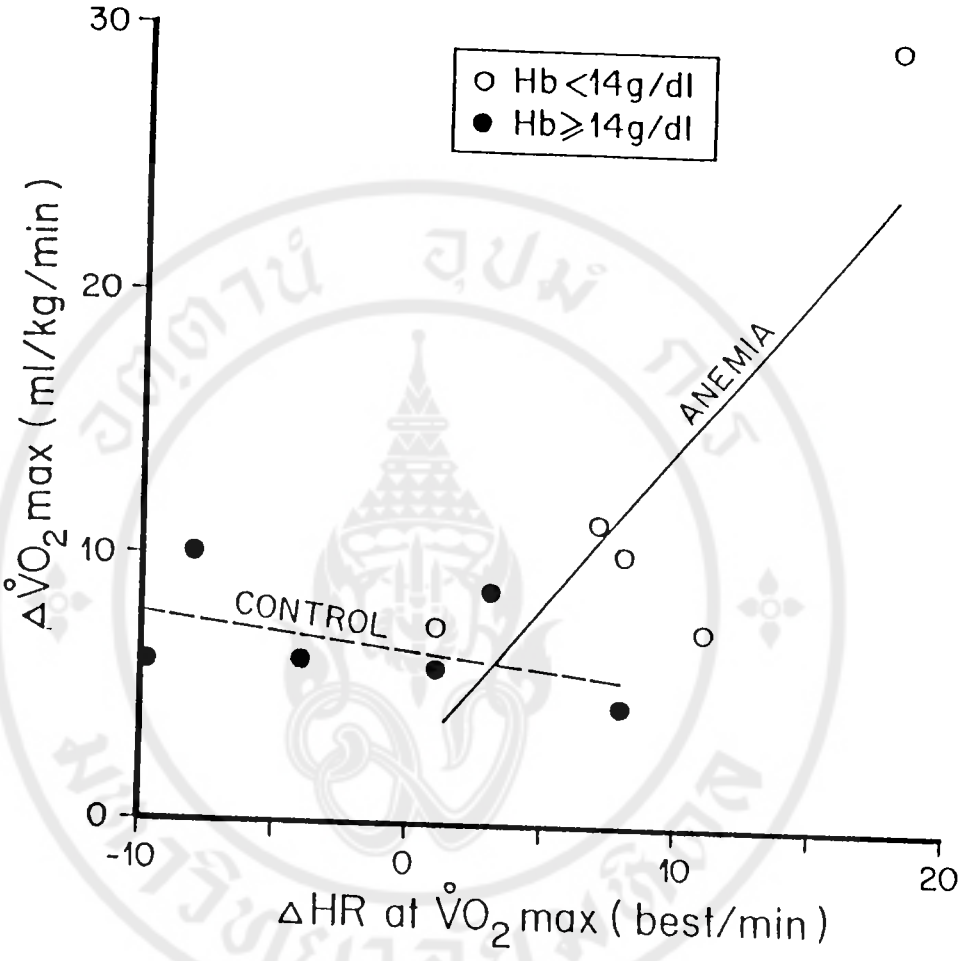


Fig 16. The reduction in $\dot{V}O_2$max at hypoxia (Δ VO_2max) plotted against the decrement in heart rate from normoxic value at the point of VO_2max (i.e. HR atnormoxic VO_2max-HR at hypoxic VO_2max; Δ HR at VO_2max).

reduction in VO_2max at hypoxia (ΔVO_2max) and the decrement in HR from normoxic value at the point of VO_2max (that is, HR at normoxic VO_2max - HR at hypoxic VO_2max or Δ HR at VO_2max) in both anemic and non-anemic subjects. Significant positive correlation was found ($r=0.82$, $p<0.05$) in anemic group but not in control. The regression equation for the anemic curve was $Y=2.3+1.2X$; where Y represented ΔVO_2max (ml/kg/min) and X represented the Δ HR at VO_2max.

Table 3 shows heart rate (HR), oxygen pulse, lactate and respiratory parameters of the control and the anemia at rest on bicycle ergometer under normoxic and hypoxic conditions. Acute exposure to hypoxia caused an increase in HR above the normoxic level in both subject groups ($p<0.05$ in control and $p<0.01$ in anemia). When comparison among groups were performed, no significant difference in resting HR under both normoxia and hypoxia were found. The hypoxia-induced change in HR expressed as percent of the normoxic level was similar among the two subject groups. Resting minute ventilation (V_E) was also enhanced by hypoxia ($p<0.05$ in both subject groups). The percent change from the normoxic value was significantly greater in the anemia than the control ($p<0.001$).

Contrast to HR and V_E, hypoxic enposure caused the decrement in resting arterial oxygen saturation (SaO_2) below the normoxic level in both subject groups ($p<0.001$ both). When comparison among groups were performed, no significant difference was found in resting SaO_2 in either

Table 3. Heart rate (HR), oxygen pulse , lactate , and respiratory parameters of control and anemic athletes at rest on bicycle ergometer in normoxia and hypoxia.

	CONTROL		ANEMIA	
Parameter	Normoxia	Hypoxia	Normoxia	Hypoxia
HR(beats/min)	65.3 ± 2.9	73.5 ± 1.4*	61.6 ± 2.5	66.8 ± 4.3**
(% Normoxia)	100	113.7 ± 5.6	100	108.6 ± 6.2
VO_2(ml/kg/min)	5.3 ± 0.4	5.6 ± 0.4	6.1 ± 1.6	4.9 ± 0.3
(% Normoxia)	100	105.3 ± 1.4	100	94.8 ± 16.2
V_E (l/min)	8.49±0.58	9.57±0.72*	8.32±1.18	11.16± 1.22*
(% Normoxia)	100	112.83±2.36	100	141.80±23.07+++
O_2pulse(ml/beat)	5.0 ± 0.6	4.6 ± 0.4	6.2 ± 1.7	4.6 ± 0.2
(% Normoxia)	100	93.9 ± 4.2	100	87.0 ± 13.0
R(VCO_2/VO_2)	0.76±0.05	0.83±0.04	0.78±0.06	0.88±0.12
(% Normoxia)	100	108.00±8.41	100	110.00±17.73
Lactate(mmol/l)	1.1 ± 0.1	1.2 ± 0.1	1.0 ± 0.1	1.1 ± 0.1
(% Normoxia)	100	107.8 ± 4.8	100	108.5 ± 6.5
SaO_2 (%)	99	91.5 ± 0.7*	99	91.0 ± 0.6***
(% Normoxia)	100	92.5 ± 0.72	100	92.0 ± 0.6

Values are means ± SEM.

Significantly different from normoxia; *p<0.05, **p<0.01, ***p<0.001

Significantly different from control ; +++p<0.001

normoxia or hypoxia. The hypoxic induced change in SaO_2 expressed as percent of the normoxic level was similar among the two subject groups. There were no significant differences in O_2 pulse, R, and blood lactate concentration between the anemic and the control subjects at rest under both normoxia and hypoxia.

Data on maximal exercise test are shown in table 4. Acute exposure to hypoxia caused a significant decrease in maximum heart rate (HRmax) below the normoxic level in the anemic group ($p<0.001$) but not in the control. When comparison among groups were performed significant difference in HRmax was found only under hypoxic condition ($p<0.05$) where the HRmax of the anemia and the control were 164.6 + 1.9 and 173.0 + 4.8 beats/min, respectively. Oxygen pulse at $\dot{V}O_2max$ was also suppressed by hypoxia ($p<0.05$ in control and $p<0.01$ in anemia). When comparison among groups were performed, no significant difference in this parameter was found either at normoxia or hypoxia. And again the percent change from the monmoxic value was similar among the two subject groups.

Like the two above parameters, maximal work load (WLmax) was also suppressed by hypoxia ($p<0.01$ in both subject groups). At both normoxia and hypoxia no significant difference in WLmax was found when comparison among groups was performed either when it was expressed as an absolute or percent change from normoxic value. Similar results were obtained when WLmax in relative to body weight was considered. The blood lactate concentration at the end of

Table 4. Maximal exercise data of control and anemia athletes in normoxia and hypoxia.

Parameter	CONTROL		ANEMIA	
	Normoxia	Hypoxia	Normoxia	Hypoxia
HRmax(beats/min)	177.0 ± 4.2	173.0 ± 4.8	172.2 ± 1.9	164.6 ± 1.9^{****+}
(% Normoxia)	100	97.6 ± 0.9	100	96.2 ± 1.2
WL_{max}(watt/kg)	4.3 ± 0.4	3.9 ± 0.3**	4.2 ± 0.4	3.7 ± 0.3*
(% Normoxia)	100	89.8 ± 1.4	100	88.2 ± 2.3
WL_{max}(Watts)	256.7 ± 6.1	230.0 ± 6.8**	260.0 ± 12.6	228.0 ± 4.9**
(% Normoxia)	100	89.6 ± 1.6	100	88.2 ± 2.3
O_2pulse at VO_2max	20.2 ± 1.2	17.5 ± 1.0*	21.4 ± 1.7	17.4 ± 0.6**
(% Normoxia)	100	99.3 ± 9.3	100	81.6 ± 4.6^{+*}
R at VO_2max	1.09 ±0.41	1.20 ± 0.02	1.10 ± 0.02	1.17 ± 0.07
(% Normoxia)	100	109.67± 2.82	100	107.8± 4.80
Lactate (mmol/l)	8.2 ± 0.3	7.5 ± 0.2**	8.7 ± 0.3	7.9 ± 0.2^{*+}
(% Normoxia)	100	91.8 ± 1.9	100	91.0 ± 1.5
$V_E$max (l/min)	73.52±2.69	72.38 ±2.41	73.46±2.63	73.81± 5.02
(% Normoxia)	100	98.80 ±2.06	100	101.00± 8.62
VO_2max(ml/kg/min)	56.1± 2.8	49.3 ± 0.9*	57.7 ± 5.4	45.0 ± 2.5^{*+}
(% Normoxia)	100	87.9 ± 1.0	100	78.4 ± 4.5^{+}
SaO_2 at VO_2max(%)	96.0± 0.8	84.8 ± 1.2***	96.8 ± 0.5	78.0 ± 0.9^{+++***}
(% Normoxia)	100	88.4 ± 1.6	100	80.6 ± 0.8^{+++}

Values are means ± SEM.

Significantly different from normoxia ;* p<0.05,** p<0.01,*** p<0.001

Significantly different from control ;$^{+}$ p<0.05,$^{+++}$p<0.001.

exercise was significantly lower at hypoxia than at normoxia ($p<0.01$) in both groups of subjects.Significant difference in blood lactate between groups was exhibited only under hypoxic condition ($p<0.05$) with the higher value in the anemic group (Table 4).

Maximal oxygen uptake (VO_2max) was, certainly, suppressed by acute exposure to hypoxia ($p<0.05$ in both subject groups). The reduction in VO_2max at hypoxia was appreciably greater in the anemic group and make its hypoxic VO_2max significantly lower than control either when expressed as an absolute or percent change from normoxic value ($p<0.05$ both). Similar results were obtained when arterial oxygen saturation at VO_2max (SaO_2 at Vo_2max) was compared between these two groups subjects.

Contrast to the six above parameters, respiratory exchange ratio at VO_2max (R at VO_2max) was enhanced by hypoxia in the control ($p<0.05$) but not in the anemia. When comparison among groups were performed, no significant difference in R at Vo_2max under normoxia and hypoxia were found. The last parameter to be considered is maximal minute ventilation (V_Emax) that showed no significant difference between normoxia and hypoxia and also between control and anemic groups.

3 Anaerobic Threshold (AT)

Table 5 illustrates the comparison in oxygen uptake (VO_2), arterial oxygen saturation (SaO_2) , heart rate (HR),O_2 pulse,work loard (WL) and minute ventilation (V_E) at anaerobic thresold (AT) of control and anemic group of subjects under normoxic and hypoxic conditions. Acute exposture to hypoxia caused a significantly decrease in VO_2 at AT below the normoxic level in both subject groups ($p<0.05$ in both groups). No significant difference in this parameter was found either at normoxia or hypoxia,when comparison among groups were performed. However,when VO_2 at AT is expressed as a percentage of VO_2max are considered,the hypoxic induced change in VO_2 at AT were remained but not significantly lower than normoxia.

Arterial oxygen saturation (SaO_2) at rest was, certainly,supressed by acute exposure to hypoxia ($p<0.001$ in both subject groups). When comparison among groups were performed,no significant difference in resting SaO_2 under normoxic and hypoxic conditions were found. Similar results were obtained when SaO_2 at AT was considered. The reduction in SaO_2 from resting to the point of AT (i.e. SaO_2 at rest-SaO_2 at AT or ΔSaO_2) was enhanced by acute hypoxic exposure ($p<0.01$ in control and $p<0.05$ in anemia). And again no significant differance in ΔSaO_2 was found when comparison among groups were performed at both normoxia and hypoxia.

Like VO_2 and SaO_2 at AT , work load and

Table 5. Anaerobic threshold data of control and anemia in both normoxia and hypoxia.

	Control		Anemia	
Parameter	normoxia	hypoxia	normoxia	hypoxia
VO_2(ml/kg/min)	36.8 ± 4.7	27.3 ± 2.8*	35.0 ± 4.6	24.2 ± 1.6*
VO_2(%VO_2max)	64.5 ± 6.1	54.7 ± 4.0	60.2 ± 3.9	54.3 ± 2.3
SaO_2(%)	98.3 ± 0.3	85.5 ± 1.6***	97.8 ± 0.8	86.8 ± 0.4***
^ SaO_2(%)	0.7 ± 0.3	6.0 ± 1.4**	1.2 ± 0.7	4.2 ± 0.4*
HR(beats/min)	135.7 ± 9.1	131.5 ± 6.9	124.6 ± 5.5	112.6 ± 2.4^{++}
O_2pulse(ml/beat)	15.9 ± 0.8	12.4 ± 0.9***	17.2 ± 1.2	13.4 ± 0.8***
WL(watts)	136.7 ±18.2	100.0 ±11.5*	136.0 ±18.3	92.0 ± 4.9*
V_E(l/min)	36.2 ± 4.0	29.5 ± 3.5	36.3 ± 3.1	31.6 ± 2.2

Values are means ± SEM.

Significant difference from normoxia : $^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

Significant difference from control : $^{++}p<0.01$.

oxygen pulse at this point were significantly decreased during hypoxic exercise. When comparison among groups were performed , no significant difference in these to parameters under both normoxia and hypoxia were found.

Minute ventilation at anaerobic threshold (V_E at AT) was not supressed by hypoxia in both groups of subjects. Similar to the three above parameters, when comparison among groups were performed, no significant differance in V_E at AT under normoxic and hypoxic conditions were found.

Does not like the above parameters, heart rate at anaerobic thresold (HR at AT) was not affected by hypoxia. Significant differace in HR at AT between the two subject groups was exhibited only under hypoxic condition ($p<0.01$) with the lower value in the anemic group (Table 5).

Table 6 showed the relationship among VO_2max, [Hb] and various AT parameters of overall subjects at normoxic and hypoxic conditions. Significant positive correlations were found between VO_2 at AT on one hand , and VO_2max,WL at AT,and V_E at AT on the other at both conditions. Such the correlations were also found between ΔVO_2 at AT on one hand,and ΔHR and VO_2 at AT on the other. No significant correlation was observed either between [Hb] and VO_2 at AT or between [Hb] and ΔVO_2 at AT.

Table 6. correlation coefficient (r) of anaerobic threshold (AT) and the corresponding parameters at both normoxia and hypoxia.

Parameter	VO_2 at AT(ml/kg/min) normoxia	VO_2 at AT(ml/kg/min) hypoxia	ΔVO_2 at AT (normoxia-hypoxia)
VO_2max(ml/kg/min)	0.78**	0.82**	
Hb(g/dl)	-0.60	0.16	-0.19
WL at AT(watts)	0.89***	0.84***	
V_E at AT(l/min)	0.73**	0.64*	
ΔHR(normoxia-hypoxia)			0.67*
VO_2 at AT(ml/kg/min)			0.88***

Significant correlation ; *p<0.05 , **p<0.01 , ***p<0.001

CHAPTER VI

DISCUSSION

A number of studies have shown that a reduction in arterial oxygen content (CaO_2), such as that occurred during acute exposure to high altitude [8,10] or to hypoxia[144], or a decrease in Hb concentration (e.g. due to blood lost [7] or anemia [11,35,36]) at sea level resulted in the decrement of aerobic work capacity and maximum oxygen uptake (VO_2max). But in the case of sports anemia that can be found in athletes who had an intensified physical training, the decrease in Hb concentration does not affected the VO_2max at sea level since these athletes still have a higher VO_2max than the normal sedentaries[12,13,62,63] this might suggest that the lowering of blood Hb level have no significant effect on the VO_2max in these highly fit athletes at sea level. It is known that individuals with normal blood Hb level, the reduction in VO_2max at high altitude (Δ VO_2max) is varied directly with the normoxic or sea level VO_2max, i.e., the more aerobically fit athlete suffered a larger decrement in VO_2max at high altitude[8-10]. However , such the effect of high altitude hypoxia on the VO_2max of athletes with sports anemia is still unknown. A question, therefore, arises; could the sports anemia in athletes who have high VO_2max aggravate the reduction in VO_2max at high altitude ? The present study was conducted to answer this question. So this experiment was conducted in

athletes to determine the reduction in aerobic capacity at hypoxia as a function of Hb concentration with the use of a multiprogressive non-steady state exercise test.

In this study the subjects were divided into two groups depending on their Hb concentration,as suggested by Pate[83] , the athletes who had blood Hb level less than 14 g/dl were classified as anemic subjects. The other group of athletes who had hemoglobin concentration more than 14 g% were stood for the control. Besides the Hb concentration, these anemic athletes also had hematocrit (Hct), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) lower than the control. The only one hematological index that was not lower than the control was mean corpuscular hemoglobin concentration (MCHC).

Lowering in hemoglobin concentration and Hct in athletes have been suggested to be due to post exercise plasma expansion [41,83]. This phenomenon has been called "post-exercise overhydration" by Refsum et al [42]. Robertson and coworkers [85] studied the changes in red cell density and its related indices in response to distance running and pointed out a marked increase in plasma volome between 48 and 72 hours after a 21 km run. Taking liquid during prolonged exercise, the shift of water from tissue space to vascular space, and the suppression of sodium and water by kidneys during exercise have been proposed to be the main causes of the postexercise plasma expansion [85,84]. Many investigators have found a decreases in hemaglobin concentration, hematocrit, and erythrocyte count in the

peripheral blood following intense training [16,58,86]. It has also been reported that the hematological parameters of erythrocytic system were low in top-class athletes in endruance disciplines [12,13,58]. The tendency to keep down the hemoglobin concentration is not an accidental phenomenon but represents beneficial adaptive change associated with a 12 to 20% plasma volume expansion which brings about blood dilution and improves rheological properties of blood. The increase in blood plasma volume, i. e. the total volume of circulating blood improves endurance capacity and resistance to exhaustion by increase in stroke volume, and improvement in the efficiency of sweating [16,66,135]. There are, however, a report, indicating no differences in hemoglobin concentration, hematocrit or erythrocyte count in well-trained compared with untrained persons after physical training that effect in an increase in VO_2max [136].

The lower MCH of the anemic athletes than the non-anemic subjects in this study did not lead to hypochromia since the MCHC of this anemic group was normal.

By considering the blood morphology, most of the subjects had normochromic normocyte except the one in anemic group (triathlete) who showed anisocytosis 1^+ and poikilocytosis 1^+. This irregularity in erythrocyte structure has also been found in 71% of the runners immediately after a marathon race and in 13% of the runners on day 10 of recovery [65,66]. However, when his blood morphology was investigated again during off season (where

the intensity and duration of training were lower than in season), such a morphological alteration of RBC was disappeared and blood hemoglobin concentration as well as Hct were increased towards normal (Hb 14.2 g%, Hct 43%). Similarly, when the blood samples of the other 4 anemic athletes were re-examined during off season, their blood Hb concentration and the Hct were also raised towards normal.

Accordingly, for all above hematological data seems likely that the lower in hematological indices and the morphological alteration of RBC of these anemic athletes were transient and might be caused by an intensified physical training since during off season where the intensity and duration of training reduced, this phenomenon was disappeared without any treatments such as iron supplementation [141,142,143].

Besides postexercise plasma expansion and iron deficiency, the other three commonly cited causes of sports anemia are hemolysis induced by intensified physical effort, losses of erythrocytes by bleeding into the digestive and urinary systems, and disterbances in erythropoiesis [15]. Since the mild macrocytosis is the one important evidence to denote the intensified hemolysis [41,145] while the MCV values of all anemic athletes in this study showed normal to mild microcytosis (Appendix III) so the anemia of these athletes should not be attributed to this cause.

Gastrointestinal bleeding [94,95] and hematuria [133] has been reported in endurance runners as well as in non-contact sports (such as swimming) [134] via the possible

mechanisms including 1) so much vasoconstriction of the renal blood vessels during severe exercise that may result in renal ischemia which causes hypoxic renal damage [134] 2) vasoconstriction of the renal blood vessels may result in an increased filtration pressure and stasis in the glomerular capillaries that leads to an increased filtration of protein and red blood cells through the glomerular membrane [132]. Although two of the athletes with low hemoglobin concentration in this study were endurance runners and one was triathlete, it is not known whether loss of erythrocyte by bleeding into the digestive and urinary systems could account for the anemia since analysis of the intestinal and renal excretions was not performed.

Another possible cause of sports anemia is the disturbances in erythropoiesis. Hallberg and Magnusson [68] suggested that training-induced an increase in 2,3-DPG leads to an increase in oxygen delivery of sensory cells of the kidney responsible for erythropoietin synthesis and there by induce a lower hemoglobin concentration and hematocrit in the peripheral blood. Moreover, the reduction of testosterone[69] as well as a reduction in the number of T4 (helper) lymphocytes andthe helper to cytotoxic suppreasors (T8) ratio [69,70] in the peripheral blood after intense physical endurance efforts can disturb the erythropoiesis system of athletes.

The main objective in this investigation was to determine the influence of hemoglobin concentration on aerobic capacity during acute exposure to hypoxia (inspired

oxygen 14.5% or approximately equivalent to an altitude of 10,000 feet). Since the two groups of subjects had the same physical fitness level under normoxic condition, but had significant difference in hemoglobin concentration (Table 2) so the effect of hemoglobin concentration on the reduction in aerobic capacity under hypoxic condition can be studied.

In this study, under hypoxic condition where the inspired O_2 was 14.5% or equivalent to an altitude about 10,000 feet, the rapid physiologic adjustments occurred to compensate for the thinner air and accompanying reduced PaO_2 [25,46]. During hypoxic resting, hyperventilation and increased cardiovascular response especially tachycardia were seen in both subject groups. However, such these two physiological compensations at hypoxia could not bring the arterial blood O_2 tension of the two subject groups toward the normoxic values since their SaO_2 fell(Table 3),and hence lowered CaO_2 at hypoxia should occur. Despite the lower in CaO_2, resting HR at hypoxia was increased while the O_2 pulse at normoxia was equal to that at hypoxia (Table 3). If the O_2 pulse mainly reflected cardiac stroke volume, such a rising HR would result in the elevation of arterial O_2 transport at hypoxia (O_2 transport = HR x SV x CaO_2). According to the fact that VO_2 is the product of cardiac output and $C(a-v)O_2$ difference (i.e.O_2 extraction by the tissues) and since the similarity in resting VO_2 was found between normoxia and hypoxia, it is possible that $C(a-v)O_2$ difference at hypoxia may be smaller than that at normoxia, if cardiac output was increased by hypoxia. A

previous report of Hartley [48] who studied the central femoral and brachial circulation during exercise in hypoxia (P_B 464 mmHg)foundthat the femoral $C(a-v)O_2$ difference at any VO_2 was less during hypoxia while the femoral flow was greater. In the present study, when comparison between anemia and control were considered, CaO_2 at hypoxia of the former group seemed to have a lower value than the latter since SaO_2 was similar while Hb concentration was lower in the anemic subjects. However,it is not known whether the $C(a-v)O_2$ difference was more decreased in the anemic group than control under hypoxic condition since the resting cardiac output was unknown. Blood lactate concentration at rest in both subject groups was not altered under hypoxia might indicate that there was enough oxygen uptake for the aerobic metabolism so that an increased anaerobic metabolism via lactic system was not required.

Our present data about maximal exercise under hypoxic condition showed that maximum oxygen uptake (VO_2max) at this condition was more markedly decreased in the anemic group of athletes than the control group (Table 4). The reduction in VO_2max at hypoxia (normoxic VO_2max - hypoxic VO_2max or ΔVO_2max) was directly correlated with normoxic VO_2max (Fig 10) but was inversely correlated with the Hb concentration (Fig 10-12).

Exposure to hypoxic atmosphere at high altitude is known to impair aerobic performance as characterized by reduced VO_2max [8,10,29,155], and the amount of reduction is proportional to the reduced in the partial pressure of O_2

in the inspired air. The relationship between the reduction in VO_2max and altitude has been estimated to be on the order of 10% (of sea level VO_2max) for every 1000 m ascended beyond an altitude of 1500 m above sea level [8,21,22,29] thus the more aerobically fit individuals who have a higher level of VO_2max do tend to suffer a larger decrement in VO_2max at altitude when compared with the less fit ones. However, the influence of aerobic fitness on the reduction of VO_2max at high altitude was controversial. In 1969, Buskirk [146] studied the results of a number of investigations and concluded that the decrement in VO_2max expressed in either ml/kg/min or % normoxic VO_2max) at high altitude was smaller for fit persons than for less fit. On the other hand, in two studies of Grover [51] and Saltin [50], the decrement in VO_2max of highly trained athletes was reported to be greater than would have been expected based on observations made on less fit individuals. So the mechanisms by which the degree of aerobic fitness as characterized by sea level or normoxic VO_2max can modify the relationship between altitude and the decrement in VO_2max has been further investigated by a number of studies [8-10,147]. In 1982, Squires and Buskirk [8] performed the experiment on twelve young men to study the effects of acute exposure to simulated altitude of 914 to 2286 m and found that during maximal exercise at an altitude of 2286 m there were significant decrease in SaO_2, minitue ventilation (V_E), carbon dioxide production (VCO_2) and systemic blood pressure. These in turn, made VO_2max significantly

decrease. According to Hartley's study [48] in which maximal exercise under hypoxic condition at an altitude of 4350 m was conducted in the sedentaries, maximum cardiac output (Qmax) and oxygen content in mixed venous blood (CvO_2) has been reported to be remain unchanged from sea level ; so the author made a conclusion that the reduction in VO_2max at high altitude may be related to a decrease in arterial oxygen content (CaO_2).

In 1985, Young et al [10] studied the influence of cardiorespiratory fitness on the decrement in VO_2max at high altitude in 51 male sea level residents and found significant positive correlation between sea level VO_2max and the reduction in VO_2max at high altitude (VO_2max) which was similar to the present study. Based on Dempsey's study which reported that at sea level, elite track athletes show significant hypoventilation and significant hypoxemia at or near their VO_2max when compared to the lower fitness athletes. So Young suggested that the individuals who have higher sea level VO_2max would suffer a greater decrease in VO_2max at high altitude. Such a conclusion about arterial desaturation does not fully explain the interaction between physical condition and the impairment of oxygen transport during hypoxia. Therefore, in 1988, further investigation was done by Shephard and coworker [9] to study the effect of physical fitness on VO_2max at hypoxia which induced by inspiration of 12% oxygen in nitrogen (equivalent) to an altitude of 4400 m). Again, they found significant positive correlation between sea level or normoxic VO_2max and the

reduction in VO_2max at hypoxia with the corresponding regression equation of Δ VO_2max (ml/kg/min) = 0.5 VO_2max (ml/kg/min) - 9.91 (r = 0.73) that was compatible with our current study in which the regression equation of over all subjects was Δ VO_2max (ml/kg/min) = 0.6 VO_2max (ml/kg/min) - 23.5(r = 0.77) where ΔVO_2max is the hypoxic change of VO_2max and VO_2max is normoxic VO_2max, the difference between the two predicted values of ΔVO_2max from these two equations were due to an altitude difference since the former equation was done at an altitude of 4400 m instead of 3040 m as done in our study.

In the present study, when the relationship between normoxic VO_2max and ΔVO_2max of the control and anemia were considered seperately, such a positive correlation remained but the rate of change in Δ VO_2max of the anemic group was greater than the control (Fig 10). In other word, at any normoxic VO_2max the anemic athletes do tend to suffer a larger decrement of VO_2max at altitude when compared with non-anemic subjects (Fig 10-11).

Moreover, when the average value of hypoxic VO_2max was compared between the anemia and the control groups it showed significantly lower in the former group with the corresponding decreased in SaO_2 and maximum heart rate (Table 4, Fig 13,14,16) while at maximal exercise the minute ventilation ($V_E max$) and respiratory exchange ratio (R) were not affected by hypoxia as well as by hemoglobin concentration (Table 4) suggesting that the limiting factors for this hypoxic exercise should not include V_E.

The pulmonary factors which may potentially limit oxygen uptake under the hypoxic exercise include total ventilation, cardiac output, ventilation-perfusion (V_E/Q) mismatch, alveolar-capillary oxygen diffusion limitation, and possibly gas phase diffusion limitation [155]. Shephard and coworker [9] observed that the subject who hyperventilated during hypoxic exercise had only a small reduction of oxygen transport, while another who hypoventilate had a larger than anticipated decrease of VO_2max. Then suggested that the drop in average $V_E$max could augmented a decrease in SaO_2. Our results, however, showed that hypoxic VO_2max and SaO_2 were certainly, lower than those of normoxia and a marked reduction in both VO_2max and SaO_2 were found in the anemic athletes, even though the change in $V_E$max was similar among the subject groups (Table 4). Since a factor which is sometimes incriminated in the limitation of exercise is the increased work of breathing at high work loads ; this could lead to an oxygen demand in excess of the increased oxygen intake achieved [156]. The cost of ventilation that exceeded the oxygen uptake is reached at level of minute ventilation above 120 l/min [160] which was not found in our subjects. Thus at least in case of our study, minute ventilation was not the limiting factor for exercising at an altitude of 10,000 feet either in the control or in the anemic group of subjects. The finding that $V_E$max was maintained at high altitude is supported by the experiments of Hughes et al. [153], Reeves et al [157], and Sutton [158] but differs from the result of Shephard

[8] who found a reduction in $V_E$max during hypoxic exercise (P_IO_2 = 12% O_2 in N_2) suggested that such a decrease in V_E may be due to bronchospasm induced by sufficient time of breathing the hypoxic gas mixture.

The more sea level or normoxic VO_2max the larger decrement in hypoxic VO_2max which could be attributed to greater diminution of oxygen transport as a result of an increase in alveolar-arterial oxygen tension gradient [154]. One factor potentially limiting oxygen transport during all-out effort is the ratio of maximum diffusing capacity($D_L$max) to the product of the slope of the oxygen dissociation curve [7] and maximum cardiac output (Qmax) (that is, $D_L$max/Qmax). In any given subject , this ratio varies from one part of the lung to another, but if the average value does not reach a cirtain minimum figure, equilibration of alveolar and capillary blood will fail to occur in the shorter capillaries [154], with resultant arterial unsaturation relative to the alveolar oxygen pressure. Since $D_L$max is reduced in hypoxia or at high altitude [9,157], and in well-trained subject this difficulty is compounded by a large Qmax [23] and a short capillary transit time [157] thus resulted in a larger decrease in $D_L$max/ Qmax ratio, an increment of alveolar-arterial oxygen difference ((A-a)O_2 difference) could be expected. A study of Torre-Bueno et al. [155] indicated that during exercise at an altitude of 10,000 ft,with exercise intensity above 1 l/min VO_2, (A-a)O_2 difference appeared and become wider with an increasing VO_2, and suggested that an increased in V_A/Q mismatch

and also the appearance of diffusion limitation occurred. Thews et al [170] also reported that during hypoxic exercise, the major cause of the $(A-a)O_2$ gradient was diffusion-limitation. Finally, West et al [152] found a decreasing SaO_2 in the face of a rising alveolar PO_2 on Mt.Everest, also suggested that it was due to diffusion limitation. There is, however,a controversial report against the appearance of diffusion limitation at high altitude. Asmussen and coworker[160] showed that diffusion resistance had no noticeable effect even during work at hypoxia.

A wide arteriovenous oxygen difference [$(a-v)O_2$ difference] in well-trained subjects is said to augment the $(A-a)O_2$ difference since it increases the impact of ventilation perfusion inequalities and frank venous-arterial shunts upon SaO_2[9]. More recently,it has been reported that in sports anemic athletes, the decrement in O_2 affinity of Hb was found together with an increase in 2,3-DPG which made a rightward shift of O_2-Hb dissociation curve[161]. this shift may create disadvantages at high altitudes[162] in that a diffusion limitation may be a determining facter in exercise tolerance[155]. In the present study, the reduction in SaO_2 in maximal exercise test in association with a reduction in VO_2max was observed and found to be more marked in the anemic athletes than the controls. This might suggest the greater limitation of pulmonary diffusing capacity during exercise under hypoxic in the anemic subjects. However, since the O_2-Hb dissociation curve and the 2,3-DPG were not determined in the present study, it is not known

wheter the shift of O_2-Hb dissociation curve to the right enhanced the diffusion limitation during exercise in hypoxia in the anemic athletes.

One of the factors which limit exercise both at sea level and altitude is the maximal cardiac output (Qmax)[23]. During submaximal exercise with reduced PO_2 in the inspired air, the lower SaO_2 is compensated for with an increased cardiac output by an increase in HR [1,153]. HRmax and Qmax were reported to be unchanged at all fraction of an inspired O_2 (F_IO_2) [153] and this also has been found during maximal exercise at an altitude of 4,000 m [1]. In addition, Cerretelli[22] suggested that acute hypoxia had no effect upon the peak HR at altitude of less than 4,000 m,and Reeves [157] also reported no significant reduction in HR of athletes during maximal exercise at 10,200 feet above sea level. All thses suport our finding in the control group in the present study (Table 4). However, there was at least one report [164] that observed as large reduction in HRmax as that found by Shephard et al.[9] during maximal exercise under hypoxic condition and they hypothesized that such a slower peak HR would be caused by hypoxia reduced myocardial contractility and/or the rate of diastolic filling that might be considered as an evidence of an impairment of myocardial function but the controversial argument was done by Sutton andcoworker [164] who reported that besides the reduction in Qmax and HRmax during hypoxic exercise (P_IO_2 = 43 mmHg) or equivalent to and altitude of 8,848 m) cardiac function which assessed by hemodynamic, echocardiography and

electrocardiography was normal with no clinical evidence of myocardial ischemia.

During maximal exercise at hypoxia, O_2 pulse was equal between the control and the anemia while HRmax was lower in the latter group (Table 4) indicated the smaller O_2 transport in this subject group since the O_2 transport $\dot{=}$ O_2 pulse x HR. Possible mechanism for this reduction in O_2 transport may refer to a marked decrement in diffusing capacity that illustrated by the larger decrement of the SaO_2 in the anemic athletes (Table 4). The marked decrease in SaO_2 together with the lower [Hb] would lead to the greater reduction in CaO_2 of the anemia when compared with the control. Hence; the lower HR and a marked reduction in CaO_2 of the anemia would cause a larger $\hat{V}O_2max$ than non-anemic athletes even though the CvO_2 may similar or decrease due to the rightward shift of O_2-Hb dissociation curve in the anemic subjects.

In this experiment, the lesser rise of blood lactate after maximal exercise at hypoxia was found in both subject groups with the corresponding lower WLmax. This finding was in agreement with the other such as Shephard et al.[9], Sutton et al.[164,166].Blood lactate concentration is determined by several interacting factors, including the rate of lactate formation from glycogenolysis and glycolysis , the rate of lactate entry into the tricarboxilic acid cycle (Krebs cycle), the rate of efflux of lactate from muscle to blood, and the rate of metabolism of lactate by the liver and other tissues, including active muscle [165].

Each factor could play apart in the present study. Given that power output was reduced during hypoxic exercise, a smaller proportion of the type II glycolytic fibers may have been activated, this in turn, caused the reduction in the rate of lactate formation [9]. This suggestion was further supported by the results of muscle biopsy which revealed that the reduced glycogenolysis and lactate formation at exhaustion with increasing simulated altitude is the importance factor for the reduction of lactate under hypoxic exercise[187]. In the present study, the hypoxic bouts also lasted 1-3 min less than the normoxic experiments, possibly allowing less time for lactate to diffuse from the active muscles into the blood stream. A decrease of plasmar bicarbonate caused by pre-exercise hyperventilation in humans has been previously been shown to inhibit lactate efflux from muscle to blood [137,185]. The pre-exercise hyperventilation was also found in this study (Table 3) this may also contribute to the reduced blood lactate concentration during maximal exercise at hypoxia. In this study, the post hypoxic exercise lactate concentration was found higher in anemic athletes even though their WLmax were similar to the control (Table 4). Gardner et al.[57] who performed the experiment about physical work capacity and metabolic stress in subjects with iron deficiency anemia suggested that the higher in post-exercise blood lactate of the anemia than the control indicated the relative contribution of anaerobic glycolysis to the overall energy demands of the exercise task. This explanation might also be

applied in our study. Although the controversial result was proposed by Beard et al.[140] who study the cardiovascular performance of high altitude males during short-term exercise testing at high altitude as a function of degree of anemia and found that the anemics had significantly lower arterial lactate concentration at maximal effort than the controls. the reason for this controversy may due to the different exercise-response between sports anemic lowlanders as in our experiment,and iron deficiency anemic highlanders.

At the beginning of progressive exercise test where the intensity of exercise is low, such an exercising energy is generated by aerobic metabolism [108,159]. As the exercise intensity increases and reach a point between 40 % and 60 % VO_2max [159] where the O_2 required by the metabolically active muscles exceed the O_2 supply, the onset of anaerobic metabolism occurs [105]. This onset corresponds to the AT described by Wasserman et al. [106]. In the present experiment, we also used these two criteria, 1) a non-linear increase in V_E and VCO_2 plus an abrupt increase in respiratory exchange ratio (R) 2) an increase in fraction of O_2 in the expired air (F_EO_2) without a corresponding decrease in F_ECO_2, for determining AT and found the VO_2 at AT at normoxia in our subjects ranged from 47 to 72 % of VO_2max for the non-endurance athletes and 58 to 84 % of VO_2max in endurance-trained athletes (Appendix III). These results were in agreement with a number of previous reports [47,114,159].

Similar to VO_2max, the VO_2 at AT was significantly

decreased at hypoxia in both groups of subjects. However, unlike VO_2max, the VO_2 at AT of the anemic athletes was not affected by their low Hb concentration since there was no significant differance in the VO_2 at AT of the anemic and that of the non-anemic athletes (Table 5). At the ventilatory AT many corresponding physiological parameters, such as SaO_2, O_2 pulse, V_E, and WL were lower at hypoxia than at normoxia in both subject groups with no significant difference between groups was observed. Interestingly, under hypoxic condition, the exercising HR at AT was lower in the anemia than the control.

Since the AT is defined as the level of exercise VO_2 above which aerobic energy production is supplemented by anaerobic metabolisms [106], acute alteration in O_2 delivery would alter the AT [108]. The evidence of this has been presented. For example, Vogel et al. [171] found that the blood lactate concentration was higher at all work rates when COHb levels were raised to 19% by breathing a carbon-monoxide mixture. The lactate at AT was also reduced by this intervention. Woodson et al. [168] used acute isovolumic anemia to alter O_2 delivery. This intervention raised the arterial lactate concentration at submaximal work rates and lower the AT. By using a ventilatory measure, the lower AT at hypoxia from the normoxic AT was also observed in the present study (Table 5). The possible mechanisms responsible for this are mention below.

In our present experiment, acute alteration in O_2 delivery by breathing 14.5% O_2 in N_2 should lead to a

marked decrease in CaO_2 since significant reduction in SaO_2 was found, and hence may lead to suppression of O_2 transport. Although it has been reported that during submaximal exercise at hypoxia, cardiac output was increased while CaO_2 decreased [1,48,153]. Such physiological compensation in response to hypoxia is to keep the normal rate of O_2 delivery to body tissues by increasing blood flow in the face of decreased CaO_2. However it is not known whether such the cardiac response also occurred in our subjects in this study.

It has also been reported that $(a-v)O_2$ difference was reduced at hypoxia [1,48] so it was reasonable to assume that O_2 extraction by the metabolic active muscles was reduced during submaximal hypoxic exercise. This might be a possible cause of the lowering in AT.

The VO_2 at AT expressed in term of ml/kg/min was found to be decreased during hypoxic exposure. However, when the AT was reported in term of percent VO_2max, such the reduction in VO_2 at AT under hypoxic condition disappeared. This is not surprising since VO_2max and the absolute VO_2 at AT were both suppressed by acute hypoxia and since VO_2 at AT was found to have a high correlation with VO_2max at both normoxia and hypoxia so under hypoxic condition where VO_2max was reduced, the onset of AT in term of VO_2 would also reduced in the same proportion of VO_2max reduction.

Nevertheless, when the reduction in VO_2 at AT due to hypoxia was compared between control and anemia, similar reduction was observed (Table 5) indicating that lower Hb

concentration,cause by sports anemia,did not affect oxygen uptake at the point up to AT when exercise was performed at an altitude of 10,000 ft.

Comparison of V_E during incremental exercise at differerent altitude could be performed at either a given relative intensity of the work such as at AT or at the same % VO_2max, or an absolute work load. During submaximal exercise at highaltitudesor hypoxia, at any given absolute work load, V_E was reported to be higher than at sea level or normoxic condition [1,157]. In this study WL at AT of both subject groups at hypoxia were lower than those at normoxia while V_E at AT was remained unchanged (Table 5).

Acute hypoxic exposure did not suppress the VO_2 at AT (when it expressed as a percentage of VO_2max) since there was no significant difference between normoxic and hypoxic values of this parameter,and this may result in the similarityinV_E at both conditions.This result corresponded well with the report of Reeves et al. [157] who performed the experiment about ventilatory regulation during exercise at 10,200 ft in athletes, and found that if the exercise intensity (in term of %VO_2max) was equal between sea level and high altitude, the altitude variable of V_E might be eliminated;that is exercise at the same percentage of VO_2max, the equal value of V_E would be observed between different altitudes. The reason why the lower Hb concentration caused by sports anemia can magnify the reduction in VO_2max at hypoxia but not VO_2 at AT (Table 4 and 5) was not exactly known. However, these results should suggest that during

submaximal exercise at the level of AT under hypoxic condition, physiological functions determining VO_2 was not deteriorated by sports anemia, but during severe exercise, the process of oxygen consumption should be disturbed. It is well known that VO_2 is determined by the rate of arterial blood O_2 transport and the O_2 extraction from the blood by tissues. Therefore, it could be suggested that such the effect of anemia on VO_2 at high exercise intensity under hypoxia was resulted from an earlier limitation of either one or both the two major physiologlcal processes which governing the VO_2.

The hypoxia-induced decrease in VO_2 at AT found in both the anemic and the control athletes (Table 5) should be due to a reduction in CaO_2 since, at hypoxia, a lowering in SaO_2 at the AT was observed. AS a result, the greater reduction in CaO_2 at AT should occur in the anemic subjects because of their low Hb concentration. In addition our results showed a marked lower HR at AT in anemic subjects while their O_2 pulse did not differ from their control. If the O_2 pulse mainly reflacted cardiac stroke volume , O_2 transport at AT (O_2 transport = HR x SV x CaO_2) should be lower in the anemia than the control. Despite the lower in O_2transport, the VO_2 at AT of the anemia remained unchanged from the control, suggesting the higher tissue extraction of O_2 at the AT in the anemic group since VO_2 is the function of O_2 transport and O_2 extraction.

During maximal exercise at hypoxia, the anemic athletes showed low HRmax with no change in O_2 pulse when compared to

the control. This may indicate that the maximum O_2 transport during exhaustive exercise under hypoxic condition in the anemic subjects was lower than their non-anemic counterparts and this may account for the decrease in VO_2max of the anemic group, if such a lowering in HRmax could reduced Qmax in theseathletes. The possible greater fall in maximum O_2 transport in the anemic athletes at hypoxia than the control could be contributed by a greater decrease in either cardiac output or CaO_2 or both. Clearly, the CaO_2 must be reduced as a result of a combination of the low Hb concentration in these anemic subjects plus the greater reduction in their SaO_2 during maximal exercise. However, it is unknown what the exact mechanisms produced such the more reduction in SaO_2 in the anemic athletes. The possibility that the anemic group possessed lower alviolar oxygen tension (P_AO_2) than the control during maximal exercise at hypoxia should be neglected since both subject groups showed similar $V_E$max. Another possible factor could be a greater reduction in lung diffusing capacity in the anemic subjects during very high intensity of exercise. However, this facter is such a speculation from extrapolation of the results obtained from non-anemic subjects reported previously. In non-anemic athletes during maximal exercise where the VO_2 is high under hypoxic condition, the diffusing capacity has been reported to be more critical than during submaximal exercise where the value of VO_2 was lower [155]. This effect of lowering diffusing capacity led to a decrease in arterial oxygen

tension (PaO_2) and hence SaO_2. An elevation in 2,3-DPG and its result in a rightward shift of O_2-Hb dissociation curve, that known to augment alveolar diffusion limitation [162] was also a possible factor in reducing the SaO_2 since such the increase in 2,3-DPG has been reported to occur in sports anemic athletes [161]. On the other hand, such an anemic state did not magnify the reduction in absolute VO_2 at AT under hypoxic condition possibly because of no diffusion limitation existed. So the lower O_2 affinity of Hb may cause a minor or no effect on this alteration in hypoxic VO_2 at AT.

Either each or combination of the possible factors mentioned above which might be resulted from anemia should exist in the anemic athletes in this study leading to a marked decrease in their VO_2max at hypoxia.

Besides the possible cotribution of the more reduction in arterial O_2 transport, the greater decrease in VO_2max of anemic athletes at hypoxia may occur in association with alteration in tissue-O_2 extraction at the point of maximal exercise. However, no supporting evidence for this can be shown.

CHAPTER VII

CONCLUSION

1. The lower Hb concentration in the anemic athletes in this study indicated sports anemia which were characterized by blood morphology (normal MCHC and MCV) and the trasient state of the low-[Hb] in these athletes (the latter characteristics were observed but data were not shown).
2. During resting at normoxic condition,the anemic and non-anemic athletes showed no significant differances in all the cardiac and respiratory parameters that were measured.
3. Besides the differance in Hb cocentration , both the normoxic VO_2max and the normoxic VO_2 at AT as well as their related parameters were similar between the anemic and the non-anemic groups.
4. During resting under hypoxic condition,hyperventilation and tachycardia occurred for compensation of the reduced SaO_2 and hence CaO_2. These changes in minute ventilation and heart rate were similar between the two subject groups.
5. Aerobic capacity,determined by VO_2max and VO_2 at AT, was decreased at hypoxia in proportion to its normoxic level;the higher in normoxic value the greater decrement in aerobic capacity at hypoxia.
6. The reduction in the aerobic capacity was attributed to

the decreased SaO_2; the larger decrement of SaO_2 the greater reduction in aerobic capacity.

7. The low Hb cocentration in the athletes could magnify ΔVO_2max but not ΔVO_2 at AT during acute hypoxic exposure.

8. The similarity in ΔVO_2 at AT between the anemic and the non-anemic athletes despite the lower in both the HR and the arterial O_2 content in the former group may indicate a higher tissue-O_2 extraction of the anemic subjects.

9. The exact mechanisms responsible for the more marked reduction in VO_2max at hypoxia in the anemia than the control were unknown. However, possible contributing factors for this might be those which caused lowering in arterial O_2 trasport. These might include the low [Hb],and the reduction in CaO_2 and HRmax.

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APPENDIX I

Calculation of inspired gas composition in equivalence to an altitude of 10,000 ft.

The density of air,thus the barometric pressure (P_B),decreases progressively as one ascends above sea level. Although dry ambient air at sea level and altitude contains 20.9 % oxygen, the PO_2 or density of oxygen molecules is lowered in direct proportion to the fall in barometric pressure upon ascending to higher elevations as in the following :

$$PO_2 = P_B \times \frac{\% O_2}{100}$$

Since the ambient air contains 20.9 % O_2,therefore

$$PO_2 = P_B \times 0.209 \quad \text{----------1}$$

At an altitude of 10,000 ft, the barometric pressure is 510 mmHg and dry ambient air still contains 20.9 % O_2. So, the PO_2 at this altitude is :

$$PO_2 = 510 \times 0.209$$

$$= 106.6 \text{ mmHg}$$

A gas mixture containing a certain fraction of O_2 which generates its partial tension of 106.6 mmHg at ambient pressure of 760 mmHg could be prepared. The percent of O_2 in the mixture can be calculated as follows :

$$\% O_2 = \frac{PO_2}{P_B} \times 100$$

$$= \frac{106.59}{760} \times 100 = 14.0 \%$$

APPENDIX II

Blood Lactate Determination

(YSI model 23L Lactate Analyzer)

Principles of Operation

The tip of the lactate probe is covered by a three-layer membrane which serves to protect the electrodes and to define a diffusion path to them. The outer layer is a polycarbonate material with a nominal pore size of 0.03 micrometers, which is large enough to readily pass oxygen, hydrogen peroxide, water, and salt, but small enough to restrict the diffusion of enzymes.The inner layer is a cellulose acetate material with a much smaller pore size which excludes ascorbic acid and most other potentially interfering substances from the electrodes while still allowing hydrogen peroxide, oxygen, water, salt, etc. to pass through. Between these membranes is a layer of glutaraldehyde-crosslinked L-Lactate oxidase.

When the L-Lactate in an injected sample diffuses through the outer membrane reaction I (below) occurs : the catalytic action of L-Lactate oxidase and flavin adenine dinucleotide (FAD) on oxygen and L-Lactate produces hydrogen peroxide and pyruvate.

$$\text{L-Lactate} + O_2 \xrightarrow[\text{L-Lactate oxidase}]{\text{FAD}} H_2O_2 + \text{Pyruvate} \qquad \text{(I)}$$

The hydrogen peroxide produced in reaction (I) diffuses through the inner layer of cellulose acetate and comes into contact with the platinum anode which is held at

a potential of + 0.70 volt with respect to the silver reference cathode. Raaction II now takes place at the platinum anode, yielding a current which is linearly proportional to the concentration of lactate in the sample.

Hydrogen peroxide (H_2O_2) $\longrightarrow$ $2H^+ + O_2 + 2e^-$ (II)

The circuit is completed by the silver reference cathode, reaction (III)

$2\ AgCl + 2e^- \longrightarrow 2\ Ag + 2\ Cl^-$ (III)

At constant chloride concentration, the potential of this reaction is practically independent of current.

The concentration of blood lactate are related to the amount of generated electron.

Reference

Manual from YSI model 23L Lactate Analyzer : General information.

APPENDIX III

Individual value of physical and hematological characteristics of 11 subjects.

	CONTROL						ANEMIA				
Parameter	1	2	3	4	5	6	1	2	3	4	5
	AN	MN	PS	JD	PT	BP	BH	AU	PJ	SS	PI
Age(yr)	22.0	28.5	24.0	21.4	21.0	21.0	23.5	22.0	28.7	20.4	29.0
Weight(kg)	77.2	53.7	74.0	46.7	54.0	61.5	68.6	73.0	59.3	58.0	54.7
Height(cm)	179	166	181	168	164.5	172	181.0	183.5	166.0	163.5	162.5
% Fat	12.6	12.9	10.5	12.9	12.2	13.1	12.9	14.7	12.2	13.1	12.8
FFM (kg)	67.5	46.8	66.2	40.7	47.4	53.4	59.8	62.3	52.1	50.4	47.7
RHR (bpm)	56.0	58.0	57.0	57.0	53.0	63.0	62.0	58.0	52.0	58.0	53.0
Hb (g%)	14.9	14.9	14.7	14.6	14.6	14.0	12.1	12.9	13.2	13.5	12.6
Hct (%)	40.6	45.0	40.6	43.0	43.0	41.2	35.8	36.0	39.3	40.0	37.0
RBC($x10^6$)	4.68	5.08	4.54	4.89	4.74	4.68	4.36	5.75	5.31	5.07	5.52
MCV (fl)	86.8	88.6	89.5	87.9	90.7	88.1	82.1	62.6	74.1	78.9	67.0
MCH (pg)	31.8	29.3	32.5	29.9	30.8	30.0	27.7	22.4	25.0	26.6	22.8
MCHC(g/dl)	36.6	33.1	36.3	33.9	33.9	34.0	33.7	35.8	33.7	33.8	34.1

Normoxic data of 11 subjects at rest on bicycle ergometer.

Parameter	CONTROL						ANEMIA				
	AN	MN	PS	JD	PT	BP	BH	AU	PJ	SS	PI
HR (bpm)	56	58	70	68	75	65	65	63	54	68	58
VO_2(ml/kg/min)	5.4	5.5	3.6	5.6	5.6	6.3	3.9	3.6	12.0	4.8	5.9
V_E(l/min)	8.3	8.0	6.3	8.6	9.2	10.6	6.7	8.0	6.3	7.7	12.9
O_2pulse(ml/beat)	7.4	5.1	3.8	3.8	4.0	6.0	4.1	4.2	13.1	4.1	5.6
R(VCO_2/VO_2)	0.8	0.9	0.7	0.7	0.9	0.7	0.8	0.9	0.6	0.7	0.9
SaO_2 (%)	99.0	99.0	99.0	99.0	99.0	99.0	99.0	99.0	99.0	99.0	99.0
[Lact](mmol/l)	1.0	1.0	1.0	1.4	1.0	1.4	1.1	0.9	0.8	1.3	-

Hypoxic data of 11 subjects at rest on bicycle ergometer.

Parameter	CONTROL						ANEMIA				
	AN	MN	PS	JD	PT	BP	BH	AU	PJ	>>	PI
HR (bpm)	72.0	76.0	71.0	78.0	75.0	69.0	84.0	65.0	61.0	62.0	62.0
VO_2(ml/kg/min)	5.5	6.1	3.7	5.8	5.8	6.8	5.5	4.2	5.4	4.1	5.1
V_E(l/min)	9.7	8.2	7.3	9.8	10.0	12.5	10.1	8.5	14.4	9.1	13.7
O_2pulse(ml/beat)	5.9	4.3	3.9	3.5	4.2	6.0	4.5	4.7	5.3	3.8	4.5
R(VCO_2/Vo_2)	0.7	0.9	1.0	0.8	0.8	0.8	0.9	0.5	1.0	0.8	0.9
SaO_2 (%)	93.0	93.0	90.0	91.0	89.0	93.0	90.0	92.0	93.0	90.0	90.0
[Lact](mmol/l)	1.2	0.9	1.1	1.4	1.2	1.5	1.0	1.1	0.9	1.4	-

Maximal exercise data of 11 subjects in normoxia.

Parameter	CONTROL						ANEMIA				
	AN	MN	PS	JD	PT	BP	BH	AU	PJ	SS	PI
HR_{max}(bpm)	188	171	169	192	174	169	169	169	170	179	169
HR at VO_2max(bpm)	188	156	169	178	174	157	169	153	170	179	169
VO_2max(ml/kg/min)	52.1	59.3	44.2	58.1	60.7	62.5	53.3	46.4	75.7	49.4	64.0
O_2pulse(ml/beat)	21.4	18.6	19.3	14.1	18.8	22.7	21.6	20.0	26.4	16.0	20.7
WL_{max}(watts)	260	280	240	240	260	260	240	240	300	240	280
$V_E$max(l/min)	72.9	66.6	83.1	72.3	67.0	79.2	79.2	74.7	77.7	71.3	65.4
SaO_2(%)	98.0	93.0	95.0	98.0	96.0	96.0	98.0	98.0	96.0	96.0	96.0
R at Vo_2max	1.02	1.10	1.12	1.17	1.07	1.07	1.13	1.13	1.07	1.09	1.01
Lactate(mmol/l)	8.6	9.0	7.2	9.2	7.6	7.6	7.8	8.8	9.5	8.9	-

Maximal exercise data of 11 subjects in hypoxia.

Parameter	CONTROL						ANEMIA				
	AN	MN	PS	JD	PT	BP	BH	AU	PJ	SS	PI
HR_{max}(bpm)	187	160	167	188	171	165	168	160	160	168	167
HR at VO_2max(bpm)	187	160	161	184	171	165	162	152	152	168	161
VO_2max(ml/kg/min)	46.2	53.2	39.7	52.1	51.9	52.5	41.9	38.9	46.1	41.9	53.8
O_2pulse(ml/beat)	19.7	18.7	18.3	13.9	14.7	19.6	17.7	18.7	18.0	14.5	18.3
WL_{max}(watts)	240	240	200	220	240	240	220	220	240	220	240
$V_E$max(l/min)	71.3	71.5	83.6	69.5	66.2	72.2	81.7	66.2	74.4	59.6	87.2
SaO_2(%)	87.0	88.0	86.0	85.0	80.0	83.0	77.0	81.0	76.0	79.0	77.0
R at Vo_{2max}	1.16	1.13	1.22	1.20	1.17	1.29	1.42	1.23	1.09	1.11	1.01
Lactate(mmol/l)	8.2	7.7	6.8	7.9	7.1	7.4	7.3	8.1	8.3	8.1	-

Anaerobic threshold data of 11 subjects at normoxia and hypoxia.

	control						anemia				
Parameter	AN	MN	PS	JD	PT	BP	BH	AU	PJ	SS	PI
NORMOXIA											
HR(bpm)	138	107	112	165	144	148	125	106	131	122	139
VO_2(ml/kg/min)	24.5	32.4	23.4	48.8	46.3	45.3	28.2	26.9	43.8	27.9	48.4
VO_2(%VO_2max)	47.0	54.6	52.9	83.9	76.3	72.5	52.9	58.0	57.9	56.5	75.6
O_2pulse(ml/beat)	13.7	16.3	15.5	13.8	17.4	18.8	15.5	18.5	19.8	13.3	19.0
SaO_2(%)	98	99	99	99	98	97	95	98	98	99	99
WL(watts)	120	100	80	160	160	200	100	120	180	100	180
V_E(l/min)	24.1	30.9	30.6	37.1	44.4	50.3	34.0	40.5	37.1	25.8	44.2
HYPOXIA											
HR(bpm)	122	111	121	157	144	134	120	109	114	106	114
VO_2(l/min)	17.5	31.2	19.3	30.0	33.3	32.3	21.4	23.1	27.7	20.3	28.4
VO_2(%VO_2max)	37.9	58.6	48.6	57.6	64.2	61.5	51.1	59.4	60.0	48.4	52.8
O_2pulse(ml/beat)	11.1	15.1	11.8	8.9	12.5	14.8	12.2	15.5	14.4	11.1	13.6
SaO_2(%)	86	90	81	90	83	83	87	87	88	86	86
WL(watts)	80	100	60	100	120	160	80	100	100	80	100
V_E(l/min)	18.0	27.5	26.0	26.7	41.5	37.5	30.9	36.2	36.7	25.1	29.3