steady-state exercise has ceased, changes have to occur to ensure a return back to normal resting physiology. Ultimately each of the cardiovascular variables (CO, BP and TPR) must return to normal resting levels. Recovery is not an immediate process, with the following factors being crucial to this (delayed) adjustment back to normal resting levels:

i. Decreased sympathetic activity, and therefore a decreased arteriolar venous tone which reduces venous return, could compound venous pooling. The venous pooling would in turn lead to EDV decreases, a lower CO and a fall in blood pressure;

ii. A decreased skeletal muscle pump mechanism reduces venous return and cardiac output and therefore results in a decreased BP;

iii. A fall in tidal volume which reduces the thoracico-abdominal pump has the effect of decreasing venous return and therefore results in a reduction of BP;

iv. Reduced levels of circulating catecholamines have the effect of constricting vessels in the lower limb which results in the venous return being substantially reduced and leads to a chain of events culminating in a reduced BP;

heart. These changes are associated with catecholamine initiated increases in cardiac output and a reduction of vasomotor tone (as a result of sympathetic nerve mediated or metabolic vasodilation of arterioles) which lead to variations in distribution of blood to certain organs. The organs which normally experience high blood flow at rest tend to encounter the greatest reductions (eg the splanchnic circulation) in blood flow during exercise; and,

iii. Lastly, the systematic and repetitive contraction of skeletal muscle leads to an increased flow of venous blood from the muscle beds. Heightened respiratory effort and cadence also elevates venous return via the thoracico-abdominal pump mechanism. These two pumps ensure a shift in venous blood from the periphery to central components.

A third factor affecting HV is myocardial contractility, the property of cardiac muscle which determines its ability to shorten independent of preload and afterload. This increased contractility is brought about by circulating catecholamines acting on beta receptors. The activation of beta receptors stimulates metabolic changes, an influx of calcium and the excitation and coupling of actin and myosin.

All of the above changes facilitate the body in supplying the increased levels of oxygen and oxidizable substrate which are required for exercise to take place. But after

In the peripheral circulatory system and ensures an elevated venous return to the heart. At the onset of dynamic exercise, systemic arterial pressure and systemic volume suddenly drop, with central venous pressure and volume abruptly rising. The dilation of vessels seen in the muscle and skin to accommodate nutrient supply and thermoregulation requirements is not fully compensated by reductions in blood flow at the splanchnic bed. As a result total peripheral resistance (TPR) falls, as does diastolic blood pressure (DBP). Even though systolic blood pressure (SBP) is maintained, or even increased, the fall in DBP is enough to decrease the mean blood pressure. The rise in cardiac filling pressure which causes the EDV to increase is attributable to an elevation in blood flow into the central circulation, accompanied by a reciprocal drop in the peripheral blood volume. This shift in blood distribution is a result of the following three events:

I. A transient reduction in peripheral blood flow which follows arteriole dilation, decreases the venous blood volume and results in a fall in venous transmural pressure. The elasticity of the more expansive veins, which are then less distended, passively expel a portion of their volume mainly from venules and small veins toward the heart. The movement of blood in this direction continues despite a declining pressure gradient, until the stage when the pressure gradient is so small that flow is reduced to zero;

II. Sympathetic nervous system initiated constriction in certain portions of the venous system ensure increased movement of blood towards the

63% of the elevated cardiac output. The remainder of the increase in cardiac output results from elevation of the SV.

Stroke volume expansion results from: elevations in venous return, and therefore in ventricular diastolic volume; adjustments in systemic vascular impedance; and enhanced myocardial contractility. These changes are facilitated by, amongst other factors, the actions of the skeletal muscle and the abdominal and respiratory pumps.

As an increase in cardiac output is a direct result of an elevated stroke volume, it is essential to establish the mechanisms which lead to such a change. One factor is the filling volume of the left ventricle - also known as preload. Another is the force or stress which the ventricle must generate and sustain in order to eject blood into the aorta (afterload). Lastly there is myocardial contractility.

Preload, measured by cardiac sarcomere length, is proportional to the left ventricular volume or to the force in the muscle wall before contraction. Although it is often thought to increase during exercise, there are limitations in the techniques used to measure the left ventricular end diastolic volume (LVEDV). Studies report increases, decreases and no change at all. However there is a direct relationship between end diastolic volume (EDV) and the force of contraction - the Frank-Starling mechanism. Thus stroke volume is directly related to EDV.

The increased preload during exercise is largely a result of adjustments to the second factor affecting stroke volume, the change in vascular impedance. This change is seen

CHAPTER ONE: LITERATURE REVIEW

1. Introduction.

1.1 Changes seen in the cardiovascular system during and after exercise.

Many reviews have discussed the changes which occur in the cardiovascular system during exercise (eg Astrand [2], McArdle[41] and Rowell [86]). These reviews indicate that at the onset of exercise there is a great increase in the need for oxygen and oxidizable substrate, and an increase in metabolism which results in the production of large quantities of CO_2. To this end both oxygen delivery and carbon dioxide removal must increase if appropriate levels of arterial and tissue gasses are to be maintained. These outcomes are mainly achieved by an increase in ventilation and an increase in cardiac output (CO).

The elevation in cardiac output is accomplished through a number of changes in cardiac function and in the peripheral circulatory system. Up to an eightfold increase in cardiac output is achieved as a result of accretions in stroke volume (SV) and heart rate (HR). One of the first changes seen at the onset of exercise is the augmentation in heart rate which results from parasympathetic inhibition and then from sympathetic stimulation. In exercise in the upright position this augmented HR is responsible for

List of abbreviations used

BMI	Body mass index
BP	Blood pressure
BV	Blood volume
C	Creatinine
CV	Red cell volume
DBP	Diastolic blood pressure
EAC	Exercise-associated collapse
Hb	Haemoglobin
Hct	Haematocrit
IV	Intravenous
MAP	Mean arterial pressure
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean cell volume
PP	Pulse pressure
PV	Plasma volume
RBC	Red blood cell
SBP	Systolic blood pressure
SD	Standard deviation
TBW	Total body water
TPR	Total peripheral resistance
U	Urea

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In summary:

To all my supporters, thanks - I couldn't have done it without you.

Abstract.

A post-exercise reduction in blood pressure (BP) may be the primary reason that athletes suffer from exercise-associated collapse (EAC) at the end of ultra-endurance running events. Plasma volume decreases, possibly caused by dehydration, may be the cause of the decrease in blood pressure. In order to determine whether there is a correlation between plasma volume changes and the post-exercise BP drop, this study evaluated alterations in pre- and post-race blood pressures and changes in blood and plasma volumes. It found that compared to resting values, systolic, diastolic and mean arterial blood pressures (mmHg) fell significantly from 119 ± 4, mean ± standard deviation, 74 ± 8, and 88 ± 5 respectively to 106 ± 14, 62 ± 12 and 77 ± 10 ($p \leq 0.05$), whereas pulse pressure failed to change. Compared to pre-race values, plasma and blood volume were found not to have changed significantly. During the race plasma urea (U) and creatinine (C) concentrations increased significantly, whereas body mass and body mass index both fell significantly. Haematocrit, haemoglobin, mean cell volume, red blood cell number, mean cell haemoglobin concentration, the mean cell haemoglobin, plasma sodium, potassium, chloride and protein concentrations, the U:C ratio and osmolality remained constant. There were no significant correlations between changes in plasma or blood volume and changes in blood pressure. These data support the idea that a post-race decrease in blood pressure does not result primarily from an intravascular fluid loss. It is likely therefore that athletes who collapse at the end of ultraendurance races due to EAC do so as a result of 'post-exercise hypotension' secondary to venous pooling, and not as a result of a reduction in plasma volume.

Declaration.

I, Ari Jack Buntman, declare that this research report is my own work. It is being submitted for the degree of Master of Science in Medicine in Applied Physiology to the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

..... 5th day of September, 1997.

INTRAVASCULAR DEHYDRATION AND CHANGES IN BLOOD PRESSURE IN ULTRA-MARATHON RUNNERS

Ari Jack Buntman

A research report to the Faculty of Medicine, University of the Witwatersrand, in partial fulfilment of the requirements for the degree of Master of Science in Medicine in Applied Physiology

Johannesburg, 1997

that very large changes in blood and plasma volume are required to produce sustained hypotension.

The question arises therefore whether exercise-induced changes in PV can be prevented. If this is possible, then a post-exercise fall in blood pressure caused by dehydration can theoretically also be prevented.

Convertino [8] and others [49] have shown that the reduced volume quickly returns to normal once exercise has ceased and they have suggested that this increase was due to the movement of protein and water back into the intravascular space [8].

Exogenous fluid replacement is also critical. Apart from Wyndham's studies, Kaminsky and Paul's paper [38] on plasma volume in athletes competing in races between 50 and 100 km, reported both haemoconcentration and haemodilution. They concluded that fluid intake played a major role in changes of plasma volume, with quantity of fluid replacement effecting final plasma volume. The runners who drank more displayed haemodilution, and the runners who drank less, haemoconcentration.

In another study of prolonged exercise in the heat it was established that plasma volume decreased to a similar degree when different replacement drinks were consumed [62]. Varying the carbohydrate content of such drinks did little to prevent intravascular dehydration. This view is supported by Kaminsky and Paul [36] who asserted that if the ingredients of the replacement drink contained sodium, this may

In response to the dehydration and haemoconcentration, several changes were seen in the cardiovascular system. The greater the dehydration, the greater the decrease in stroke volume (with a maximum reduction of 27%). This reduced volume was accompanied by increases in heart rate which resulted in similar forearm blood flows for the varying levels of dehydration. These findings were consistent until the time when plasma volume decreased below the 8.5% mark. Around this point forearm blood flows became 20 - 22% lower than the group who had only experienced weight losses of 1.1± 0.1%. Changes in forearm blood flow were seen despite no change in forearm venous volume.

The study of Montain and Coyle led them to conclude that the cardiovascular system compensates adequately (ie maintains BP) until stroke volume has fallen by about 10% and plasma volume by about 8.5%. Further reductions in stroke and plasma volume lead to a decrease in blood pressure.

This viewpoint is supported by both Guyton [25] and Caroline [7]. The former asserted that reductions in blood volume of 10% resulted in "no significant effect on either arterial pressure or cardiac output" , and the latter suggested that cardiovascular homeostasis was preserved until BV decreases by 16 percent. In addition acute haemorrhage amounting to 8% blood loss has no effect on BP provided that baroreceptor reflexes are intact [61]. The findings of Montain and Coyle and those of Guyton and Caroline imply

figures portrayed a drop in body weight of 4% and a 16 - 18% decrease in plasma volume, which was considerably more than that measured by Sawka [67].

In Costill's study [11] the total reduction in plasma volume could be separated into immediate and delayed changes. The initial reduction in plasma volume (12.2%) seen at the onset of exercise was attributed to a "transcapillary" fluid flux into working musculature, and the remaining decrease (3.6%) was noted to take place over the next 110 minutes of exercise.

Having established that plasma volume does in some cases reduce, it is important to evaluate the effect of this haemoconcentration. The ability of the cardiovascular system to adjust to decreases in plasma volume was evaluated by Montain and Coyle [42]. Their study on cyclists yielded very interesting results which illuminated the cardiovascular response to different levels of dehydration. In their experiment subjects cycled at 62-67% of maximal oxygen consumption for two hours, while ingesting varying quantities of fluid, resulting in graded levels of dehydration.

In the first 40 minutes of the experiment blood volume changes were not different between the various fluid-intake groups. After 40 minutes subjects in the moderate and large fluid intake groups (who experienced a total weight loss of 1.1± 0.1 to 2.3 ± 0.1%) had maintained their plasma volumes. However the men in the no-fluid and low-fluid group (these athletes experienced a decrease in body weight of between 3.4 ± 0.1 and 4.2 ± 0.1 kg) displayed a decrease in plasma volume 2-3% below resting levels.

Nevertheless Kolka did note that haemodilution might be present even if a subject is dehydrated (5.4 kg body mass loss) [39].

On the other hand, evidence of a decrease in plasma volume during exercise was noted by Fortney and Senay [20]. Their study of women exercising at 40% VO_2 max. (in both a hot and a cooler environment) showed that exercise resulted in a decrease in plasma volume - with the exercise in the heat eliciting a 7% greater plasma volume decrease than it did in the cold. In addition it appeared that females may exhibit a greater tendency to reduce their plasma volume than do men exercising in similar conditions[20].

Reductions in plasma volume were also noticed in Myhre's study [43] of middle aged marathon runners. At six kilometres into the race Myhre recorded a 1% decrease in body weight and a plasma volume reduction in the region of 6,5%. Although the plasma volume stabilized from the six-kilometre mark onwards, the reduction in body weight continued, with an additional fall of 3.2%.

Myhre's results were supported by Sawka [57] who showed that subjects who were dehydrated by 4.9 ± 0.4 % had similar decreases in their plasma volume (5.0 ± 6.0%). These findings in turn were supported by Costill et al [11] who showed that a drop in body weight, induced either by exercise or exposure to heat, was associated with a decrease in plasma volume. Costill et al [11] further illustrated a greater percentage decline in plasma volume than the percentage decrease in total body weight. Their

1.2.1 Theory One: Exercise-associated collapse as a result of hypovolaemia.

During both endurance (longer than an hour but less than two-and-a-half hours) and ultra-endurance (longer than two-and-a-half hours) exercise the plasma volume has been reported to either increase [35, 39, 45, 57], decrease [11, 20, 26, 43, 57], or not to change at all [36].

If plasma volume increases during exercise it is important to justify the cause of this increase. Many researchers have found a linear relationship between the hydration status of the athletes and their plasma volume. Both Sawka [57], and Kaminsky and Paul [35], demonstrated an increase in plasma volume during exercise. In Sawka's study the subjects were all euhydrated, which led him to deduce that external fluid replacement was influential in maintaining body weight and increasing the plasma volume. Kaminsky and Paul [35] suggested that the plasma volume expansion is the result of haemodilution secondary to a high fluid intake. They showed that athletes competing at a heart rate of 130 beats. min^{-1} for three hours had an increase in their plasma volume during exercise.

In another study of marathon runners, haemodilution was identified by the end of the race [30]. However this increase in plasma volume appeared to be artefactual and was attributed to positional variation: the initial plasma volume estimations were made in an upright position, whereas final readings were taken while the subjects were supine.

due to a marked exercise induced vasodilation of the vascular tree in the legs, and secondly to a failure of the muscular venopressor mechanism in the legs to continue to work after exercise has ceased.

On cessation of exercise the ideal response would be for the body to automatically reverse the effects previously described. Significant arteriolar vasoconstriction in the legs would have the effect of maintaining venous return, in the absence of the 'muscle-pump', which would then ensure an adequate blood pressure and tissue perfusion. However Elchna found the body's response was dissimilar to the 'ideal resp ' required. Rather the body failed to respond as the exercise ceased resulting in a decreased venous return and collapse. Syncope was the body's natural mechanism to re-establish a normal BP and a normal level of consciousness. Noakes described this phenomenon, "post-exercise (postural) hypotension" [3b], by suggesting that there is a drop in central blood volume which is caused by a pooling of blood in the peripheral veins.

In summary, it is possible, therefore, to postulate that EAC develops as a result of rapidly occurring, severe hypotension. This reduced blood pressure would be secondary to either a fall in plasma and blood volume, caused by heat-induced dehydration, or as a result of profound and persistent post-exercise venous pooling.

Their findings were fascinating.

> "Of 33 men subjected to acute exhausting physical work approximately one-half (19 or 57.6%) developed post-exertional orthostatic hypotension, with nine (27.3%) in the syncopal group and 10 (30.3%) in the abnormal group. Thus, every other man developed post-exertional orthostatic hypotension and one man in four had syncope [16]."

A second intriguing aspect of Eichna et al's study was the physical observations made about those subjects who did collapse and about those who nearly collapsed.

> "Almost invariably present were marked fatigue, drowsiness, apprehensiveness, increasing discomfort, nausea, abdominal cramps, lightheadedness and dizziness, and the sensation of impending collapse. In the more severe instances ... vomiting, disorientation, inability to move or obey commands ... and crumpling at the knees, at which time the men were laid flat. ... Once supine, all symptoms quickly improved or disappeared completely [16]."

At no stage in their study was any IV therapy administered, and there was also no medical intervention apart from lying the patients in a supine position. Although not conclusively proven, all indications were that a decrease in venous return was responsible for the circulatory failure. This decrease, they postulated [16], was probably

dehydrated, rarely collapse, [51] and clinically serious levels of dehydration have never been recorded in any large group of athletes competing in a modern ultra-endurance event [51].

The argument against the 'hyperthermic dehydration-model' leads to the formulation of a second school of thought which purports that athletes collapse as a result of peripheral venous pooling. This pooling is thought to lead to reduced venous return, a diminished cardiac output and a decreased systolic BP [50]. Assuming that the hypotension is not caused by a drop in intravascular volume [51], the treatment for such a condition would be to simply lie the patient in a supine position, elevate their feet and pelvis [49], thereby enhancing venous return and normalising BP. To justify this theory Noakes turned to the work of, among others, Elchna, Horvath and Bean [16] who in 1947 postulated that non-hypovolaemic ("post-exertional") hypotension was associated with a cessation of exercise.

In Elchna et al's study[16] BP, pulse and all other relevant signs and symptoms of 33 well trained men who had completed certain exercise regimens, which included endurance and power exercises, were monitored. Measurements were taken in both vertical and supine positions at specified intervals.

The article by Wyndham and Strydom [66] marked the start of a period in which administrators and the medical profession began to aim at ensuring that endurance athletes drank more. Those who failed to take heed of the warnings and later collapsed from what was thought to be dehydration and/or heatstroke, were 'resuscitated' by replacing what was thought to be lost fluid. The medical staff at ultra-endurance races believed that the cardio-vascular system of collapsed athletes was effective and still intact. Therefore the only factor that could be causing the hypotension, taking into consideration the weight loss experienced by athletes, was a decreased amount of blood (fluid) which they believed should be replaced intravenously.

This dogma found much popularity until it was challenged by Noakes [49], who argued that dehydration and fluid loss was not the primary reason for collapse. The main thrusts of his argument are: firstly, most (> 80%) ultra-marathon runners develop EAC after they have stopped running [34], therefore suggesting that there is not a substantial decrease in the athletes' blood volume; secondly, those athletes suffering from EAC show no signs of circulatory shock in the supine position, indicating that their intravascular contents are intact; and thirdly, most EAC runners have core temperatures (rectal temperatures) within normal limits and are not hyperthermic [1, 34, 44].

These assertions are supported by evidence from both the Two Oceans and Comrades ultra-marathons which indicates that the majority of runners who require medical assistance after collapsing are undertrained, hyperhydrated and finish in the last hour of the race [56]. In contrast, the fastest runners, who are the hottest and most

appropriate aetiology there is a chance that the treatment could be inappropriate and unnecessary, or even harmful [37].

In general there are two major theories regarding EAC. The first theory revolves around the concept that most collapsed athletes experience a reduction in plasma and blood volume which in turn reduces the quantity of circulating blood and results in a hypotensive episode [9, 22, 33, 45, 51, 54, 66, 67]. This condition has primarily been blamed on hyperthermia, exacerbated by dehydration [33, 66]. In order to correct this 'dehydration' the traditional treatment for these athletes has been to infuse intravenous (IV) fluids, thus replenishing their intravascular volume and elevating their blood pressure. Taking into consideration that the hypotensive symptom is usually reversed after IV therapy there is an assumption that the treatment is appropriate.

As Noakes noted [60], one of the first attempts to describe this phenomenon in detail was that of Wyndham and Strydom [66]. They demonstrated a direct relationship between hyperthermia (elevated rectal temperatures) and inadequate water intake. From their findings they concluded that heat-related complications during prolonged exercise could be reduced or even avoided if fluid losses were replaced appropriately. As the title of their paper "The danger of an inadequate water intake during marathon running" suggests, they recommended increased "water intake" to avoid dehydration and hyperthermia. In another paper Wyndham [67] asserted that marathon runners consumed far too little fluid which, associated with marked weight reductions, high sweat losses and massive heat production, led to heatstroke and collapse.

increased number of participants has been a greater number of casualties [40]. Of the athletes who enter ultra-endurance events, 0.16% to 4.7% will collapse during or after the race [22].

The aetiology of collapse can be divided into two groups. The first group includes those instances where a known medical condition can be clearly identified as being the cause of the collapse. A few examples of this may be hypothermia[45], hypoglycaemia [22, 58, 62], hyponatraemia [46], gastroenteritis [34] or myocardial ischaemia[34]. The second type of collapse is that which occurs without obvious cause. These latter patients usually respond very well to emergency treatment and walk out of the medical facility a short while later. This latter type of collapse will be termed "exercise-associated collapse". [52] Exercise-associated collapse (EAC) has been defined as "an inability to stand or walk unaided as a result of light-headedness, faintness, dizziness, or syncope [34,56]."

One of the most basic tenets of physiology is that a normal blood pressure is essential if one is to sustain bodily function. Without an adequate BP the body will fail to perfuse vital organs and peripheral tissues adequately resulting in a state of shock. If one is to look for a common characteristic in most collapsed athletes, it is undoubtedly their inability to stand as a result of hypotension.

For the medical profession to treat these people appropriately, it is imperative to understand the pathophysiology of the athletes' ailment. Without understanding the

v. The continued post-exercise thermoregulation, which causes vessels in the skin to remain dilated, results in an expanded peripheral blood vessel volume. This results in a decreased total peripheral resistance and causes a lower DBP and a reduced MAP;

vi. Oxygen debt results in an increased post-exercise demand for oxygen, and ensures that recovery is not an immediate process. The continued demand for a higher than normal oxygen requirement is supplied by increased blood flow to muscles which lowers the TPR; and,

vii. Dehydration with reduced plasma and/ . volume (BV), if present, may also reduce venous return.

In summary this continued elevation of circulatory demands lead to a staggered reversal of changes in the circulatory system which accompany the onset of exercise and a return to normal resting function can be delayed. During this period of delayed recovery, some athletes are unable to maintain adequate blood pressures, and collapse.

1.2 Exercise-associated Collapse.

Over the last two decades endurance sport has grown in popularity and stature to a stage when events can attract in excess of 10 000 athletes. Accompanied by the

consideration, it was decided that venous blood samples would be used exclusively, and that for the purposes of this study all samples would be drawn in the erect posture

In order to further reduce any chance of error, venous blood samples were taken from the subjects' arm in a position similar to the contralateral arm from where blood pressures were assessed. This was done to eliminate inaccurate readings associated with positional variations. An example of such a problem is that if one compares blood samples taken from the antecubital vein of a pendant arm to blood samples taken from the same arm in a horizontal position, there is a change in haematocrit equivalent to a 3% decrease in blood volume[17].

In consultation with Professor B Mendelow and Mr D Clifford of the haematological laboratory of the South African Institute of Medical Research (SAIMR), it was decided that analysis of blood would be most accurate if results were obtained as soon as possible after having drawn the sample. To this end, the eight-day pre-race samples were analysed in the SAIMR laboratory using an automated device (Coulter STKS). The one-hour pre- and post-race samples were also analysed by the SAIMR, however this time a portable automated analyser (Sysmex K 4500) was utilized. These two instruments are regarded by the SAIMR as being equally accurate. The procedure followed therefore was that within an hour after sampling, a blood aliquot from each subject was analysed for Haemoglobin (Hb) content and Haematocrit (Hct). No correction was made to the packed cell volume for either trapped plasma or for differences between venous and whole packed cell volume[14, 23]. A second sample was

It was assumed that the automatic sphygmomanometer used for this study was calibrated, and that drift was minimal. Even if these assumptions are false, the blood pressure data generated remain valid. The rationale for this assertion is that the main aim of the study was to assess changes in blood pressure over an eight day period. Any errors therefore are most probably systematic as calibration errors of a non-linear nature are very unlikely. Therefore it is assumed that relative values are correct even if the absolute values are slightly inaccurate.

1.5 Blood Analysis and Sampling.

While the subjects were standing upright venous blood samples were drawn from a superficial vein in the left antecubital fossa. The arm was supported at about 30° to the horizontal in each subject. Using the Vacutainer system, blood samples were placed in both red-top (containing no anti-coagulant) and purple-top tubes, the latter containing di-potassium ethylene-diamine-tetra-acetic acid (EDTA (K_3)).

This blood sampling protocol was designed to avert the problems associated with changes in blood composition allied to variations in posture. Secondly it was decided not to utilize arterial blood samples in order to avoid any complications of withdrawing such a sample. The extraction of arterial blood samples is difficult, more time consuming and can have serious side-effects (eg. extensive extravasation). Even though the composition of venous blood differs somewhat from that of arterial blood (for example venous blood has a higher Hct and lower chloride concentration) it was felt such differences would produce a systematic error. Taking all factors into

1.4 BP Measurement.

To measure BP each subjects' right arm was completely supported, a medium-sized cuff was placed approximately three centimetres proximal to the antecubital fossa and the arm was elevated in such a manner as to ensure that the cuff was level with the subjects' heart. Blood pressure was then taken using a Dinamap 8100 monitor (Johnson and Johnson, Johannesburg, South Africa). The Dinamap provided SBP and DBP. Using the SBP and DBP, pulse pressure and mean arterial pressure were calculated.

Campbell [5] asserted that auscultatory methods of measuring BP post-exercise are inaccurate and that errors of up to 30mmHg have been reported. To eradicate errors during field and laboratory studies (such as incorrect cuff deflation rate, venous congestion during repeated measurement, and external noises which could possibly effect a researcher's ability to hear Korotkoff sounds) a number of researchers have used automatic sphygmomanometers [18]. Although there is some criticism that these devices lose accuracy [6], many exercise physiologists believe in their merits. Cade et al [3] used a Dinamap 850 automatic blood pressure measuring device to measure BP in a standing position, and a Dinamap 8100T was used by Holtzhausen [24] to measure BPs in the field. Further support for the use of these devices is contained in the finding that measurements taken by a Dinamap correlate extremely well with interarterial catheter pressures, especially over normal BP ranges (SBP:37-109mmHg, DBP 21 - 78mmHg) [32].

To this end great care has been taken in the experimental design of this study to prevent the occurrence of posture-related changes in plasma volume. As mentioned previously blood composition, blood pressures and intravascular volumes are all affected by posture. Thus to reduce the possibility of this as a source of error, all measurements pertaining to blood pressure and haematological indices were taken in the erect position.

1.3 Subjects.

Eight healthy males volunteered for the study which was sanctioned by The University of the Witwatersrand's Committee for Research on Human Subjects (Medical) - protocol # M 950806. Informed written consent was attained from each subject.

The subjects first met in Johannesburg at 07h00, eight days before the race. The time of 07h00 corresponded to the time the ultra-marathon would begin and thus reflected early morning physiological status of the subjects. They had been instructed to eat and drink over the preceding 24 hours as they would the day before the race. They were weighed on a Seca, Alpha 770 (Vogel and Halke, Hamburg, Germany) scale in socks, running shorts and a T-shirt and their height was measured. The subjects were allowed to walk around freely before being instructed to stand quietly for about five minutes. During this period (10 - 15 minutes in all) vascular and other volumes were expected to equilibrate [39] and the subjects to have become comfortable with the surroundings.

documented that posture also affects plasma volume and that a plasma volume reduction of greater than 11% can occur when a person suddenly assumes a motionless erect position after having been in a supine position [27, 60]. Other studies have shown that when a person moves from a reclining position to a standing position there is a shift of body water from plasma to interstitial spaces [11]

One of these studies was conducted by Pivarnik [53] who noted a reduction in plasma volume when assuming a seated position from supine. A further reduction was experienced when exercise began. He concluded that the first reduction is a result of "vascular fluid" being "sequestrated in the subcutaneous spaces of the legs" and that exercise leads to further decreases in plasma volume as a result of movement of plasma out of the circulating volume into the intramuscular compartment. This view has been supported by Gore et al [23] and Hagan et al [26].

As a result of his experiment in runners and cyclists, Gore [23] concluded that the plasma volume reduction evident when runners began running was not a result of the exercise itself but was rather caused by a positional change when the subjects moved from a seated to an erect position.

Hagan et al's [26] paper supported previous researchers [11, 26, 53] in that he described how plasma volume changes when humans assume an erect position after being in a supine position and vice versa. Redistribution of fluid between the various fluid compartments, rather than loss of the fluid volume, seem therefore to be an important factor affecting plasma volume.

The runners were all based in Johannesburg (altitude approximately 1800m) and travelled to Durban (sea-level) for the race. They were at the coast for a maximum of two days prior to running the Comrades marathon. Table 5 shows that several of the measured variables differed between Johannesburg (eight-day pre-race measurement) and Durban (one-hour pre-race measurements). None of these differences were attributed to a change in altitude as runners were at sea-level for too short a time to have acclimatised [41]. Therefore the changes in the variables from Johannesburg to Durban were considered not to be altitude-related and any effect that altitude might have had has been considered to be negligible.

This study set out to evaluate if blood volume and/or blood pressure changed during an ultra-marathon race. If a significant fall in BP occurred without a change in plasma or blood volume then it could be concluded that venous pooling had occurred. If on the other hand both plasma volume and BP fell significantly then it could be deduced that the fall in plasma volume resulted in the reduced blood pressure. It is also possible that each theory is not mutually exclusive and that both play some role in the drop of blood pressure which occurs on the cessation of exercise.

1.2 Posture.

Great care has been taken in this study to eliminate the possible effect of postural changes on intravascular fluid dynamics. The studies mentioned later in this chapter investigate the measurement of plasma volume during and after exercise. In addition to the difficulties in obtaining accurate measurement of plasma volumes it is well

CHAPTER TWO. MATERIALS, METHODS AND RESULTS.

1. Materials and Methods.

1.1 Experimental Design.

To assess whether a change in blood volume is related to an altered blood pressure, BPs, blood and plasma volume, body mass and various blood variables were evaluated before and after an ultra-marathon in eight subjects. The ultra-marathon was the 87km Comrades Marathon from Durban to Pietermaritzburg, South Africa, which took place on Monday, June 18, 1996.

Pre-race assessments were carried out twice, once eight days before the race and the second an hour prior to the race start. A post-race evaluation was conducted immediately after the subjects completed the event. Thus in this study each subject acted as their own control, and problems which can confound studies that compare two groups, were eliminated.

During the race the average ambient temperature was $23.6 \pm 4.1\ ^{0}C$. Each subject was permitted to drink and eat *ad libitum* during the race, but most restricted themselves to rehydrating with water and Coca Cola or a mixture of the two. After completing the race the subjects immediately walked to the official medical tent. Once there, BP and body mass were measured and a third set of blood samples were drawn.

The main thrust of the second theory is that at the completion of ultra-endurance events, certain athletes suffer from significant venous pooling in their lower limbs which can lead to a decreased blood pressure and collapse.

In the literature review each theory has been examined, as have other aspects which are central to understanding the merits of each argument. As both theories have been investigated it remains to be tested which of intravascular volume depletion or venous pooling is the greater contributor to a post-exercise reduction in blood pressure and ultimately to exercise-associated collapse. The primary aim of this study is to evaluate therefore if there is a correlation between changes in intravascular volumes and changes in blood pressure in subjects who have completed an ultra-distance marathon.

al [34] to argue that the most likely mechanism for the EAC was "orthostatic hypotension", a mechanism which Noakes's [49] and Hagan's [26] data support.

In a later paper Holtzhausen [35] defined 'post-exercise postural hypotension' as "a decline in systolic blood pressure of at least 20mmHg below supine values on assuming the upright (erect) posture, associated with syncopal symptoms." This definition, and the mechanism of EAC which it implies, is gaining recognition as an important cause of EAC. Whether this mechanism occurs independently of changes in plasma volume is however unknown.

Although concluding that orthostatic hypotension was the major cause of EAC in her subjects, Holtzhausen et al [35] also found that the EAC group showed greater plasma volume change than did her control group. The study conducted for this short report attempts to clarify therefore whether EAC is associated with venous pooling and/or hypovolaemia.

1.3 Summary.

In summary, there are two primary theories which attempt to explain why athletes who are otherwise asymptomatic collapse at the end of ultra-endurance sporting events. In the first theory it is argued that heat-induced dehydration causes a drop in plasma and blood volume which leads to a lowered blood pressure and collapse.

and then elevating their legs and pelvis - which has the effect of both increasing their central and circulating blood volumes. The central volume increases as a result of a gravity-induced autotransfusion of blood which has pooled in the lower limbs [48], and the circulating volume rises from an influx of fluid into the intravascular compartment from the surrounding interstitial spaces [11]. The latter aspect was supported in theory by Hagan[26] who asserted that when a resting individual moves from an erect to a supine position, there is a net increase in plasma volume of about half a litre. The therapeutic effect of such a change in plasma volume could be enhanced if change in posture was applied to a runner whose blood volume had been pooled in the lower half of their body.

One of the most significant studies which attempted to explain that EAC was a result of venous pooling was carried out by Holtzhausen et al [34]. She and her fellow researchers reported that the athletes' mean erect systolic BP was 10mmHg lower than their supine measurement five minutes after completing a race. They also reported that their subjects' post-race supine measurement was 10 mmHg lower than their normal supine measurement . This drop was not present 24 hours later. Holtzhausen et al concluded that the collapsed athletes, who were otherwise asymptomatic, suffered from a hypotensive response. The athletes also had the following factors in common: 85% of those who collapse did so at the end of the race, their collapse was associated with increased effort (as it occurs more at medal cut-off times) and EAC runners exhibited greater plasma volume changes than did the control group. This lead Holtzhausen et

contains an adequate amount of glucose and electrolytes. Although there is much debate regarding the physiological response to exercise, it is fair to support Fellman who said that :

> "Changes in plasma volume during exercise can include haemodilution or haemoconcentration depending on the type of exercise, intensity and ambient conditions. In most cases, and systematically if exercise is performed in a hot environment, haemoconcentration is the dominant response [19]. "

1.2.2. Theory Two: EAC as a result of venous pooling of blood.

Compared with studies conducted to evaluate the changes in plasma volume, very few researchers have investigated post-exercise venous pooling. One of the few who have reported on the subject was Senay [58]. Although not referred to directly, he alluded to the possible mechanism for collapse at the end of races. He detailed how at the onset of exercise changes in peripheral vascular resistance, the beginning of muscle pump action and increased perfusion of muscle tissue, result in an increased volume of blood in the lower limbs. At the cessation of exercise the body's inability to rapidly reverse these changes would result in a decrease in the central blood v... an acute hypotensive episode would follow and these could lead to syncope and EAC.

If this idea is correct then reversal of venous pooling will cause a recovery. The treatment for EAC proposed by Noakes [49] involves lying a patient in a supine position

have the effect of reducing hyponatraemia in haemodiluted runners, even if it did not reduce haemoconcentration. They argued that quantity of the fluid ingested, and not the content, plays the most important role in predicting plasma volume changes.

On the other hand Criswell's study[12] on oral fluid replacement showed that replacement with a glucose-polymer electrolyte drink resulted in lower plasma volume losses than ingesting water alone. In addition, he showed that the more stable plasma volume was not the result of differences in plasma concentration of either vasopressin and/or aldosterone.

Having assessed numerous different studies it appears that the research has led to conflicting findings - with some studies indicating that the content of a replacement drink has little to do with ultimate plasma volume and others indicating that it plays a very important role.

When one evaluates performance, Cade et al [3] have shown that runners who replace lost fluid with water alone, show a greater deterioration in performance when compared to a group who ingested a glucose-electrolyte solution. It is also interesting to note that the runners who drank water alone, were the only group who displayed plasma volume decreases of 10% or more.

In all likelihood it is probably accurate to predict that peak performance is only possible when an athlete replaces lost fluid with the appropriate quantity of fluid which

TABLE 1 : ANTHROPOMETRIC, TRAINING AND COMPETITION DETAILS.										
VARIABLE	SUBJECTS								MEAN	SD
	1	2	3	4	5	6	7	8		
Height (cm)	191	181	194	174	174	170	185	171	180	9
Age	42	36	29	35	48	50	43	48	41	7
Weekly training km	55	70	95	90	80	80	70	70	76	12
# of weeks spent training for 1996 Comrades	20	14	20	20	20	27	24	13	20	4
Total km trained	1150	980	1900	1800	1800	1830	1000	910	1396	399
# of previous Comrades completed	2	0	1	8	10	3	0	29	6.83	9.6
Best Comrades time (min)	537	0	613	516	448	550	0	403	511	78

2.5 Intravascular Volume Changes.

Using the formulae described by Dill and Costill [14] to determine changes in intravascular fluid volumes, it was found that the subjects' average blood and plasma volume failed to significantly change either before or during the race, as shown in Table 7.

2.6 Changes in Plasma Volume and Blood Pressure.

Table 8 shows that overall there was no change in plasma or blood volume, either before or during the race. The post-race blood pressure measurement however changed significantly from resting levels (measured eight days prior to the race being run (Table 5)). When these two variables were correlated with one another (Table 9), no significant correlations were found.

2.3 Biochemical Results.

Table 5 shows that the 1-hr pre-race values recorded for sodium, chloride, urea and the U:C ratio were significantly different from the values recorded 8 days previously. However potassium, creatinine, protein and osmolality values failed to change in the period before the race. During the race, values for urea and creatinine changed significantly compared with the 1-hr pre-race values, while sodium, potassium, chloride, osmolality, the U:C ratio and protein remained unchanged.

2.4 Blood Pressure Changes.

Tables 5 and 6 show that compared to eight-day pre-race measurements, the DBP, MAP and PP evaluated immediately before the race, had failed to change whereas SBP increased significantly. Comparing the post-race measurements with the one-hour pre-race values showed that during the race each blood pressure variable (SBP, DBP and MAP), except the pulse pressure, decreased significantly. When the eight-day pre-race BPs are compared to the post-race blood pressure values (rationale discussed in Chapter Three), one sees significant decreases in SBP, DBP and MAP.

More specifically the mean of the 8-day pre-race measurement of SBP was 119 mmHg and in the hour preceding the race it was 131mmHg, therefore increasing by 12 mmHg. By comparison the DBP only increased by 1mmHg. Compared to the one hour pre-race values mean SBP post-race was 25mmHg lower, DBP 13mmHg lower, MAP 15mmHg lower and PP moved from 56 to 44mmHg.

2. Results.

The subjects' anthropometric data are shown in Table 1. Haematological, biochemical and blood pressure values for each of the eight subjects, and the mean ± SD are listed in Tables 2, 3 and 4. Changes noted between the mean values for each of the three measuring sessions and their statistical significance are detailed in Table 5.

2.1 Anthropometric Results.

The subjects completed the race on average in 574 minutes (range: 468 - 649 min), in other words in about 9½ hours. This finish time corresponds to an average speed of 9.2 ± 0.9 $km.h^{-1}$. Before the race the subjects' mean body mass rose significantly by an average of 1.8kg, from 78.2 ± 7.1 kg to 80.0 ± 7.6 kg. During the race their body mass fell significantly from pre-race values to 76.8 ± 7.3 kg. Associated with the change in body mass, body mass index also changed significantly both before and during the race. (Table 1)

2.2 Haematological Results.

Table 5 summarizes the changes in the values recorded for the six haematological variables assessed (Hb, Hct, MCV, RBC, MCHC and MCH). None of these changed significantly either before or during the race.

In order to assess if the changes in blood and plasma volume were significant, a one sample nonparametric test was used. This tests whether the parameters differ significantly from zero. A *P* value of less than 0.05 was considered to be significant.

Graphpad's Instat Software, San Diego version 2.0 was used for statistical analysis.

been established, the Hct readings are used to estimate the percentage change in plasma and cell volumes. The formulas used to evaluate the above changes are as follows:

$$BV_A = BV_B (Hb_B / Hb_A)$$

$$CV_A = BV_A (Hct_A)$$

$$PV_A = BV_A - CV_A$$

Therefore:

$$\Delta BV, \% = 100 (BV_A - BV_B) / BV_B$$

$$\Delta CV, \% = 100 (CV_A - CV_B) / CV_B$$

$$\Delta PV, \% = 100 (PV_A - PV_B) / PV_B$$

The subscripts B and A refer to 'before' and 'after' an event (eg a marathon), respectively, and BV_B is taken to be 100 %.

1.7 Statistical Analysis.

All the results were calculated as the mean and standard deviation (SD). Statistical significance ($P < 0.05$) was determined for pre and post-race variables using an ANOVA one way analysis . In order to determine if the changes in blood pressures (SBP, DBP, MAP and PP) could be associated with the change in plasma volume, Pearson's product moment correlation coefficients were calculated. Significance was accepted at P values < 0.05.

three values. Admitting that there are some inherent 'leakage' problems [11, 20, 28, 30, 43, 46, 58, 59], Cade et al [3] argued that calculating the change in plasma volume using protein concentration does have some advantages but illuminates certain trends rather than providing exact figures .

The problems associated with 'leakage' may have some validity. Most of the above techniques rely on the assumption that MCV remains constant. Should this however alter, it would result in inaccurate measures of change in plasma volume. van Beaumont [64] argues that an increase in plasma osmolality of greater than 5 mosmol/kg H_2O accompanied by the blood pH remaining within 0.1pH units from resting values, will effect MCV and could therefore invalidate change in plasma volume readings. MCV swelling is usually seen when blood pH is less than 7.10, despite 20 mosmol/kg H_2O increments in plasma osmolality. Having said that, Kolk [39] reported that there was no significant change in MCV from initial values after competing in a standard marathon. Harrison [27] concluded:

> "In general the magnitude of change in plasma volume induced by thermal stress, exercise or a change in posture is similar whether calculated from changes in the haematocrit and haemoglobin concentration or from changes in total plasma protein concentration."

In this short report changes in plasma and blood volumes were estimated using the protocol of Dill and Costill [14]. This protocol utilizes the Hb content to first establish a percentage change in total blood volume. Once a change in total blood volume has

proportionately higher than the changes in Hct seem to indicate. To this end they recommended that if one only uses Hct to measure a plasma volume change, a proportionality factor of (100/(100 - Hct)) should be applied.

Possibly the most influential article discussing change in plasma volume is that of Dill and Costill [14]. They contended that there is adequate evidence that a decreased plasma volume is not a result of the loss of a protein-free filtrate, but that as plasma volume decreases so does the quantity of circulating protein. They calculate the extent of this intravascular loss to be 6% of total protein, for a 4% reduction in body weight, and they proposed that relative changes in plasma volume should be calculated from both haemoglobin and haematocrit and not haematocrit alone. The rationale for not using haematocrit alone is that Hct is distorted by alterations in the volume of red blood cells.

The procedure described by Dill and Costill [14] has found much support in the literature, with many researchers calculating change in plasma and blood volume using their protocol [12, 21, 30, 34, 36, 38, 39, 43, 52, 53, 57].

Despite the popularity of this method [14], Cade et al [3] argued that these results may not be accurate. The rationale for such criticism is that in their study they saw evidence of significant haemolysis in approximately 57% of their subjects. Instead of using Hct and Hb, they calculated relative changes in plasma volume using the change in concentrations of albumin, globulin and total plasma protein and [illegible] averaging the

A refinement of these methods of measuring changes in plasma volume is the protocol described by van Beaumont and his co-workers [64], which uses venous Hct (Hct_v) alone. Before one can assume that this method is an accurate form of measuring plasma volume the following must be true: the volume of circulating red corpuscles must remain constant, the ratio between Hct_v and whole body haematocrit must not alter and the red blood cell size must remain constant. If any of these have changed, which they generally do not, the result will be inaccurate [10, 11].

Greenleaf et al [24] asserted that in order to measure change in plasma volume one can use either Hct alone or Hct and Hb. If one is to use Hct on its own, the number of red blood cells (RBC) must remain constant as must the red cell volume (MCV). However they pointed out that in exercise of greater than two hours duration, the MCV may change, therefore invalidating this technique as an accurate measure of change in plasma volume.

However the above concerns of Greenleaf [24] appear to have been allayed by the findings of a number of studies. Harrison [20] reported only a 1% decrease in RBC volume during light and moderate exercise lasting 50 minutes. Sawka [57] found little change in subjects who began to exercise in an euhydrated state and Dill et al [15] demonstrated a 2% increase in red cell volume in five hours of moderate exercise.

van Beaumont et al [64] also investigated the assessment of plasma volume changes. In their study they evaluated if changes plasma volume were mimicked by proportional changes in Hct readings. They found that the plasma volume changes are

It has therefore been argued that relative changes in plasma volume can more accurately be estimated from measurements of Hb, rather than Hct, although Harrison, Edwards and Leitch [31] have suggested that most evidence indicates that the volume of circulating red cells remain constant during exercise and thermal stress. Harrison[28] therefore has argued that using Hb alone is the best method to measure a change in plasma volume for the following reasons:

i. Hct alone is inaccurate, as water is lost from the red cells during moderate exercise.

ii. Plasma proteins may be "translocated" during exercise (ie. they may be shifted from the extravascular space to the intravascular space).

iii. The increased concentration of plasma protein in the intravascular compartment increases oncotic pressure which favours water retention during and after exercise.

However by 1981 [30] Harrison's previous view [28] had obviously changed as he used both Hct and Hb, according to the protocol of Dill and Costill [14], to measure relative changes in plasma volume. Plasma volume changes can also be assessed using another method proposed by Harrison [27] whereby the corresponding values of Hb and the packed cell volume are measured. This method was utilized by Gore [23] in his study of plasma volume changes in runners and cyclists.

protein in the blood and equilibrates in the intravascular compartment. This enables the researcher to withdraw a sample and measure its concentration to calculate plasma volume. Concentration of the dye is measured using absorption spectrophotometry. The substances generally injected for this purpose, are Evans Blue and radioiodine (^{125}I and ^{131}I) albumin.

Fellman[19] has suggested that protein labelling is only reliable for steady state plasma volume measurement. She is supported by Harrison [28] when he stated:

> "The dilution technique, although suited to the discrete measurement of blood volume, is not generally regarded as suitable for continuous measurement of a changing volume because test substances tend to be lost from the intravascular compartment."

In order to overcome the problem of losing contents from the vascular system a number of other methods have been considered. All of these methods depend on measurements of haemoglobin (Hb) and/or haematocrit (Hct) and on the conviction that the red blood cells do not leave the vascular compartment. The first alternative is the method described by van Beaumont [64], which assesses changes in plasma volume from changes in Hct. However Costill et al [11] criticized this method and assert that many researchers fail to take into account the fact that an altered Hct can be indicative of a reduction in red cell size. Consequently Costill et al believe that plasma volume changes are underestimated when this method is utilized.

centrifuged at 500rpm for ten minutes. Plasma was then removed and frozen in preparation for later biochemical analysis.

Blood volume, plasma volume and other cardiovascular variables are affected by the chemical status of body fluids. In order to monitor changes of biochemical compositions in body fluids, six variables were measured (plasma sodium, potassium, chloride, urea, creatinine and osmolality). In addition the U:C ratio was calculated to assess changes in kidney function. Biochemical measurements were evaluated by the SAIMR using a Hitachi 747 analyser, and Boehringer reagents.

1.6 Fluid Volume Changes.

Studies on changes in PV are confounded by difficulties of measurement. As plasma volume is central to theories of EAC it is essential that intravascular contents are measured accurately; inaccurate and unreliable measurements would reduce the validity of this study. Due to the nature of plasma, it is impossible to measure the exact volume of blood and plasma in a live human. Therefore one can, at best, look at various techniques to estimate the volume. The problem with this approach is that plasma volume is constantly in a state of flux, and any measuring techniques must consider that plasma contents are free to flow into and out of the intravascular compartment.

The techniques used generally make use of a dilution method whereby a specific amount of a substance with a known concentration is injected into the vascular system. In so-called 'protein labelling' protocols the volume of injected dye attaches to the

changes in blood pressure were assessed comparing eight-day pre-race BP's to post-race measurements.

In attempting to explain these changes in blood pressure one has to again evaluate the physiological adjustments seen when a person exercises in an ultra-endurance event. As described in chapter one, a return to a normal resting physiology and blood pressure is a staggered process that begins on cessation of exercise. This inability for the body to revert immediately back to its normal resting physiological state is a result of the numerous changes which occur as exercise begins.

Amongst these factors which play a role in athletes' delayed recovery are the decreased muscle pump, the decreased abdomino-thoracic pump and cutaneous vasodilation. These three factors all have the effect of reducing venous return. From Starling's Law, the decreased venous return results in the reduction of stroke volume and therefore a drop in cardiac output is seen. With an attenuated cardiac output, systolic blood pressure falls.

After an ultra-endurance marathon has been run, there is also decrease in vascular tone[41] on completion of the event. This reduced tone results in the diastolic blood pressure decreasing. If the SBP and the DBP both drop, the MAP will mimic these falls. To this end the significant falls in SBP, DBP and MAP are explained in the aforementioned fashion.

assessing these BP measurements it is essential to remember that the most significant aspect is the data indicating a change in blood pressure and not the actual values, as read off the Dinamap. The reason for this statement is that there is a possibility of systematic error in the device used. However when one takes into consideration the ranges of blood pressures measured, the values are thought to be accurate.[32] In addition if there was a systematic error in the device and the values are somewhat inaccurate, it is still believed that assessed changes in blood pressures are not invalidated, as relative change of blood pressure variables is the most important aspect for this study.

When considering the changes in blood pressures, one sees that the SBP, DBP and MAP all changed significantly. Further analysis of this information leads to the belief that the blood pressure measurements taken in the hour prior to the race are elevated above normal resting levels. This elevation is thought to be a result of a pre-race catecholamine release due to anxiety and anticipation. This heightened blood pressure is not considered to be representative of the subjects' normal resting blood pressures, because at the same time of day eight days previously, systolic blood pressures where nearly 12mmHg lower.

As a result of the above anomaly, when one compares post-race blood pressures to eight-day pre-race figures, one sees a decrease in SBP of 14mmHg as opposed to a decrease of 26 mmHg between one-hour pre-race and post-race values. In percentage terms, the post-race SBP dropped 10.8% when compared to eight-day pre-race values and 19% when compared to one-hour pre-race values. Accordingly,

Therefore when one assesses the above findings, one sees that both circumstantial evidence and direct measurement of certain variables, lead to the conclusion that the quantity of the intra-vascular contents did not fall substantially during the race.

My findings suggesting no change in intra-vascular volume differ somewhat from that of Holtzhausen et al [35], who also evaluated changes in intra-vascular volume and blood pressure seen during an ultra-distance marathon. However it is felt that the study[35] is somewhat flawed as the blood pressure measurements and plasma volume changes described by Holtzhausen do not accurately reflect the haemodynamic status of the subjects in an erect position (ie. the physiological state that they would be in on completion of an ultra-marathon). In Holtzhausen's study erect blood pressure measurements were only taken after the subjects lay in a supine position for 10 minutes and all blood samples were taken in a seated position. Using this protocol, plasma volume decreases of 12.8 ± 9.1% were reported. As described previously, postural changes can alter plasma volumes. Therefore it is believed that the reported losses are exaggerated and that the reduction in plasma volume was in all probability caused when the subjects assumed an erect position after being supine for 10 minutes. The decreases reported are therefore largely a result of subjects' positional variations. Consequently these data should not be compared to the results of my enquiry which show that overall the subjects exhibited no change in plasma or blood volume, either before or during the race.

Having established that on average neither blood nor plasma volumes changed significantly, it is important to now consider the fluctuations in blood pressure. When

race increase of sodium and chloride appear to indicate a dehydrated state, this trend did not continue during the race where they failed to change significantly. The fact that electrolyte concentration did not continue to increase during the race is a further indication that an intra-vascular contents decrease did not occur. As sweat is hypotonic, a loss of intra-vascular contents would in all liklihood result in an electrolyte concentration increase. Data showing that such an increase (electrolyte) did not occur is still further evidence that the plasma volume did not fall.

The reduction in urea values seen prior to the race is likely to be a direct result of carbohydrate loading, which reduces protein catabolism[47]. The significant increases in levels of plasma urea and creatinine seen during the race are consistent with the findings of Décombaz et al [13] who studied biochemical changes in a 100km run. In keeping with their explanation, it is fair to assume that these changes are "compatible with a stimulation of gluconeogenesis at the expense of the amino acid pool without induction of muscle protein catabolism[13]."

Finally one can assess the U:C ratio to gauge if the plasma volume did indeed increase. As perfusion of the kidneys can be assessed from the U:C ratio, it is possible to evaluate if changes in kidney perfusion occurred. The significant increase of the U:C ratio before the race and then not during the race offers further explanation that during the race plasma volume did not change in any substantial quantity. If plasma volume losses had occurred, kidney perfusion would surely have decreased.

After careful planning it is felt that the measurement of these variables was exceptionally accurate and reliable. In addition, the method used to assess if the altered variables indicated a change in plasma volume was also considered to be accurate and valid. Using the method of Dill and Costill it can therefore be concluded that the direct measurement of plasma volume provided evidence that plasma volume failed to change.

A second indication of a change in intravascular volume could be a fluctuation in body mass. In this study there was a significant increase in pre-race body mass and BMI which could indicate a plasma volume increase. However a more likely explanation is that the athletes were hyperhydrated prior to the beginning of the race, because plasma volume was the same eight days before the race was run. The post-race reduction of mass and BMI could have been related to changes in plasma volume and dehydration. However in this case, it is more likely that the substantial reduction of body mass was a result of extravascular fluid losses, which were lost as a consequence of sweat.[15] These findings appear to support other evidence that plasma and blood volumes failed to change.

The third method to evaluate if the plasma volume had reduced, was to assess changes in biochemical variables. If plasma volume was to have dropped, concentrations of biochemical variables would surely increase. Once again one finds very little evidence which would indicate intra-vascular dehydration or explain the significant drop in blood pressure experienced after the race. Prior to the race sodium and chloride increased significantly by 2.1% and 4.8% respectively. Although this pre-

CHAPTER THREE : DISCUSSION AND CONCLUSIONS.

1. Discussion.

This study set out to establish if there was a correlation between blood volume variations and a change in blood pressure during an ultra-marathon. It was hoped that the results would add to the debate about whether a change in blood volume or post-exercise venous pooling, plays a greater role in decrease of blood pressure post-exercise and ultimately in exercise-associated collapse. The data in this study strongly suggests that it is the latter, as a significant reduction in blood pressure is found in conjunction with no change in blood and plasma volume following an ultra-endurance running event. This appears to suggest that venous pooling, and not a change in intravascular volume, is largely responsible for the post-endurance fall in BP and ultimately for exercise-associated collapse.

Evidence to support the above conclusion depends on showing that blood and plasma volume did not change whilst blood pressure declined significantly. In this discussion proof that plasma volume did not change will be provided by the evaluation of measurement techniques, body mass changes and alterations in biochemical variables. In addition justification will be provided for the substantial and significant fall in blood pressure.

Firstly actual measurements and calculations were used to assess if plasma volume did indeed alter. These calculations were based on measurements of both Hct and Hb.

TABLE 8: ONE -SAMPLE NON-PARAMETRIC TESTS		
	P VALUE	SIGNIFICANT ?
ΔPV Pre - race	0.563	No
ΔPV During race	0.5781	No
ΔBV Pre - race	0.469	No
ΔBV During race	0.3125	No

TABLE 9 : CORRELATION COEFFICIENTS			
VARIABLES	PEARSON'S R VALUE	P VALUE	SIGNIFICANT ?
Δ SBP and ΔPV	0.566	0.144	No
Δ DBP and ΔPV	-0.10	0.982	No
Δ PP and ΔPV	0.528	0.178	No
Δ MAP and ΔPV	0.244	0.560	No

TABLE 6: BLOOD PRESSURE CHANGES						
VARIABLE	6-DAY PRE-RACE VS 1-HR PRE-RACE	SIGNIFICANT ?	1-HR PRE-RACE VS POST-RACE	SIGNIFICANT ?	6-DAY PRE-RACE VS POST-RACE	SIGNIFICANT ?
SBP (mmHg)	12	Yes	-26	Yes	-13	Yes ($p<0.05$)
DBP (mmHg)	1	No	-13	Yes	-12	Yes ($p< 0.05$)
PP (mmHg)	10	No	-12	No	-2	No
MAP (mmHg)	4	No	-15	Yes	-11	Yes ($p<0.01$)

TABLE 7 : PERCENT CHANGE IN PLASMA AND BLOOD VOLUME				
	BEFORE RACE		DURING RACE	
SUBJECT	BLOOD VOLUME	PLASMA VOLUME	BLOOD VOLUME	PLASMA VOLUME
1	-0.6	0	-9.4	-12.6
2	0.7	0	-5.8	-7.5
3	-2.3	-1.2	0.6	1.5
4	0	0.2	-4.3	-8.1
5	9.8	10.4	-0.6	1.1
6	-0.7	-0.5	3.4	8.7
7	-1.3	-2.3	-0.7	-1.2
8	-1.3	-1.2	0.7	0
MEAN	0.5	0.7	-2.1	-2.3
SD	3.9	4.0	3.9	6.8

TABLE 5: CHANGES							
Variable	Change bt/ 8 days pre-race and 1-hr pre-race.	Change bt/ 1-hr pre-race and Post-race	Friedman Statistic	P Value	Significance	8-Day Pre-race vs 1Hr Pre-race	1Hr pre-race vs Post-race
MASS (kg)	1.8	-3.2	40.399	<0.0001	Significant	Yes	Yes
BMI ($kg.m^{-2}$)	0.6	-1	53.284	<0.0001	Significant	Yes	Yes
Hb (g/dl)	-0.2	0.4	0.850	0.448	Not	No	No
Hct %	-0.002	0.003	0.364	0.701	Not	No	No
MCV (femtolitres)	-1.2	-0.9	0.928	0.418	Not	No	No
RBC ($x10^{12}/l$)	0.07	0.08	1.482	0.261	Not	No	No
MCHC %	0.4	-0.4	5.127	0.021	Significant	No	No
MCH (picograms)	-0.7	0.2	0.773	0.480	Not	No	No
SODIUM (mmol/l)	2.9	0.4	5.884	0.014	Significant	Yes	No
POTASSIUM (mmol/l)	-0.1	0.5	3.076	0.078	Not	No	No
CHLORIDE (mmol/l)	4.5	-2.1	9.912	0.002	Significant	Yes	No
UREA (mmol/l)	-2.9	1.74	36.367	<0.001	Significant	Yes	Yes
U/C	-26.2	7.2	35.736	<0.001	Significant	Yes	No
CREATININE (umol/l)	-5.6	23.1	12.545	0.001	Significant	No	Yes
PROTEIN (g/l)	-1.2	3.4	3.175	0.073	Not	No	No
OSMOLALITY (mmol/kg)	-2	-2	0.398	0.679	Not	No	No
SBP (mmHg)	11.5	-24.9	2.845	0.046	Significant	Yes	Yes
DBP (mmHg)	1.3	-12.5	6.524	0.010	Significant	No	Yes
PP (mmHg)	10	-12	3.416	0.062	Not	No	No
MAP (mmHg)	3.4	-15.2	12.341	0.001	Significant	No	Yes

TABLE 4: POST-RACE VALUES										
VARIABLE	SUBJECTS								MEAN	SD
	1	2	3	4	5	6	7	8		
MASS (kg)	88.2	77.7	79.6	66.4	74	74.1	84.3	69.7	76.6	7.3
BMI ($kg.m^{-2}$)	24.2	23.6	21.2	21.9	24.4	25.6	24.6	22.8	23.7	1.4
Hb (g/dl)	17	15.6	17	16.4	16.5	14.7	15.3	15.3	16.0	0.9
Hct %	48.0	44.1	47.3	48.2	44.9	40.5	44.1	43.6	45.1	2.6
MCV (femtolitres)	89.1	87.5	87.4	82.1	90	85.3	86.9	88.8	87.1	2.5
RBC ($x10^{12}/l$)	5.38	5.04	5.41	5.87	4.98	4.75	5.09	4.91	5.18	0.36
MCHC %	35.4	35.4	35.9	34	36.7	36.3	34.7	35.1	35.4	0.9
MCH (picograms)	31.5	30.9	31.4	27.9	33.1	30.9	30	31.2	30.9	1.5
SODIUM (mmol/l)	146	142	142	143	143	135	143	144	142	3
POTASSIUM (mmol/l)	4	4.2	5.3	5.2	4.3	4.1	5.3	4.1	4.6	0.6
CHLORIDE (mmol/l)	109	110	109	108	110	104	113	112	109	3
UREA (mmol/l)	4.9	6.4	5.2	6.1	4.5	4	4.8	6	5.2	0.9
U/C	40.6	49.2	47.7	45.2	33.3	35.1	41.4	54.1	43.3	7.1
CREATININE (umol/l)	121	130	109	136	135	114	116	111	121	11
PROTEIN (g/l)	83	82	78	84	71	79	73	74	78	5
OSMOLALITY (mmol/kg)	299	290	290	293	288	272	290	295	290	8
SBP (mmHg)	104	99	100	83	130	105	111	119	106	14
DBP (mmHg)	76	68	65	48	60	58	47	80	62	12
PP (mmHg)	28	31	35	35	70	47	64	39	44	16
MAP (mmHg)	84	78	76	59	83	73	68	92	77	10

TABLE 3: 1-HOUR PRE-RACE VALUES										
VARIABLE	SUBJECTS								MEAN	SD
	1	2	3	4	5	6	7	8		
MASS (kg)	82.3	80.5	84.2	71.1	76.4	75.5	87.8	72.4	80.0	7.8
BMI ($kg.m^{-2}$)	25.3	24.6	22.4	23.5	25.2	26.1	25.7	24.8	24.7	1.2
Hb (g/dl)	15.4	14.7	17.1	15.7	16.4	15.2	15.2	15.4	15.6	0.8
Hct %	44.1	43.0	47.8	46.0	45.6	43.4	43.8	43.2	44.6	1.7
MCV (femtolitres)	89.1	89.4	87.7	82.9	91.2	87	86.6	90.4	88.0	2.7
RBC ($x10^{12}/l$)	4.95	4.81	5.44	5.55	5.02	4.99	5.06	4.78	5.06	0.28
MCHC %	34.9	34.2	35.8	34.1	35.8	35	34.7	35.6	35.0	0.7
MCH (picograms)	31.1	30.6	30	28.3	32.7	30.5	30	32.2	30.7	1.4
SODIUM (mmol/l)	141	142	143	140	144	140	143	142	142	1
POTASSIUM (mmol/l)	3.9	3.8	4.1	4.4	3.7	4.4	4.2	4.6	4.1	0.3
CHLORIDE (mmol/l)	109	112	113	110	113	111	113	111	112	2
UREA (mmol/l)	3	3.7	3.6	3.3	2.9	3.2	3.7	4.8	3.5	0.6
U/C	33.7	41.1	37.5	34.7	26.6	31.4	38.9	44.9	36.1	5.8
CREATININE (umol/l)	89	90	96	96	109	102	95	107	97.9	7.4
PROTEIN (g/l)	72	73	76	73	70	79	71	75	74	3
OSMOLALITY (mmol/kg)	285	291	291	286	288	291	289	294	290	3
SBP (mmHg)	147	133	115	116	141	130	137	131	131	11
DBP (mmHg)	80	79	85	65	74	64	83	72	75	8
PP (mmHg)	67	54	30	51	67	66	54	59	56	12
MAP (mmHg)	101	96	94	81	86	85	100	91	92	7

TABLE 2: 8 DAY PRE-RACE VALUES										
VARIABLE	SUBJECTS								MEAN	SD
	1	2	3	4	5	6	7	8		
MASS (kg)	89.6	79.3	82	68.8	74.6	73.7	85.1	72.4	78.2	7.1
BMI ($kg.m^{-2}$)	24.6	24.2	21.8	22.7	24.6	25.5	24.9	24.8	24.1	1.2
Hb (g/dl)	15.3	14.8	16.7	15.7	18	15.1	15	15.2	15.7	1.1
Hct %	44,4	42,6	48,4	46,1	46,1	43,5	43,2	43,2	44,7	2.0
MCV (femtolitres)	89.1	87.5	101.3	79.8	92.4	86	86.1	91.1	89.2	6.2
RBC ($x10^{12}/l$)	4.98	4.87	4.78	5.78	4.99	5.06	5.02	4.74	5.03	0.33
MCHC %	34.3	34.8	34.8	33.9	34.6	34.7	34.7	35.1	34.7	0.4
MCH (picograms)	30.7	30.4	34.9	27.2	36.1	29.8	29.9	32.1	31.4	2.9
SODIUM (mmol/l)	141	138	140	140	139	138	141	136	139	2
POTASSIUM (mmol/l)	4.3	3.9	4.2	4.3	4.0	4.5	4.2	4.2	4.2	0.2
CHLORIDE (mmol/l)	108	108	105	109	107	106	110	104	107	2
UREA (mmol/l)	5.2	7.0	5.8	5.2	7.2	6.6	6.2	6.2	6.4	1.0
U/C	51.5	79.6	52.7	52	69.9	60.5	64.6	67.8	62.3	10.0
CREATININE (umol/l)	101	88	110	100	103	109	96	121	103.5	10.0
PROTEIN (g/l)	74	71	85	79	68	77	70	76	75	6
OSMOLALITY (mmol/kg)	290	297	290	292	285	294	291	294	292	4
SBP (mmHg)	123	116	116	122	123	114	123	121	119	4
DBP (mmHg)	72	77	77	71	71	60	77	87	74	8
PP (mmHg)	51	39	39	51	52	54	46	34	46	7
MAP (mmHg)	88	89	89	87	88	78	91	97	88	5

64 van Beaumont, W., Underkofler, S., van Beaumont, S. Erythrocyte volume, plasma volume, and acid-base changes in exercise and heat dehydration. *J Appl Physiol.*, 50(6) 1255 - 1262, 1981.

65 van Beaumont, W., Greenleaf, J.E., Juhos, L. Disproportional changes in haematocrit, plasma volume, and proteins during exercise and bed rest. *J Appl Physiol.*, 33(1) 55 - 61, 1972.

66 Wyndham, C.H., Strydom, N.B. The danger of inadequate water intake during marathon running., *S Afr Med J.*, 43:893 - 896, 1969.

67 Wyndham, C.H. Heat stroke and hyperthermia in marathon runners. *Ann N Y Acad Sci.*, 301:128 - 138, 1977.

56 Sandell, R.C., Pascoe, M.D., Noakes,T.D.: Factors associated with collapse during and after ultra-marathon footraces: A preliminary study. *Phys Sportsmed.*, 16:9, pp 86 - 94, 1988.

57 Sawka, M.N., Francesconi, R.P., Pimental, N.A., et al. Hydration and vascular fluid shifts during exercise in the heat. *J Appl Physiol.*, 56(1): 91 - 96, 1984.

58 Senay, L C. Early response of plasma contents on exposure of working men to heat. *J Appl Physiol.*, 44(2):166 - 170, 1978.

59 Senay, LC., Mitchell, D., Wyndham, C.H. Acclimatization in a hot, humid environment: body fluid adjustments. *J Appl Physiol.*, 45(5) 786 - 796, 1976.

60 Senay, L.C. Jnr, Pivarnik, J.M. Fluid shifts during exercise. *Ex Sport Sci Rev.*, 13:335 - 387, 1985.

61 Shepherd, J.T., The cardiac catheter and the American Heart Association. *Circulation.*, 50(3) 418 - 428, 1974.

62 Sutton, J., et al. The medical problems of mass participation in athletic competition. The City-to-Surf race. *Med J Aust.*, 2:127 - 133, 1972.

63 Thomas, J.E., Schirger, A., Fealey, R.D. et al. Orthostatic hypotension. *Mayo Clin Proc.*, 56: 117 - 125, 1981.

49 Noakes, T.D. The collapsed endurance athlete - time to rethink our management ? *Sports Train Med Rehab.*, 2: 171 - 191, 1991.

50 Noakes, T.D. Dehydration during exercise: what are the real dangers? *Clin Sports Med.*, 5(2):123 - 128, 1995.

51 Noakes, T.D.: Sportsmedicine forum: "Why endurance athletes collapse." *Phys Sportsmed.*, 16:9, 1988.

52 Owen, M.D., Kregel, K.C., Wall, P.T. et al. Effects of ingesting carbohydrate beverages during exercise in the heat. *Med Sci Sports Exerc.*, 18(5) 568 - 575, 1986.

53 Pivarnik, J.M., Goetting, M.P., Senay, L.C. Jr. The effect of body position and exercise on plasma volume dynamics. *Eur J Appl Physiol.*, 55:450 - 456, 1986.

54 Roos, R. Medical coverage at endurance events. *Phys Sportsmed.*, 15:11, 1987.

55 Rowell, L.B., Sheperd, J.T., editors. Handbook of physiology. Section 12. Exercise: regulation and integration of multiple systems. 1996. Oxford University Press.

41 McArdle, W.D., Katch, F.L., Katch V.L. 1991. *Exercise physiology: energy, nutrition and human performance.* 3rd ed. Lea and Febiger.

42 Montain, S.J., Coyle, E.F. Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. *J Appl Physiol.*, 73: 1340 - 1350, 1992.

43 Myhre, L.G., Hartung, G. H., Nunnenley, S.A., et al. Plasma volume changes in middle-aged male and female subjects during marathon running. *J Appl Physiol.*, 59(2): 559 - 563, 1985.

44 Myhre, L., Lutt, U.C., Venters, M.D. Response of non-athletes to lower body negative pressure and acute dehydration. *Med Sci Sports Exerc.*, 19:187 - 194, 1987.

45 Nash, H.L.: *Phys Sportsmed.*, 13:134-144, 1985.

46 Nelson, P.B., Robinson, A.G., Kapoor, W. et al. Hyponatremia in a marathoner. *Phys Sportsmed.*, 16:10, pp 78 - 87, 1988.

47 Newsholme, E.A., Leech, A.R. *Biochemistry for the medical sciences.* John Wiley & Sons, 1983.

48 Noakes, T.D. Response to letter. *Med Sci Sports Exerc.*, 23(7) 884, 1991.

35 Holtzhausen, L-M., Noakes,T.D. The prevalence and significance of post-exercise (postural) hypotension in ultra-marathon runners. *Med Sci Sports Exerc.*, 27(12): 1595 - 1601, 1995.

36 Irving, R.A., Noakes, T.D., Burger, S.C., et al. Plasma volume and renal function during and after ultra-marathon running. *Med Sci Sports Exerc.*, 22(5): 581 - 587, 1990.

37 Irving, R.A., Noakes, T.D., Buck, R. et al. Evaluation of renal function and fluid homeostasis during recovery from exercise induced hyponatraemia. *J Appl Physiol.*, 70: 342 - 348, 1991.

38 Kaminsky, L.A., Paul, G.L. Fluid intake during an ultra-marathon running race: relationship to plasma volume and serum sodium and potassium. *Sports Med. Phys. Fitness.*, 31: 417 - 419, 1991.

39 Kolka, M.A., Stephenson, L.A., Wilkerson, J.E. Erythrocyte indices during a competitive marathon. *J Appl Physiol.*, 52(1) 168 - 172, 1982.

40 Laird, R.H. Medical care at ultra-endurance triathlons. *Med Sci Sports Exerc.*, 21:8, pp S222 - S225, 1989.

28 Harrison, M.H., Edwards, R.J., Leitch, D.R. Effect of exercise and thermal stress on plasma volume. *Eur J Appl Physiol.,* 39(6):925 - 931, 1975.

29 Harrison, M.H., Edwards, R.J. Measurement of change in plasma volume during heat exposure and exercise. *Aviat Environ Med.*, 47(10): 1038 - 1045, 1976.

30 Harrison, M H., Edwards, W.J., Graveney, M.J. et al. Blood volume and plasma protein responses to heat acclimatisation in humans. *J Appl Physiol.,* 50(3) 597 - 604, 1981.

31 Harrison, M H., Edwards, W.J., Leitch, D.R. Effect of exercise and thermal stress on plasma volume. *J Appl Physiol.*, 39(6) 925 - 931, 1975.

32 Hartford,C.G., Marcos,E.F., Rogers, G.G. Noninvasive verses invasive blood pressure measurement in normotensive and hypotensive baboons. *Lab Animal Sci.*, 46(2) 231 - 233, 1996.

33 Hiller, W.D., O'Toole, M.L., Fortess, E.E. Medical and physiological considerations in triathlons. *Am J Sports Med.*, 15:164 - 167, 1987.

34 Holtzhausen, L-M., Noakes, T.D., Kroning, B. et al. Clinical and biomechanical characteristics of collapsed ultra-marathon runners. *Med Sci Sports Exerc.,* 26(9) 1095 - 1101, 1994.

21 Fortney, S M., Nadel, E.R., Wenger, C.B. et al. Effect of blood volume on sweating rate and body fluids in exercising humans. *J Appl Physiol.*, 51(6) 1594 - 1600, 1981.

22 Gerstein, S.M. Risk factors for collapse of runners. A report on the 1988 Toronto Marathon. *Physician Sportsmed.*, 18:12, 1990.

23 Gore, C J., Scroop, G.C., Catcheside, P.G. et al. Plasma volume, osmolarity, total protein and electrolytes during treadmill running and cycle ergometer exercise. *Eur J Appl Physiol.*, 65:302 - 310, 1992.

24 Greenleaf, J.E., Convertino, V.A., Mangseth, G.R. Plasma volume during stress in man: osmolarity and red cell volume. *J Appl Physiol.*, 47(5):1031 - 1038, 1979.

25 Guyton, A.C. 1991. *Textbook of medical physiology*. 8th ed. WB Saunders and Company. 264 p.

26 Hagan, R.D., Diaz, F.J., Horvath, S.M. Plasma volume changes with movement to supine and standing positions. *J Appl Physiol.*, 45(3): 414 - 418, 1978.

27 Harrison, M H. Effects of thermal stress and exercise on blood volume in humans. *Physiol Rev.*, 65(1): 149 - 209, 1985.

14 Dill, D.B., Costill, D.L. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol.*, 37(2):247 - 248, 1974.

15 Dill, D.B., Soholt, L.F., Oddershede, I.B. Physiological adjustments of young men to five-hour desert walks. *J Appl Physiol.*, 40 (2): 236 - 242, 1976.

16 Eichna, L.W., Horvath, S.M., Bean, W.B.: Post-exertional orthostatic hypotension. *Am J Med Sci.*, 213:6, 1947.

17 Eisenberg, S. Effect of posture and position of the venous sampling site on the haematocrit and serum protein concentrations. *J Lab Clin Med.*, 61: 755 - 760, 1963.

18 El-Sayed, H., Hainsworth, R. Relationship between plasma volume, carotid baroreceptor sensitivity and orthostatic tolerance. *Clin Sci.*, 88(4) 463 - 470, 1995.

19 Fellman, N. Hormonal and plasma volume alterations following endurance exercise. *Sports Med.*, 13 (1), 37 - 43, 1992.

20 Fortney, S.M., Senay, L.C. Jr. Effect of training and heat acclimation on exercise responses of sedentary females. *J Appl Physiol.*, 47(5) 978 - 984, 1979.

7 Caroline, N.L. *Emergency Care in the Streets.* 5th ed. Little, Brown and Company, 1995. 194 p.

8 Convertino, V A. Blood Volume: its adaption to endurance training. *Med Sci Sports Exerc.*, 23(12): 1338 - 1348, 1991.

9 Costill, D.L.: Sweating: its composition and effects on body fluids. *Ann N Y Acad Sci.*, 310:160 - 174, 1974.

10 Costill, D.L., Branam, L., Eddy, D, et al. Alterations in red cell volume following exercise and dehydration. *J Appl Physiol.*, 37(6): 912 - 916, 1974.

11 Costill, D L., Fink, W.J. Plasma volume changes following exercise and thermal dehydration. *J Appl Physiol.*, 37(4) 1594 - 1600, 1974.

12 Criswell, D., Renshler, K., Powers, S.K., et al. Fluid replacement beverages and maintenance of plasma volume during exercise: role of aldosterone and vasopressin. *Eur J Appl Physiol.*, 65:445 - 451, 1992.

13 Décombaz, J., Reinhardt, P., Anantharman, K et al. Biochemical changes in a 100km run: free amino acids, urea and creatinine. *Eur J Appl Physiol.*, 41: 61 - 72, 1979.

REFERENCES.

1 Armstrong, L.E., Hubbard, R.W., Kraemer, W.J. et al. Signs and symptoms of heat exhaustion during strenuous exercise. *Ann Sports Med.*, 3:182 - 189, 1987.

2 Åstrand, P., Rodahl, K. *Textbook of work physiology - Pysiological bases of exercise.* 3rd ed. McGraw-Hill Book Company, 1986, 173 p.

3 Cade, R., Packer, D., Zauner, C. et al. Marathon running: physiological and chemical changes accompanying late race functional deterioration. *Eur J Appl Physiol.*, 65:485 - 491. 1992.

4 Campbell, N.R.C., McKay, D.W., Chockalingam, A. et al. Errors in assessment of blood pressure: blood pressure measuring technique. *Can J Pub Health.*, 85 (Sept - October) S18 - S21, 1994.

5 Campbell, N.R.C., McKay, D.W., Chockalingam, A. et al. Errors in assessment of blood pressure: patient factors. *Can J Pub Health.*, 85 (Sept - October) S12 - S17, 1994.

6 Campbell, N.R.C., McKay, D.W., Chockalingam, A. et al. Errors in assessment of blood pressure: Sphygmomanometers & blood pressure cuffs. *Can J Pub Health.*, 85 (Sept - October) S22 - S25, 1994.

The data presented in this study therefore supports the conclusion that blood pressure decreases occur despite no change in plasma volume. Accordingly an unexplained post-exercise decrease in blood pressure is a result of mean arterial hypotension. Consequently it could be argued that EAC is a result of this drop in blood pressure, and that EAC should rather be defined as a sudden decrease in mean arterial blood pressure on the cessation of prolonged exercise in the upright position, associated with syncopal symptoms.

2. Conclusion.

In my study all the athletes had a decrease in blood pressure, accompanied by no change in blood and plasma volume and no correlation between plasma volume and blood pressure. The changes in blood pressure therefore cannot be explained by the insignificant changes seen in intravascular volume.

This data strongly supports the idea that the majority of athletes who collapse at the end of ultra-endurance races, do so not as a consequence of dehydration and/or a decrease in plasma volume, but rather as a result of venous pooling in the pelvis and legs at the cessation of exercise. The pooling results in a decreased systolic, diastolic and mean arterial blood pressure. This drop in MAP in turn leads to a decreased cerebral blood flow, lightheadedness and an inability to stand upright. Heat-induced dehydration or changes in plasma volume will, however, exacerbate the cardiovascular component of EAC, but are in all likelihood not the primary cause of EAC, as has been previously argued.

In an attempt to further explain BP changes one must look at possible fluctuations in the intravascular volume. The post-race reduction in blood pressure was expected and has been explained in the past by arguing that this is a result of heat-induced dehydration[33, 66]. But if one looks at the data presented in this study, it can be seen that insignificant plasma and blood volume changes (ΔBV: -2.1%, ΔPV: -2.3 %) fail to explain the decreased blood pressures experienced by the subjects. As discussed earlier (page number 16) changes in intravascular contents of between 1% and 2% cannot alone be responsible for changes in SBP of between 10.8% and 19% [7, 25, 42].

After having evaluated the changes in blood pressure and lack of variation in intravascular volume it remains to be finally assessed if the drop of blood pressure is in any way related to a deviation in plasma volume. As all the above calculations and conclusions relate to average changes, it remains to be tested if individuals exhibited any relation between changes in plasma volume and changes in blood pressure. In order to achieve this aim, the plasma volume and blood pressure changes were correlated with one another to assess if their was any relationship between the two variables. Consequently the eight-day to post-race differences in BP were correlated with changes in plasma volume. These calculations yielded no significant associations. (Table 9)

These results are similar to those of Holtzhauzen et al [35] (even though her intravascular dehydration results appear to be incorrectly inflated) in that she also failed to find a significant correlation ($r = 0.06$; $p > 0.1$) between plasma volume losses and a reduction in post-race systolic blood pressure.