EFFECTS OF ACUTE PASSIVE HEAT EXPOSURE

by

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A THESIS

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BACKGROUND: Passive heat therapy (regular hot tub or sauna use) has gained attention for its potential to improve cardiovascular health, and recent evidence suggests that it produces beneficial vascular adaptations. However, the cardiovascular responses to a single bout of hot water immersion have not yet been characterized; therefore the mechanisms that produce long-term adaptations are not yet fully known. PURPOSE: To examine the acute physiological and perceptual effects as well as the safety and acceptability of a 60 minute bout of hot water immersion. METHODS: Thirteen healthy, young (23 ± 1 years) subjects were immersed to heart level (both arms out) in 40.5°C water for 60 min (average peak rectal temperature: 38.7 ± 0.1°C). All measurements were taken at baseline prior to and during immersion. Subjective experiences were measured with scales of perceived exertion, skin wettedness, and thermal sensation. Heart rate was measured by commercially available chest strap, blood pressure by an automated sphygmomanometer, and blood glucose with a commercially available glucose monitor. Cardiac output was measured with an open-circuit acetylene wash-in method. Carotid and brachial artery diameter and blood velocity were measured using Doppler ultrasonography. Values were used to calculate
blood flow and shear rate, a frictional force exerted on the endothelium by blood which is associated with beneficial vascular adaptation. Skin blood flow was measured using laser Doppler flowmetry and is presented as a percentage of maximal cutaneous vascular conductance (%CVCmax; CVC = laser Doppler flux/mean arterial pressure), determined by local heating to 43.5°C at the end of hot water immersion. Temperatures were measured with thermocouples on the skin, a rectal thermistor, tympanic, and sublingual probes. Peak changes were compared to baseline using Student’s paired t-test, and significance was set to P<0.05. Data are presented as mean ± S.E. RESULTS: Heart rate increased from 60 ± 2 at baseline to a peak of 119 ± 4 bpm (p<0.01) during immersion. Cardiac output increased from 6.3 ± 0.4 to 10.2 ± 0.6 L/min (p<0.01). Blood flow increased in the carotid (618.7 ± 26.1 to 1057.3 ± 56.8 ml/min; p<0.01) and brachial (56.4 ± 9.4 to 470.6 ± 38.0 ml/min; p<0.01) arteries. Total shear rate (4 x velocity / diameter) also increased in the carotid artery (205.7 ± 13.5 to 278.6 ± 17.8 s-1; p<0.01) and even more so in the brachial artery (93.2 ± 10.5 to 508.9 ± 50.2 s-1 p<0.01). Skin blood flow reached a plateau of 50.5 ± 3.4 %CVCmax (p<0.01) during immersion. CONCLUSION: Hot water immersion caused substantial increases in core temperature, cardiac output, arterial blood flow, skin blood flow, and shear rates. These changes are similar to those seen during a single bout of exercise, which suggests that repeated hot water immersion may cause beneficial vascular adaptations through similar mechanisms.
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Background

Cardiovascular disease (CVD) is the leading cause of death in developed countries and encompasses a variety of disorders including heart failure, arrhythmia, heart valve disorders, and stroke. The majority of CVD pathologies are products of atherosclerosis, a progressive hardening and thickening of arterial walls that disrupts the normal flow of blood. Damage to the endothelium, a single layer of cells that lines blood vessels and plays a large role in contraction, dilation, and protection of vessels, is the preliminary stage of atherosclerosis. Many studies have linked endothelial dysfunction to risk factors of atherosclerosis.

When endothelium is damaged it increases the expression of adhesion molecules allowing lipids, mostly low density lipoproteins (LDLs) to leak from the blood into the smooth muscle of vessel walls. Immune cells, specifically monocytes which differentiate into macrophages once they reach the intima, react to the injury of the endothelium and attempt to digest LDLs. However, ingestion of these LDLs causes macrophages to become foam cells. These build up over time and become what is known as an atheromatous plaque. Plaque becomes problematic as it first decreases the elasticity of the arterial wall by causing the deposition of dense connective tissue and then as increasing build-up begins to narrow the artery, causing disruptions in blood flow. Arteries are more easily ruptured due to these degenerative areas in vessel walls which leads to hemorrhaging. In addition, there is a greater occurrence of thrombosis as thrombi are more easily formed due to the rougher surface of atheromatous plaque. Thrombosis in the coronary arteries accounts for two thirds of the deaths due to vascular
disease, while the other third is due to thrombosis or hemorrhage in the brain or other organs.\textsuperscript{14}

The effects of exercise as a potent preventative measure against atherosclerosis have been well described.\textsuperscript{13, 14, 27, 39, 47, 52, 53, 54} Exercise is thought to improve endothelial function via shear stress, the frictional force experienced by the endothelial lining of arteries as a result of blood flow.\textsuperscript{14, 52, 54} During exercise, cardiac output, the volume of blood pumped from the heart per minute, is increased as the amount of blood flow required by the body increases.\textsuperscript{56} With a larger cardiac output there is greater blood flow, especially to working muscles\textsuperscript{14} and therefore greater shear stress.\textsuperscript{52} Vascular adaptations to exercise have been shown to be highly influenced by shear stress, as are improvements to endothelial function and vascular remodeling that appear to be atheroprotective.\textsuperscript{18, 53, 54} Adaptations to exercise have also been attributed to increased core temperature, and even 30 minutes of moderate exercise may raise core temperature as much as 1°C.\textsuperscript{12}

However, exercise is difficult for many patient populations. Even with an otherwise healthy lifestyle, these populations are at greater risk of CVD because they are mostly sedentary.\textsuperscript{49} It is necessary, then, to find an alternative way to combat cardiovascular disease for these individuals.

In recent years, heat therapy, defined as repeated acute body core temperature elevations using hot water immersion or sauna, has received attention for potential cardiovascular health benefits. Heat therapy has not only been seen to improve endothelial function as a possible preventative measure,\textsuperscript{18, 23} but studies have also shown a variety of beneficial cardiovascular effects associated with passive heating in
subjects with chronic heart failure. Some of these benefits include improved hemodynamics, reduction in clinical symptoms, and reduced occurrence of arrhythmias which are associated with sudden cardiac death. Chronic sauna use, a specific type of heat therapy, has also been linked with decreased incidence of sudden cardiac death and all-cause mortality in a non-specific population. Applying a long-term passive heating protocol to a population with impaired cardiovascular health has the potential to dramatically improve vascular responses to heat, improve insulin sensitivity, and overall improve cardiovascular health. Heat therapy could even be restorative for patients who have difficulty exercising as it provides many benefits similar to those of exercise, but in a passive manner.

The majority of the studies examining the beneficial effects of passive heating are chronic. Researchers ask subjects to repeat a standard protocol multiple times over weeks up to months, with measurements made before any heating and after the weeks or months are complete. Relatively few studies have examined the acute effects of passive heating that are possibly therapeutic. Little is known about the acute physiological effects of longer bouts (i.e. 60 minutes) of hot water immersion. To better understand the mechanisms through which heat therapy may cause these beneficial adaptations, the acute effects of hot water immersion must be examined.

**Shear stress**

Defined above as the frictional force exerted by the blood on the endothelial lining of vessels, shear stress has been connected to beneficial cardiovascular adaptations. Endothelial cells have been observed to reorient in response to shear
stress, causing them to become a more streamlined surface. Sections of arteries that are subjected to low mean shear stress do not undergo reorientation and are strongly correlated with endothelial dysfunction while areas that experience high mean shear stress appear to be protected from atherosclerosis. More specifically, arterial areas that experience partial retrograde shear, a force induced by blood moving back towards the heart, have an impaired endothelial response to stresses and are correlated with higher incidence of atherosclerotic plaques. Arterial areas that experience mostly anterograde shear, induced by blood moving away from the heart, experience the most endothelial benefit and therefore greatest decreased risk of atherosclerosis. Due to these findings, studies have begun to look at ways to increase shear stress as a preventative measure against atherosclerosis.

**Blood flow**

Blood flow, specifically to areas such as muscle and skin, is considerably lower at rest than what the body is capable of achieving. Changes in position, activity level, climate, and even psychological stress may alter blood flow as the cardiovascular system responds to meet the needs of the body. Of particular interest are the changes in blood flow and the cardiovascular responses that make those changes possible during exercise as these have been shown to benefit cardiovascular health, and whether these changes may be replicated with heat therapy.

Working muscles require greater blood flow than resting tissues since they have an increased demand for nutrients such as glucose to provide energy and higher production of metabolic wastes. Blood acts as a transport system, bringing more
nutrients to the muscles and carrying away metabolic wastes. Increased blood flow is achieved as the sympathetic nervous system causes the heart to beat faster and ventricles to contract to a greater extent. Venous return also increases during exercise due to a decrease in the capacitance of the venous system, or a decrease in the amount of blood being held in the veins. This decrease comes about when skeletal muscles begin to contract around the veins and the smooth muscle within the walls of the veins contracts due to an increase in sympathetic output. External factors, such as pressure exerted on the body or gravity, may also affect venous return. Since the amount of blood the heart can pump out is determined by the amount coming in, increasing venous return means that the heart has a greater volume of blood to circulate. Greater blood flow results in greater shear stress being exerted upon the endothelium which is, as discussed above, beneficial to the cardiovascular system.

It is thought that a similar increase in blood flow, and therefore shear stress, may be elicited via passive heating. Significant increases in skin blood flow have been previously noted with hot water immersion. Increasing skin blood flow is a thermoregulatory response, often paired with sweating. Sweat evaporates from the surface of the skin, and the change in state of the liquid water to a gas transfers a large amount of heat energy from the skin. Blood circulating through the skin capillaries cools via this transfer of energy, and the cooled blood travels to other areas of the body and cools them. The greater the amount of blood circulating through the skin, the more cooling may occur.

Skin or cutaneous vasculature is extremely compliant in that a large volume of blood may circulate through it, up to 8L/min. The average resting amount
of blood being circulated by the heart is 5.5L/min.\textsuperscript{14} Therefore, systemic cutaneous vasodilation has the capacity to dramatically increase normal blood flow.\textsuperscript{21}

**Cardiac Output**

Defined above as the volume of blood pumped from the heart per minute, cardiac output is determined, among other things, by venous return or the rate at which blood returns to the right atrium, via the venous system, from peripheral tissues and increasing arterial pressure.\textsuperscript{14, 56} As a result, cardiac output represents a sum of all the local regulations of blood flow occurring throughout the body.\textsuperscript{14} As discussed earlier, cardiac output during exercise is amplified as the amount of blood flow required by the body increases.\textsuperscript{56}

Cardiac output has also been observed to increase during hot water immersion.\textsuperscript{41} This increase, unlike that observed during exercise, is mainly due to large increases of cutaneous, or skin, blood flow and possibly also due to increased hydrostatic pressure.\textsuperscript{4} The thermoregulatory response of diverting blood to the skin has been observed to nearly double cardiac output during passive heating, with half or more of the increased blood flow going to the skin.\textsuperscript{4} The mechanism of this increased cardiac output is likely the increased heart rate associated with heat stress as it has been suggested that stroke volume does not change very much.\textsuperscript{4, 8} However, it has also been suggested that hydrostatic pressure from immersing the body in water results in an increased venous return to the heart which would also increase cardiac output.\textsuperscript{50} Stroke volume has been seen to decrease during passive heating, yet the heart maintains and even increases cardiac output during heat stress probably due to increased contractility.\textsuperscript{4, 6} Johnson et
al. suggest that during whole body heating there is a demand for elevated cardiac output that, paired with the lack of skeletal muscle pump returning blood to the heart, provides a challenge to the heart.21

**Blood Glucose**

The concentration of glucose within the blood is closely regulated in healthy individuals, but insulin sensitivity and/or diabetes, can cause blood glucose levels to rise.33 Too much blood glucose can dehydrate tissues and damage the cardiovascular system, increasing the risk of stroke, heart attack, and other serious conditions.14 Fasting blood glucose has been shown to decrease significantly following two weeks of heat therapy in the form of sauna bathing.18 It was suggested that the increased blood flow resulting from heat stress going to skeletal muscles was the cause of increased glucose uptake.13,18 In addition to this, fasting plasma glucose in patients with type 2 diabetes mellitus was seen to decrease following three weeks of regular heat stress, this time provided with hot water immersion.17 Blood glucose levels over the course of a single hot water immersion session have not been measured in healthy individuals.

**Safety and Acceptability of Heat Therapy**

In order for heat therapy to become more widely accepted there are several considerations that must be made. First of all, the safety of hot water immersion must be confirmed. A part of safety during hot water immersion is monitoring temperature, but a more effective method is needed for situations outside of the research laboratory.
Consideration must also be made for the subjective experience and comfort of those who undergo hot water immersion.

In addition, concerns have been raised about the safety of spending more than 20 minutes in heat immersion, specifically that it causes decreases in blood pressure to the point that people may lose consciousness. Therefore the traditional suggested maximum time limit on hot tubbing is between 15-30 minutes. However, maintenance of body core temperature at or above 38.5°C is considered to be necessary for inducing many of the beneficial physiological adaptations, and to achieve this, longer periods of immersion are required. Ideally, 60 minutes would be spent in hot water immersion to achieve threshold temperature and then allow time for this stimulus to affect the body.

The main safety concerns with hot water immersion are the decrease in blood pressure that occurs as blood vessels vasodilate in response to heat, in particular compliant vascular beds such as the skin, as well as the increase in core temperature itself. Several studies have marked the safety of short periods of hot water immersion, generally 10-20 minutes as is generally accepted. These have gone so far as to examine the safety of hot water immersion for hypertension patients and patients with stable coronary artery disease. However, safety has not been a specifically measured parameter for studies that did examine longer bouts of hot water immersion.

Temperature

Another possible mechanism that increases health with heat therapy is the increase in core temperature. Sufficient increases in core temperature or heat stress can stimulate expression of various heat shock proteins. These proteins are currently under
investigation for their potential roles in enhancing cardiovascular and metabolic health. Passive heating can increase core body temperature to a sufficient extent to induce the expression of heat shock proteins.

In addition to tracking possibly beneficial effects, increases in core temperature must be monitored closely for the sake of subject or patient safety. In the research setting this accomplished using rectal thermistor, which tracks changes in core temperature with a high degree of accuracy. However, this standard laboratory practice may not be considered acceptable for many people using heat therapy outside of a lab setting. If a patient wishes to utilize heat therapy in a home or gym setting they would likely prefer to track temperature through less invasive means. Tympanic thermometers, commonly seen in physician offices, and sublingual or oral thermometers are potential alternative methods to track temperature during hot water immersion. Neither is as accurate as rectal thermistor for measuring core body temperature, but if one closely correlates to core temperature it could be used as a surrogate.
Purpose

The purpose of this study is to further examine the acute effects of a hot water immersion protocol used in heat therapy. To accomplish this, the current study observes physiological responses during one 60 minute bout of hot water immersion to see whether the acute effects of passive heat are similar to those of exercise. Specifically it examines blood flow and shear rate experienced by arteries as these are thought to be key stimuli of atheroprotective measures, cardiac output, skin blood flow, blood glucose, blood pressure, core temperature, and heart rate. Subject safety was monitored to minimize concern over heat therapy’s safety. Subject perceptual responses were measured to determine acceptability. Finally, several means of body temperature measurement are examined to determine suitability for use in heat therapy protocols.
Methods

Subjects

Seven male and six female for a total of thirteen subjects who were healthy, young (23 ± 1 years), and engaged in recreational exercise (< 7 hours per week and were not training for any particular event or sport) participated in this study. All subjects had never been diagnosed with long term health problems such as cardiovascular disease, hypertension, or diabetes. Subjects were not taking any prescription medication, were nonsmokers, and had not had anorectal, vaginal, or prostate surgery within the past 6 months. A urine pregnancy test was taken by each female subject immediately prior to their study to confirm a negative result. Subjects abstained from heavy exercise, over-the-counter medication, vitamins, and supplements for 24 hours prior to their study time. Subjects also abstained from caffeine and alcohol for 12 hours prior, and food for 2 hours prior. The Institutional Review Board at the University of Oregon provided approval for this study, and each subject provided their oral and written informed consent for all protocols prior to participation.

Protocol

Health and activity histories were taken during an initial screening session and a single study date agreed upon if subjects met study criteria. An email was sent to each subject the day prior to their study date reminding them to abstain from certain substances and exercise.
Upon arrival to the laboratory, subjects answered a questionnaire as to whether they had abstained from medications, supplements, vitamins and exercise for 24 hours, caffeine and alcohol for 12 hours, and food for 2 hours. Subjects were then reminded of study protocols, and instructed upon the proper placement of a sterile rectal thermistor (YSI Series 400, Yellow Spring Instruments, Yellow Springs, OH, USA) which they completed following a nude body weight measurement. Subjects then reclined in their bathing suits for 20 minutes of rest. During these 20 minutes subjects were instrumented with: two Laser Doppler probes (Laser Doppler Perfusion and Temperature Monitor DRT4; Moor Instruments Ltd., Axminster, England) located on their left forearm, thermocouples (Squirrel Data Logger 2020 Series; Grant Instruments Ltd., Cambridge, England) located on their left upper back, left upper chest, and left forearm, an automated sphygmomanometer (Cardiocap/5; Datex-Ohmeda, Louisville, CO, USA) on the left upper arm, and a Polar heart rate monitor (Polar; Lake Success, NY, USA) around the chest at heart level. Laser Doppler probes continuously measured forearm skin blood flow throughout the protocol as thermocouples continuously measured skin temperature in the three areas they were placed. Blood pressure was measured using the automated sphygmomanometer at baseline and every five minutes during heating and recovery as was heart rate, measured by the Polar chest strap.

Other baseline measurements included tympanic temperature (Braun Thermoscan; Kaz USA, Inc., Southborough, MA, USA), sublingual temperature, rectal temperature, and subjective scales monitoring subject perceived exertion, skin wettedness, and thermal sensation (Image 1). After baseline, these measurements were also taken every five minutes throughout heating and recovery. Measurements of blood
velocity and vessel diameter in the carotid and brachial arteries were taken for 60 seconds using high-resolution Doppler Ultrasonography (Terason t3000cv, Teratech, Burlington, MA) with a 10.0MHz linear array ultrasound transducer probe. Recordings were collected at 20 frames per second (Camtasia®, TechSmith®, Okemos, MI, USA) during baseline and once every fifteen minutes during heating. Cardiac output was measured at baseline and every twenty minutes during heating using an Open Circuit Acetylene Wash-In method (Beck Integrated Physiological Testing Systems, Saint Paul, MN, USA). Blood glucose was measured during baseline and every thirty minutes of heating with a commercial blood glucose meter (Precision Xtra; Abbott Diabetes Care Inc., Alameda, CA, USA).

Once baseline measurements were complete, subjects transferred to a 40.5°C hot tub where they reclined on a bench until they were immersed to heart level with both arms remaining out of the water. Subjects remained in this position for the duration of the 60 minutes of hot water immersion. An electric fan was turned on high and angled toward the subject once subject core body temperature reached 38.5°C. Measurements were taken as described above and subjects were encouraged to drink water throughout immersion, the amount of which was closely monitored.

After 60 minutes of immersion, subjects exited the hot tub with as little physical exertion as possible. All instrumentation remained attached during this transfer to ensure continued monitoring in the same area as during hot water immersion. Subjects reclined in a recovery chair immediately after exiting the hot tub and remained there for at least 15 minutes or until their core temperature declined sufficiently to indicate that they were returning to baseline. During this time, local heaters surrounding laser
Doppler probes were turned on and heated the skin to 43.5°C to induce maximal vasodilation in the cutaneous vasculature. Measurements of subject perceptual scales, temperatures, and blood pressures continued throughout the recovery period. A final nude body weight was taken after all other final measurements and de-instrumentation. Pre and post nude body weights and the weight of the water consumed by the subject were used to determine sweat loss and dehydration level as a way of ensuring that subjects did not leave the laboratory in a dehydrated state.

Image 1. Perceptual scales used to compare subjective experiences between subjects.

**Schematic of Protocol:**

- **U/S** = Ultrasound: measurement of Arterial Blood Flow/Shear
- **Q** = Cardiac Output Measurement
- **SkBf** = Skin Blood Flow
- **★** = Rectal, Tympanic, Sublingual, and Skin Temps, Perceptual scales, Heart Rate, Blood Pressure

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**SKIN WETTEDNESS SCALE**

| DRY  | 0  |
| SLIGHTLY WET | 4  |
| DAMP/HUMID | 8  |
| WET  | 12 |

**THERMAL SENSATION SCALE**

| COLD  | 6  |
| COOL  | 7  |
| SLIGHTLY COOL | 8  |
| NEUTRAL | 9  |
| SLIGHTLY WARM | 10 |
| WARM  | 11 |
| HOT  | 12 |

| VERY, VERY LIGHT | 13 |
| VERY LIGHT | 14 |
| FAIRLY LIGHT | 15 |
| SOMEWHAT HARD | 16 |
| HARD | 17 |
| VERY HARD | 18 |
| VERY, VERY HARD | 19 |
| MAXIMUM EFFORT | 20 |

**BORG SCALE**

| RATING OF PERCEIVED EXERTION | 6  |
| VERY, VERY LIGHT | 7  |
| VERY LIGHT | 8  |
| FAIRLY LIGHT | 9  |
| SOMEWHAT HARD | 10 |
| HARD | 11 |
| VERY HARD | 12 |
| VERY, VERY HARD | 13 |
| MAXIMUM EFFORT | 14 |
Measurements

Arterial Shear stress and Blood flow

Arterial blood flow and shear stress are physiological values that may be calculated from the direct measurement of blood velocity and vessel diameter. Doppler ultrasonography is a widely accepted method used to image vessels and track blood velocity. Velocity is measured as a portion of the high frequency sound waves emitted by the ultrasound head are reflected from red blood cells within arteries. Reflected waves return to the ultrasound head, but at a lower frequency due to the Doppler Effect since blood is moving away from the receiving apparatus. The Doppler Effect describes the change in frequency of soundwaves depending on whether the source of the sound is moving towards or away from the receiver. In this case, the blood cells are the source of the sound being received at the ultrasound head even though it was the ultrasound that originally created the sound. Change in diameter and frequency, once measured, may then be used to calculate blood flow through a particular artery:

$$\text{Flow} = \pi \left( \frac{\text{diameter}}{2} \right)^2 \times \text{velocity} \quad (1)$$

Shear stress is also calculated from these measurements:

$$\text{Total shear} = 4 \times \left( \frac{\text{velocity}}{\text{diameter}} \right) \quad (2)$$

Skin Blood Flow

Skin blood flow may be measured using Laser Doppler probes placed over an area of skin. A concentrated beam of light shone from the probe is transmitted onto and through the skin where it scatters, hitting a limited area of tissue from all different
directions in a diffuse sphere of the same frequency of radiation. However, when the light/radiation hits a cell that is moving, i.e. a blood cell, it causes the radiation’s frequency to change from that coming from stable cells in that same Doppler Shift.\textsuperscript{38} The change in frequency is equal to:

\[ \Delta f = \left( \frac{\text{velocity of moving cells with respect to the observer}}{\text{velocity of the initial wave}} \right) \times f \text{ of stable cells} \quad (3) \]

By measuring the change in frequency and knowing both the velocity of the initial wave and the frequency of radiation coming from stable cells, it is possible to calculate the velocity of the moving cells with respect to the observer or the probe.\textsuperscript{38} Laser Doppler probes are unable to compute flow precisely as flow is a unit of volume per time and the probes cannot accurately measure blood volume. Therefore, measurements are made in terms of flux and are adjusted for the mean arterial pressure (MAP) since changes in blood pressure may appear to be changes in cutaneous blood flow when truly they are not. This adjustment causes the units of skin blood flow to become Cutaneous Vascular Conductance (CVC):

\[ \text{CVC} = \frac{\text{Laser Doppler flux}}{\text{MAP}} \quad (4) \]

Experimental values are adjusted to CVC measurements of maximum vasodilation in the skin, achieved through local heating to 43.5 °C or local administration of a vasodilatory drug, so that they may be compared to values obtained at other sites or in other subjects. The value reported is then %CVC\textsubscript{max} or the percentage of the current CVC as compared to maximum CVC.
Cardiac Output

Several methods for measuring cardiac output have been developed, and many of these are tested against the direct Fick method which is considered to be the gold standard of cardiac output measures.\textsuperscript{20, 37, 38} The direct Fick method is an invasive procedure that requires insertion of a catheter into the antecubital vein that is then threaded up to and through the heart until it reaches the pulmonary artery. A catheter is also placed in the radial artery such that blood samples of both mixed venous and arterial blood may then be taken at opportune moments.\textsuperscript{20} After catheterization, expired air is collected into a Douglas bag for an exact amount of time, at least a minute but preferably longer.\textsuperscript{5} During gas collection, arterial and mixed venous blood samples are drawn. Analysis of carbon dioxide and oxygen in blood samples and expired air samples are then used to calculate cardiac output.\textsuperscript{5}

Such an invasive method may be accurate, but can also be dangerous, expensive and time consuming. Therefore, several non-invasive measurements have been developed including acetylene rebreathe, acetylene wash-in, electrical cardiography, Doppler, and carbon dioxide rebreathe.\textsuperscript{37} Each have their limitations, but the acetylene methods have been validated when compared to invasive techniques.\textsuperscript{20}

The method used in the current study is the Open circuit Acetylene wash-in (OpCirc). With OpCirc, subjects breathe a mixture of gasses, one soluble the other insoluble.\textsuperscript{20} There is a large reservoir of these mixed gasses available for the subject to breathe, and the subject exhales into open air which allows them to breathe normally throughout measurement. Expired air is analyzed by a mass spectrometer which measures concentrations of acetylene and helium. The soluble acetylene concentration
upon exhale is used to estimate pulmonary blood flow while the insoluble helium concentration is used to track lung volume and alveolar dead space. Pulmonary blood flow estimation makes noninvasive cardiac output measurements possible due to the closed circuit nature of the cardiovascular system.

Blood enters pulmonary circulation via the pulmonary artery and is, at this point, deoxygenated. The pulmonary artery branches into smaller and smaller vessels until these vessels become capillaries which surround the smallest component of the lung, the alveoli. Gas exchange takes place here, where the tissue between the blood and inspired air is the thinnest. Carbon dioxide is released from the blood and oxygen is bound to hemoglobin. Using the OpCirc method, this is also where acetylene dissolves into the blood. Blood from the capillaries then travels to venules which become pulmonary veins that return oxygenated blood to the heart to be circulated throughout the body. The rate at which blood returns to the heart from the lungs determines the volume of blood that the heart can pump per unit time. In other words, venous return determines cardiac output. The rate acetylene is take up into the blood is determined by perfusion or blood flow through the lungs that then carries the acetylene away as it returns to the heart. Because of this it is possible to calculate pulmonary blood flow away from the lungs to the heart and therefore cardiac output.

OpCirc measurements were taken as subjects breathed into a mouthpiece that was attached to a pneumotach (Pneumotach; Hans Rudolph Inc., Kansas City, MO, USA). The pneumotach was, in turn, attached to a mass spectrometer (MGA 1100; MA Tech Services Inc., Saint Louis, MO, USA), a pneumotach amplifier (Series 1110; Hans Rudolph Inc., Kansas City, MO, USA) that sent information to the OpCirc software
(Beck Integrated Physiological Testing System), and a Sliding-Type™ pneumatic
directional valve (4285 Series; Hans Rudolph Inc., Kansas City, MO, USA). The valve
was attached to a Douglas bag (Hans Rudolph Inc., Kansas City, MO, USA) filled with
a mixed gas containing 0.593% acetylene, 9.06% helium, 21.0% oxygen, and balanced
with nitrogen (Device-Lung Diffusion Mixture; Norlab Calibration Gas, Boise, ID,
USA) so that the air the subject was breathing could be switched from room air to that
contained in the Douglas bag. Subjects also wore a nose clip to ensure that all of their
inspired and expired air would flow through the pneumotach.

Subjects breathed on the above apparatus for approximately 2 minutes to get
accustomed, during this time they also began to breathe in rhythm with a metronome.
Once the subject appeared comfortable, the gas they were inhaling was changed from
room air to the acetylene gas mixture using the directional valve. Subjects took 8-10
breaths of the acetylene gas mixture before they were changed back to inhaling room air
and removed the apparatus. Cardiac output was then calculated by the OpCirc module
of BIPS software (Beck Integrated Physiological Testing System).

Analysis

Recordings of Doppler ultrasonography were analyzed using software equipped
to with vessel edge-detection abilities (DICOM, Perth, Australia). With this,
measurements of vessel diameter and blood velocity were taken for at least 45 seconds
of each recording. Calculations of average blood flow, total shear, anterograde shear,
and retrograde shear were then possible. Skin blood flow was averaged for
approximately 60 seconds in areas of interest and then converted to CVC and
%CVC\text{max}.

One-way repeated measures Analysis of Variance (ANOVA)s were
conducted to determine whether changes were significant when compared to baseline,
alpha level set to P<0.05.
Results

During hot water immersion core rectal temperature increased steadily, becoming significantly elevated from baseline at 15 minutes (p<0.01) of hot water immersion and remained elevated (Figure 1). Heart rate increased rapidly for the first 20 minutes of immersion, becoming significant by 5 minutes (p<0.001), before plateauing for the remaining time (Figure 2).

Skin Blood Flow and Temperature

Skin blood flow increased rapidly between 0 and 20 minutes of heating, becoming significantly higher by 10 minutes (p<0.01), before it too plateaued (Figure 3). Skin temperature increased at a slower rate for the first 35 minutes before steadily decreasing (Figure 4). The Chest skin temperature site was significantly higher than
baseline from 20-50 minutes (p<0.01), the Forearm site became significantly higher at 20 minutes (p<0.01) and remained elevated throughout immersion, while the Back site was significantly elevated from 25 to 45 minutes of immersion (p=0.019).

**Hemodynamic Measurements**

Cardiac output increased significantly compared to baseline at 20 minutes (p<0.01) and continued to increase throughout immersion (Figure 5). Arterial blood flow in both carotid and brachial arteries increased significantly by 15 minutes (p<0.01 and p<0.001, respectively) and remained elevated during hot water immersion (Figure 6). Total and anterograde shear in the brachial artery both increased significantly at 15 minutes (p<0.001, p<0.001 respectively) and stayed elevated throughout immersion (Figures 7 and 8). Total and anterograde shear in the carotid artery also increased significantly at 15 minutes (p<0.01, p<0.01 respectively), but less drastically than brachial (Figures 7 and 8). Retrograde shear in the brachial artery decreased significantly by 15 minutes (p<0.001), and remained attenuated for the remainder of
immersion (Figure 9). There was no significant change in carotid retrograde shear (Figure 9).

Figure 5. Cardiac output at baseline (0min) and during hot water immersion. * Denotes significant (p<0.05) difference compared to baseline.

Figure 3. Brachial and carotid arterial blood flow at baseline (0min) and during hot water immersion. * Denotes significant (p<0.05) difference compared to baseline.

Figure 7. Total shear in brachial and carotid arteries at baseline (0min) and during hot water immersion. * Denotes significant (p<0.05) difference compared to baseline.
Acceptability and Safety Measures

Systolic blood pressure (SBP) increased during hot water immersion, only becoming a significant elevation when compared to baseline at 45 minutes (p=0.048). Diastolic blood pressure (DBP) decreased significantly by 5 minutes and remained significantly decreased throughout heating (p<0.001), resulting in an overall decrease in mean arterial blood pressure (MAP) which also decreased significantly by 5 minutes (p<0.01) and remained attenuated during immersion (Table1). Perceived exertion, thermal sensation, and skin wettedness each increased steadily through heating, thermal sensation reaching a plateau followed by perceived exertion at 15 and 20 minutes, respectively (Table 1). There was no trend or significance in blood glucose measurements (Means (g/dL): 0min = 82 ± 1.9, 30min = 84 ± 3.1, 60min = 82 ± 2.4).
<table>
<thead>
<tr>
<th>Measurement</th>
<th>0min (baseline)</th>
<th>20 min</th>
<th>40 min</th>
<th>60 min</th>
<th>75 min</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAP</strong></td>
<td>87 ± 1.4</td>
<td>81 ± 1.5*</td>
<td>81 ± 2.0*</td>
<td>80 ± 1.8*</td>
<td>83 ± 1.6</td>
</tr>
<tr>
<td><strong>SBP</strong></td>
<td>119 ± 2.1</td>
<td>118 ± 2.6</td>
<td>127 ± 4.0</td>
<td>126 ± 3.6*</td>
<td>118 ± 2.1</td>
</tr>
<tr>
<td><strong>DBP</strong></td>
<td>71 ± 1.7</td>
<td>63 ± 1.8*</td>
<td>58 ± 1.8*</td>
<td>57 ± 1.5*</td>
<td>65 ± 2.0</td>
</tr>
<tr>
<td><strong>Perceived Exertion</strong></td>
<td>6 ± 0.1</td>
<td>11 ± 0.9</td>
<td>13 ± 0.8</td>
<td>11 ± 0.7</td>
<td>7 ± 0.4</td>
</tr>
<tr>
<td><strong>Thermal Sensation</strong></td>
<td>12 ± 0.4</td>
<td>17 ± 0.3</td>
<td>18 ± 0.4</td>
<td>16 ± 0.5</td>
<td>11 ± 0.6</td>
</tr>
<tr>
<td><strong>Skin Wettedness</strong></td>
<td>0 ± 0.01</td>
<td>7 ± 0.8</td>
<td>10 ± 0.6</td>
<td>7 ± 0.9</td>
<td>2 ± 0.4</td>
</tr>
</tbody>
</table>

Table 1. Blood pressure measurements and perceptual scales at baseline (0min) and during immersion.
* Denotes significant (p<0.05) difference compared to baseline.
Discussion

This study examined acute physiological and perceptual responses to a 60 minute bout of hot water immersion. Key findings include: 1) significant increases in core and skin temperatures likely influencing the dramatic increase in skin blood flow; 2) significantly elevated heart rate, cardiac output, arterial blood flow and shear stress 3) slight but significant decrease in MAP; 4) subjects reported increases in perceived thermal sensation, exertion and skin wettedness; 5) an insufficient relationship between tympanic, sublingual, and core temperatures for either tympanic or sublingual methods to replace core temperature measurement.

Blood Flow

Changes in skin blood flow, whether increasing or decreasing, represent the main cardiovascular adjustments in response to thermal challenges. Sweating and cutaneous vasodilation are thought to be initiated as a function of elevated core temperature, and large increases in skin blood flow have been observed with hot water immersion and other passive heating protocols. Skin blood flow is known to rise locally when one area of the body experiences an elevation in temperature, and it has been shown to increase systemically in response to increased whole body skin temperature and core temperature. Even tolerable increases in whole body skin and core temperatures have been shown to stimulate maximal skin blood flow systemically. A similar response can be seen in our results (Figure 3). Forearm skin blood flow increased from about 8% of max CVC at baseline during rest to over 50% of
max CVC at plateau during heating, increasing steadily as core and skin temperatures increased. The plateau in skin blood flow began as skin temperature began to increase less drastically and remained at a plateau when skin temperature began to decrease possibly due to increased core temperatures.

**Cardiac output**

During hot water immersion, cardiac output nearly doubled (Figure 5). This was largely due to the elevated hear rate (Figure 2) and a partial maintenance of stroke volume during heating, and was likely driven by elevations in skin blood flow. Increased blood flow to a large area of skin results in large changes in the distribution of blood throughout the body and increased cardiac output. A previous study noted increased cardiac output with hot water immersion, but with a considerably different protocol from the one used presently. Systemic cutaneous vasodilation, if not compensated for by elevated cardiac output and a redistribution of blood from other organs, would cause a dramatic decrease in arterial blood pressure. However, the body closely regulates arterial blood pressure and makes adjustments to maintain a relatively stable mean arterial pressure (MAP). The combination of elevated heart rate and increased cardiac output are similar demands to mild to moderate exercise on the heart. Additionally, increased cardiac output during hot water immersion without help from the skeletal muscle pump, used during exercise, may work the heart harder possibly influencing the improved cardiac function noted with heat therapy.
Shear Stress

Elevations in the required blood flow to cutaneous beds and subsequent elevations in cardiac output may explain increases in arterial blood flow and shear stress observed in this study (Figures 6-9). Previous studies have noted improved endothelial function following heat therapy, but few suggest an explanation for these improvements. Increases in shear stress, specifically increased anterograde paired with decreased retrograde, are connected to enhancements in endothelial function. Such increases are often noted to occur during exercise. Therefore it is possible that improved endothelial function noted in studies examining heat therapy may occur due to similar mechanisms as improvements seen with exercise. Improved endothelial function and possible increases in cardiac function may be central influences of the overall improved cardiovascular health that is being observed with the use of heat therapy.

Acceptability of Hot Water Immersion Protocols

The safety of hot water immersion has been examined by several groups, but the majority of those focused on safety test the standard 10-20 minutes in patient populations. They found that hot water immersion that lasted 10-15 minutes is relatively safe for patients with stable coronary artery disease and stable hypertension. Studies that included a longer period of hot water immersion (60-75 minutes) reported no instances of subjects fainting or feeling unwell due to their protocols. In both studies, slight but significant decreases in MAP were observed. Significant
increases in heart rate and core temperature, nothing past what the body would experience with mild to moderate exercise, were also observed.\textsuperscript{12, 35, 41}

The current study’s findings mirrored those of the literature. Heart rate and core temperatures increased to levels significantly above baseline, but within the scope of observed increases with exercise.\textsuperscript{14} MAP decreased significantly, dropping during the first 15 minutes of immersion before recovering at a slightly lower level than baseline. Even with this decrease in blood pressure, only three subjects experienced mild to moderate lightheadedness. An additional finding of this study was that a 60 minute bout of hot water appeared to have no effect on blood glucose concentrations. Young healthy individuals will probably not experience dramatic decreases in blood glucose leading to adverse symptoms within these parameters. Therefore, a reasonable amount of care should be taken when utilizing hot water immersion. Caution especially in entering and exiting the tub as slipping is a major hazard around water, and awareness of any lightheadedness with standing. Similar to sitting after high intensity exercise, it is unwise to stand too quickly as systemic vasodilation may lead to venous pooling and an increased risk of fainting. Still, the risk of fainting after longer periods of hot water immersion in young healthy people appears to be minimal if they are aware of its effects and react accordingly.

Subjects’ responses to perceptual scales showed that they experienced a rapid change in thermal sensation from neutral to quite hot upon entering the hot tub. That sensation increased over time, but significantly decreased once a fan was turned on and pointed in their direction. Similarly, perceived exertion levels increased upon entering
the hot water and continued to increase before a fan was turned on. Skin wettedness followed a similar pattern.

**Temperature**

Some temperature measurement methods had more success than others at estimating core temperature. Tympanic temperature at first appeared to mirror core temperature during heating; however, when comparing exact values less than half of tympanic temperatures were similar within 1°C of core temperatures and varied up to 3°C. With such a wide range compared to core temperatures, tympanic temperature measured with a standard thermometer was not accurate enough to be used as a safe replacement. Variation from core temperature could have been caused by circulating air cooling the head, warm air from the hot tub heating the ear canal, or even that the tympanic thermometer did not reach far enough into the ear canal to get an accurate reading. Sublingual temperature was very much reliant upon the amount the subject was speaking and the timing of drinking water. Overall, this method appears to be very unreliable in this setting since the consumption of water during hot water immersion is encouraged to prevent dehydration. Other methods of temperature measurement should be investigated for use with hot water immersion outside of the research lab.
Conclusion

60 minutes of hot water immersion appears to cause increases in core temperature and key hemodynamic variables similar to increases seen with exercise. Therefore, it is possible that cardiovascular improvements seen with heat therapy are brought about through similar mechanisms as exercise. Body temperature and any adverse symptoms associated with heat exposure should be monitored throughout immersion, but an acceptable alternative measurement to core temperature still needs to be found. In addition, a reasonable amount of care in transferring and recovering from hot water immersion should be taken.


