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# The role of the hydrostatic indifferent point in governing splanchnic blood pooling during orthostatic stress

Ursula Anne Diehl  
*University of Iowa*

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**THE ROLE OF THE ABDOMINAL HYDROSTATIC INDIFFERENT POINT IN  
GOVERNING SPLACHNIC BLOOD POOLING DURING ORTHOSTATIC  
STRESS**

by  
Ursula Anne Diehl

A thesis submitted in partial fulfillment  
of the requirements for the Master of  
Science degree in Exercise Science  
in the Graduate College of  
The University of Iowa

May 2011

Thesis Supervisor: Associate Professor Don D. Sheriff

Graduate College  
The University of Iowa  
Iowa City, Iowa

CERTIFICATE OF APPROVAL

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MASTER'S THESIS

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This is to certify that the Master's thesis of

Ursula Anne Diehl

has been approved by the Examining Committee  
for the thesis requirement for the Master of Science  
degree in Exercise Science at the May 2011 graduation.

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To my husband Evan, who impresses me every day and inspires me to work harder.  
To my family, for their support, and especially for my mother Rachell, for her  
encouragement, motivation, and for teaching me to never give up.  
Thank you and I love you

## ACKNOWLEDGMENTS

Thank you to Dr. Don D. Sheriff for his support and guidance throughout this endeavor. His motivation and dedication to knowledge have encouraged me to expand my thinking and continue to seek answers for my questions.

My sincerest thank you goes out to the faculty and professors within the department of Health and Human Physiology, especially Dr. Harald Stauss, Dr. Ray Fagenbaum, and Dr. Clay Peterson. Their help and investment in my endeavors throughout my undergraduate and graduate studies have exceeded my expectations and I'm tremendously grateful.

Thank you to my husband for your optimism and confidence in my abilities. Your love and encouragement helps me rise up to face new challenges.

Thank you to my family and friends for your moral support and abundance of love. I'm extremely blessed to have you in my life.

## ABSTRACT

The response of the circulatory system to gravity and hydrostatic forces has been well studied, for example the hydrostatic indifferent point (the location at which pressure does not change with posture) of the venous system has been established to be an important determinant of orthostatic responses and it has been found to be located near the diaphragm. However, the role of the abdomen has been less researched; for example, it appears that the concept that the abdominal compartment may have its own hydrostatic indifferent point has been overlooked. The goal of the present study was to establish the location of the abdominal hydrostatic indifferent point ( $HIP_{ab}$ ) and to test the hypothesis that binding of the lower abdomen would shift the location of the  $HIP_{ab}$  cranially. Intra-abdominal pressure was measured using a modified wick needle technique in the supine and upright posture before and after binding of the lower abdomen in 7 anesthetized rats. In the unbound condition, the  $HIP_{ab}$  was located  $5.2 \pm 0.3$  cm caudal to the xyphoid, meaning the hepatic veins were exposed to relatively large negative interstitial pressures during head-up tilt. Binding of the lower abdomen significantly ( $p < 0.05$ ) shifted the  $HIP_{ab}$  cranially by 1.7 cm. Thus, the relatively caudal location of the  $HIP_{ab}$  causes a relatively large hepatic transmural pressure owing to the fall in interstitial pressure during upright posture. The cranial shift of the  $HIP_{ab}$  by binding of the lower abdomen lessens the fall in hepatic extramural pressure and thereby protects the hepatic veins from distension.

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## CHAPTER I

### INTRODUCTION

#### Orthostatic Intolerance

Orthostatic intolerance is a condition in which gravitational affects on the body in the upright position lead to the development of pooling of blood in the lower extremities, which reduces the volume of blood returning to the heart. The large, sudden fall in blood pressure produces cerebral malperfusion which can lead to syncope, falls, and injuries. Falls resulting from syncope account for 3% of all visits to the emergency room (28). Falls are also the leading cause of accidental deaths in the elderly, specifically persons over 65 years of age (11).

Orthostatic intolerance affects an estimated 500,000 people in the United States and four times as many females as males (28). Upon standing, those suffering from orthostatic intolerance experience a feeling of lightheadedness, weakness, heart palpitations, and hyperpnea (4, 28). Other triggers for this syndrome include substantial weight loss, spaceflight (28), a warm environment, and emotionally stressful situations (5).

The circulatory system functions as a hydrostatic column of fluid. Although both arteries and veins are affected by hydrostatic forces, the thin-walled veins are more vulnerable to their debilitating effects. While standing upright, about 75% of the blood volume is located in the veins and approximately 70 to 75% of the total blood volume is below the level of the heart (21). Cardiac output may be reduced by 40% (18). Most humans spend much of their day successfully in the upright position, indicating that the body has mechanisms to compensate for the fall in cardiac filling induced by gravity. In people with orthostatic intolerance, these mechanisms prove inadequate.

## Acute Mechanisms to Compensate for Decreased Cardiac

### Filling

When a person transitions from the supine position to upright posture, blood begins to pool in the compliant veins in the lower extremities, resulting in a decrease in blood flow returning to the heart. The resultant decreased cardiac filling leads to a decrease in stroke volume, cardiac output, and blood pressure, which is sensed by the stretch-sensitive baroreceptors in the carotid sinus and aortic arch. The information from the baroreceptors is sent to the nucleus tractus solitarius of the medulla. The decrease in baroreceptor firing leads to an increase in sympathetic outflow and a decrease in parasympathetic activity, resulting in increased systemic vascular resistance, increased heart rate, and increased contractility, all of which function to maintain blood pressure. Unfortunately, the partial restoration of blood pressure is sometimes only temporary. Baroreceptors in the aortic arch and carotid sinus are able to adapt to the lower pressure, so long-term regulation requires hormonal and renal mechanisms. The concepts of these long term mechanisms to regulate blood pressure are beyond the concept of this paper.

### Adverse Consequences of Gravity

Because we spend a great proportion of our waking hours in the upright posture, gravity presents significant challenges for the arterial and venous components of our cardiovascular system.

### Arterial

While in the supine position, arterial pressure is relatively equal at the level of the feet, heart, and head. Upon standing, additional pressure caused by the hydrostatic column of blood within the arteries below the heart is added to the dynamic pressure generated by the heart. The height of the column of blood is proportional to the increase in pressure. Thus, the local arterial pressure is greatest at the level of the feet and can rise from 100 mm Hg in the supine position to 200 mm Hg standing upright (21). But

because arteries are relatively stiff and have a thicker wall compared to veins, the large rise in pressure due to gravity is better tolerated.

Above the heart, the negative hydrostatic pressure causes a decline in arterial pressure and thus a fall in cerebral arterial pressure. Hydrostatic arterial pressure falls to -40 mm Hg at the level of the head, while the arterial pressure from the heart's pumping action doesn't change. Therefore, the local arterial pressure at the head falls from ~100 mm Hg supine to ~60 mm Hg standing upright. Cerebral blood flow, which is dependent on cerebral arterial pressure, is maintained until arterial pressure falls below ~60 mm Hg via cerebral autoregulation. Thus the ability to maintain arterial pressure above the heart is crucial to sustaining cerebral blood flow and thus consciousness (18).

### Venous

The affects of gravity on the venous system are somewhat more complex compared to the arterial system. Like arterial pressure, while lying down, venous pressure is essentially the same in the locations of the foot, heart, and head. Upon standing up, the distensible veins below the heart engorge with blood due to the large increase in hydrostatic pressure. While the driving force for blood to flow from the heart to the capillaries is about 80 mm Hg, the pressure promoting venous return to the heart from the venules is only 15-20 mm Hg (21). As mentioned previously, with nearly 75% of the total blood volume below the level of the heart within the extremely distensible veins, the human cardiovascular system must overcome a very difficult challenge when in the upright posture.

Above the heart, the veins cannot withstand the increasingly negative pressure and collapse. Pressure within the veins continue to fall above the level of the heart and can become as low as -40 mm Hg at the top of the head (21). Cerebral vessels within the rigid skull are tethered to surrounding tissues and thus held open, which helps maintain blood flow. Thus the intraluminal artery to vein pressure gradient above the heart falls

leading to reduced cerebral blood flow, and is constant below the heart, resulting in reduced cerebral perfusion pressure, venous pooling in the lower extremities, reduced stroke volume, and reduced cardiac output.

After several hours of upright posture, fluid begins to leak out of the capillaries. Filtration out of the capillaries is heavily dependent on the hydrostatic pressure within the veins, thus, hours of upright posture lead to edema in the lower extremities. Filtration and edema persist, in order to increase the interstitial pressure to delimit the high hydrostatic blood pressure within the vessel (lower the transmural pressure, which is further explained below). Unfortunately, syncope usually precedes the equalization of these pressures (21).

### Transmural Pressure

The amount of blood that is displaced to the veins is determined by vessel diameter, which in turn is governed by transmural pressure. Transmural pressure ( $P_{TM}$ ) is defined as the pressure inside the vessel ( $P_{inside}$ ) minus the pressure outside the vessel ( $P_{outside}$ ), also known as the interstitial pressure.

$$P_{TM} = P_{inside} - P_{outside}$$

With transmural pressure rising, vessel diameter increases as well, and the extent of pooling increases. While standing upright, pressure in the veins above the heart fall and the veins collapse. The greatest amount of pooling occurs in the legs where the interstitial pressure ( $P_{outside}$ ) is approximately 0 mm Hg and therefore  $P_{TM}$  is equal to intravascular pressure ( $P_{inside}$ ). As mentioned previously, venous pressure is highly influenced by hydrostatics, and thus,  $P_{inside} = \rho gh$  ( $\rho$  is the density of blood ( $\text{kg/m}^3$ ),  $g$  is the gravitational acceleration ( $\text{m/s}^2$ ), and  $h$  is the height of column of fluid (m)).

$$P_{outside} = 0, P_{TM} = P_{inside} = \rho gh$$

However, as discussed below, within the abdominal compartment,  $P_{outside}$  is high enough to restrict  $P_{TM}$ , vessel diameter, and thereby reduce splanchnic blood pooling.

### Valves in the Venous System

Unlike the arteries, the veins contain a series of one way valves that function to direct blood back to the heart and help combat the effects of gravity. Upon standing, blood travels from the arteries to the veins and the hydrostatic column of blood in the first segment below a valve within a vein increases. The venous segments fill sequentially until eventually all of the valves are forced open until there is one long column of blood below the heart, and this leads to a substantial accumulation of blood volume in the lower extremities.

The skeletal muscle pump is a physical defense mechanism that works to propel blood from the lower extremities back to the heart. By contracting the muscles of the legs, there is a physical compression of the vein and the pressure inside the vessel increases. With the increase in pressure, the valve superior to the compressed area of the vein opens and blood is moved towards the heart, while the valve inferior to the compression remains closed. Once the muscle relaxes, the pressure within the vessel falls causing the superior valve to close and the inferior valve to open. This fall in pressure directs blood from inferior segments to flow into more superior segments and the process repeats with each contraction (18).

Individuals with insufficient venous valves or congenitally absent valves experience severe orthostatic intolerance (21, 25). Without valves to prevent the fall in blood in the veins towards the feet, assumption of upright posture leads to a continuous column of blood below the heart. The immediate pooling in the extremities leads to a fall in stroke volume, cardiac output, and syncope.

### Abdominal Binding

Treatments of orthostatic intolerance include lifestyle and behavioral changes and in severe cases, medications that improve vasoconstriction and increase blood volume. Physicians specializing in orthostatic intolerance agree that a steady intake of water or

other fluids, at least two liters per day, reduces most symptoms (5). While these treatments have shown to be effective in combating orthostatic intolerance they may exacerbate hypertension (24).

Smit et al. (24) demonstrated that abdominal binding raises arterial blood pressure and can relieve the symptoms of orthostatic intolerance. Binding, like the action of the skeletal muscle pump, is presumed to constrict vessel diameter by increasing the intra-abdominal pressure, and thus reduce local transmural pressure. The reduction in local transmural pressure therefore prevents splanchnic pooling and constricting vessel diameter directs blood back towards the heart. The increase in venous return and stroke volume helps alleviate the fall in cardiac filling that accompanies upright posture (24). Although the increases in standing blood pressure may be small, for example systolic blood pressure increased by an average of only 12 mm Hg, Tanaka et al. (26) showed that this small increase was effective enough to raise cerebral perfusion and lessen symptoms.

#### Venous Hydrostatic Indifferent Point

While studying the circulatory system as a continuous hydrostatic column, it is important to discuss the location at which venous pressure does not change with posture, known as the venous hydrostatic indifferent point ( $HIP_v$ ) (12, 21). With head-up tilt, above the location of the  $HIP_v$  pressure falls. Conversely, during head-up tilt, below the location of the  $HIP_v$ , pressure rises and pooling in the lower limbs ensues. The extent of the rise or fall in pressure is proportional to increasing distance from the  $HIP$ .

According to Rowell,  $HIP_v$  is located close to the level of the diaphragm. Its location is determined by the distribution of venous compliance. It has been shown that anything that would reduce lower body compliance such as activation of the muscle pump during exercise would shift the  $HIP_v$  upward and raise cardiac filling pressure (21).



### Rushmer's Model

While studying the effects of gravity on the circulatory system, it is important to examine the fluid dynamics of the abdomen. Rushmer's studies proposed that the contents of the abdomen exert a counter pressure that protects the veins of the splanchnic circulation from dilation and thereby opposes pooling (23). He demonstrated that the abdomen appears to act as a liquid-filled container, open at the top, with a density equal to blood, approximately 1.0 g/ml. As a result of gravity, the pressure within the abdomen behaves as a hydrostatic type of pressure and is dependent on the vertical height of the column of visceral contents above the point of measurement. He noted that intra-abdominal pressure somewhat balances venous pressure, reducing the amount by which the vein walls must support venous pressure. He believed this would decrease the tendency for splanchnic vessel dilation and as a result oppose the pooling of blood within them (23).

While Rushmer never used the term, his model implies that the abdomen has its own HIP ( $HIP_{ab}$ ) and the HIP of his "open container" would be located at the open end. Rushmer's model places the  $HIP_{ab}$  at the level of the diaphragm and has an intra-abdominal pressure equal to 0 mm Hg (23) and rising to 30 mm Hg at the pelvic floor. Because abdominal veins are the same length and density as the viscera, venous pressure will undergo an identical change in pressure of 30 mm Hg. As a result, transmural pressure would remain unchanged within the abdomen and blood would not pool when gravity imposed hydrostatic forces. Rushmer's model has led some to believe that the splanchnic veins are perfectly protected from the affects of gravity. Others still disagree, citing more recent studies that reveal increased splanchnic blood volume during upright posture, as discussed below (21, 27).

### Our Model

Some major alterations must be made to Rushmer's model. The abdomen is obviously a closed compartment and the specific gravity of the viscera is actually closer to 0.9 g/ml (as opposed to 1.0 g/ml). With generally constant compliance throughout the abdomen, we would expect the  $HIP_{ab}$  to be located near the middle of the abdomen, not at the top. With the  $HIP_{ab}$  located near the middle, we would therefore expect to see a rise in pressure below this point and a fall in pressure above during head-up tilt. With these adjustments, we would also expect that the intra-abdominal pressure can be negative at the cranial portion of abdomen. With low, possibly negative pressures near the cranial portion of the abdomen, the liver, also located in cranial part of the cavity, may experience consequences from a rapid change in transmural pressure. If the pressure outside the liver falls to negative values, transmural pressure will rise, causing the liver to engorge with blood. The liver is the most compliant of the abdominal organs (21) and contains about 15% of the total blood volume (18), making it an important reservoir for the cardiovascular system. Therefore, with a  $HIP_{ab}$  located near the middle of the compartment, the liver may be subject to pooling of blood during head-up tilt.

Contrary to Rushmer's model, Taneja et al. (27) showed that splanchnic blood volume actually increases during head-up tilt by more than 10%. This increase in blood volume within the abdomen consequently contributes to the reduction in cardiac output and orthostatic intolerance. Rushmer also assumed that visceral density was equal to the density of blood. In reality, visceral density is less than that of blood, and so the degree of change in pressure will not be equal between the abdominal and venous compartments. Abdominal pressure will only increase by 90% of the change in pressure seen in the splanchnic veins.

Finally, Rushmer calculated that resting intra-abdominal pressure was approximately 0 mm Hg in humans and dogs. A more recent study found normal intra-

abdominal pressure was about 5-7 mm Hg in humans (8). Resting intra-abdominal pressure in rats however, ranges closer to 0-2 mm Hg (16, 17).

### Implications and Purpose

Although the circulatory system's response to gravity and hydrostatic forces has been well-studied, the abdomen's response has been less researched. As Rushmer first proposed, the abdomen's effects on venous return and cardiovascular function are important in understanding the relationship of the cardiovascular system and gravity. More information about the pressure dynamics of the abdominal compartment may also have significance in treating orthostatic intolerance through abdominal binding.

We have several goals for this study. First, we plan to develop a measurement system for measuring intra-abdominal pressure in rats with a high degree of reproducibility and repeatability. The second goal is to establish the normal intra-abdominal pressure in supine, anesthetized rats and establish its degree of reproducibility and repeatability. Next, we'll measure the change in intra-abdominal pressure during 90 degree head-up tilt as well as the effects on intra-abdominal pressure while binding the lower and upper abdomen (in succession).

In order to establish the effective density of the viscera within the abdominal compartment, we'll also simultaneously measure intra-abdominal pressure at two different locations along the z-axis during 90 degree head-up tilt. Lastly, we'll use the data from the intra-abdominal pressure recordings to determine the location of the abdominal hydrostatic indifferent point and the influence of binding the lower and upper abdomen. We hypothesize that binding the abdomen will increase intra-abdominal pressure and lower compliance, and therefore alter the location of the  $HIP_{ab}$ . With this rise in intra-abdominal pressure, there may no longer be a negative intra-abdominal pressure, thereby reducing distension of the splanchnic veins. Binding should also reduce

the pooling of blood within the abdomen by increasing venous return, which is why binding is a suitable treatment for orthostatic intolerance.

## CHAPTER II

### METHODS

#### Experimental Animals

All experiments were performed on seven female Sprague-Dawley rats (Harlan, Indianapolis, IN) having a median body weight of 184 grams (162-200 g). Rats were housed in clear plastic cages, and temperature ( $21 \pm 2^{\circ}\text{C}$ ) and light periods (12-h light-dark cycle; light on between 6:00 AM and 6:00 PM) were controlled. All rats received a standard chow diet *ad libitum*. Experiments were performed in accordance with the “Guiding Principles for Research Involving Animals and Human Beings” of the American Physiological Society (1) and were reviewed and approved by the Institutional Animal Care and Use Review Committee of the University of Iowa.

#### Experimental Protocols

The rat was weighed and then placed in an induction chamber and anesthetized with isoflurane (induction 5% in oxygen). Once the rat was sufficiently anesthetized, it was transferred to a servo-controlled, heated surgical table set to maintain the rat’s body temperature at  $37^{\circ}\text{C}$  as measured by a rectal probe. The rat was then restrained supine on the table. Anesthesia was maintained by fitting a cone over the nose and mouth for delivery of isoflurane (maintenance 1-2% in oxygen).

Once secured, the hair on the abdomen and thorax were removed using electric clippers. The rat’s thorax was palpated to find the location of the xyphoid and this location was marked on the rat using a permanent marker. We also measured 2 to 5 cm caudal to the xyphoid, depending on the experiment, and marked those locations.

#### Modified Wick Technique

To measure abdominal pressure in the anesthetized rats, we used a modified wick technique based on technique described by Fadnes et al. (10). A 2- 4-mm-long opening

was filed into the side of a 22 gauge, 1-inch long hypodermic needle (Becton, Dickinson, Franklin Lakes, NJ). This side-hole was located 1 cm from the needle tip and on the side opposite of the bevel. A ~4-5 cm length of 4-0 nylon monofilament suture (Monocryl, Ethicon) was inserted into the needle, protruding slightly from both the tip and the base of the needle. The following parts were filled with normal saline and connected together taking great care not to introduce air bubbles. A 22 gauge tubing connector was connected to the plastic dome of a pressure transducer (P10EZ, Ohmeda, Madison, WI). This tubing connector was connected to a 10 cm length of polyethylene tubing (PE50, Becton Dickinson, Sparks, MD) which led to another 22 gauge tubing connector and a male-male stainless steel Luer slip-tip which led to another 22 gauge tubing connector to which the side-hole needle was connected.

At times, when the needle tip was exposed to air, a wicking-action developed in which fluid in the needle and tubing was pulled toward the tip of the needle creating a negative pressure at the transducer. Therefore, the needle tip was immersed in a small droplet of saline to prevent this wicking action and thereby maintain the pressure stable at zero when the needle was outside of the body.

The modified wick technique was used to measure abdominal interstitial fluid pressure because of its simplicity and reliability (10). For example, insertion of an unmodified needle could lead to the tip of the needle becoming plugged with tissue and a continuous water column would no longer be available between the interstitial fluid and the needle lumen. This would result in irregularities in the recorded pressure. Using a side-hole modified wick technique needle, if the tip became plugged, the side-hole would allow for a continuous column of fluid and pressure would be measured correctly.

#### Head-Up Tilt Protocol

The needle connected to the transducer was fully inserted into the abdomen of the rat approximately 1 cm below the ventral surface of the abdomen. The needle transducer

was secured to the table in a manner that kept it parallel to the tilt table. A 10 cm by 10 cm gauze sponge (Kendal Curity, Mansfield, MA) was unfolded and rolled into an approximately 40 cm by 2 cm strip. This strip of gauze was wrapped around the lower abdomen 4-6 cm below the xyphoid of the rat and secured in place with a loose knot. The set-up was then allowed to equilibrate for a few minutes. The rat then underwent three 90° head-up tilts (HUT) each lasting 30 seconds. The first HUT was performed and then the rat was returned to the original position to rest for 30 s.

The rats then underwent the tilting protocol illustrated schematically in Figure 1. For each tilt, the table was manually rotated such that the rat experienced “pitch” rotation (15) about its Y-axis to the 90 degree head-up position which was maintained for 30 s after which the rat was pitched back to the supine posture. Movement times were approximately 1 s (90 degree/s). The animal was then allowed to recover for at least 30 s. The gauze strip was tied more snugly around the abdomen of the rat with the aim of raising abdominal pressure by about 2 cm of viscera. At least 30 s was allowed after binding the rat’s abdomen before the second HUT was performed. The rat was then returned to its rest position for another 30 s, after which the piece of gauze was loosened, allowing abdominal pressure to fall. Finally, the third HUT was performed for 30 s and returned to the original supine rest position. This counterbalanced design was employed to minimize potential time affects stemming from repeated gravitational stress. After the third HUT, the needle-transducer in the abdomen was removed and the tip was immediately placed in a small pool of saline in order to prevent occurrence of the wicking-action described above.

This protocol of tilting the rats was then repeated twice more, for a total of nine HUTs. It was deemed important to make measurements with the needle introduced three separate times to test the repeatability and reproducibility of the measurement system. Throughout the experiment, the rat’s ventilation was monitored to ensure it was adequate even if the abdomen was bound.

### Binding the Upper Abdomen

In all seven of the rats, the HUT protocol was repeated by binding the upper portion of the abdomen instead of the lower abdomen. Here, the gauze was tied approximately 1-2 cm below the xyphoid. Schematic illustration of the experimental protocol is shown in Figure B1.

### Two Needle Transducers in the Abdomen

In three of the rats, two needle transducers were inserted into the abdomen, one 2-3 cm caudal to the xyphoid and the other 4-5 cm caudal to the xyphoid. This was done in order to measure density of viscera as well as to provide a means of simultaneously estimating the location of the abdominal HIP from two separate pressure measurements.

### Postmortem Measurements

Upon completion of the protocol the animals were euthanized. The abdomen and thorax were then cut open in order to measure the distance from the xyphoid to the right atrium, the distance from the xyphoid to the dome of the diaphragm, and the distance from the xyphoid to the pelvic floor.

### Data Collection

A second pressure transducer was secured to the table and connected to a water filled tube running along the length of the table for measurement of tilt. The abdominal pressure transducer was secured to the tilt table. Both transducers were connected to signal conditioners (model 6600, Gould Instrument Systems, Valley View, OH). These signals were digitized at 250 Hz and written to a fixed disk of a microcomputer with the use of commercially available software (PONEMAH Physiology Platform, P3, Gould Instrument Systems) for later analysis.



### Data Analysis

The analysis was done on 1 s averages of the digitized data starting 10 seconds before tilt and ending 30 seconds after tilt started. Ten second averages were taken at 10 seconds before tilt, the first 10 seconds of tilt, and the last 10 seconds of tilt to provide baseline, early tilt response, and responses in the steady state.

### Technical Considerations

#### Introduction of Air

While examining previous experiments and research performed, we discovered several technical details important to take into account. First, in Rushmer's research in which he tilted dogs to study intraperitoneal pressure, a balloon covered fluid-filled manometer was inserted into the abdomen through a surgical incision (23). This surgical procedure allowed air to be introduced into the abdominal cavity. Rushmer stated that care was taken to remove air that entered the intraperitoneal cavity. The problem of air entering the abdominal cavity was also discussed by Stephen Loring et al. in their studies on gravitational pressure gradients in the abdomen of dogs. In this experiment, a fluid-filled catheter was inserted on a guide wire into the peritoneal cavity through a small incision. They also stated that care was taken to prevent the entrance of air by compressing the abdominal wall manually while inserting the catheter (19). Although Rushmer and Loring et al. (19) had confidence in their methods, it is possible that not all of the air was removed from the peritoneal cavity. Air in the abdominal compartment does not act like a fluid and these studies made no independent measure to directly verify that all the air was removed. To avoid this, we sought to employ a minimally invasive approach for which we settled on a 22 gauge, side-hole modified wick intra-abdominal needle system. By inserting the needle directly into the abdomen without an incision, we greatly decreased the opportunity for air to enter the cavity.

### Location of Pressure Recordings

Rushmer also studied intra-abdominal pressure in humans by recording intra-rectal pressure using an air-containing balloon similar to the method used in the study noted above (23); the biggest difference being the balloon's location in the rectum instead of the abdomen. The difficulty in measuring intra-rectal pressure is that the rectum can be viewed as its own container, pressured to its own potentially different baseline pressure. There also may be effects on pressure recordings from gastrointestinal peristalsis. In our study, we originally attempted intra-rectal pressure but results were unstable and therefore, the approach was abandoned.

### Gradients in Abdominal Pressure

The challenges imposed by the non-homogenous abdominal contents were addressed by Loring et al. (19) in the study of gradients in pressure within the abdomen. For example, even in the supine posture, depending on needle placement within the abdomen, the needle could be pinched between two solid structures and measure a higher pressure than would be recorded elsewhere. With tilting, and the potential for shifting of abdominal contents, a location that was previously not pinched could become pinched. In order to overcome such problems stemming from the non-homogenous nature of the abdominal contents, we took measurements in triplicate and removed and/or repositioned the needle between each measurement. The median was taken in order to not be heavily influenced by extremely high or low pressure recordings stemming from such an occurrence.

### Modified Wick

As discussed earlier within the methods, the use of a non-modified hydrostatic needle presents potential problems. While inserting the needle into the abdomen, the end may become obstructed and no longer contain a continuous column of fluid. Without the continuous column of fluid, pressure recordings could be erratic and unreliable. To avoid

this, we employed a modified wick-technique as outlined above. The side-hole provides for a continuous column of fluid and insertion of a single monofilament facilitates the action of wicking fluid in. We made one substitution to the Fadnes et al. (10) description of the modified wick technique by substituting a single monofilament material for strands of nylon fibers within the needle. We found this modified approach also provided stable and reproducible results.

#### Blind Insertion

An obvious potential problem with our protocol is that we inserted the needle blindly into the abdomen of the rat. Inserting the needle among the abdominal contents has the opportunity to pierce an organ or blood vessel. If such a structure was pierced and blood spilled into the abdominal compartment, the local pressure would change and we could have observed unpredictable pressure recordings. To control for this potential problem, after we performed all head-up tilts, we opened the abdominal cavity to ensure the contents were intact and unharmed. Also the location of the insertion of the needle was chosen to minimize possible damages to the kidneys, bladder, spleen, and liver.

#### Tilting Protocol

Using a tilt-table presents potential for the rat to slip or for needles to move in which case our recordings would be altered and impaired. The rats, needles, and transducer tubing were secured to the tilt table and monitored during the tilt to ensure nothing shifted.

#### Abdominal Binding

A potential complication that could arise with abdominal binding is that it may restrict venous return from the lower body. Abdominal hypertension can impair perfusion of abdominal organs and organ dysfunction beyond the abdominal cavity due to the close relationship among nearby cavities (9). De Waele et al. (9) reported patients

with intra-abdominal hypertension, blood flow to and from the kidneys were impaired caused by decreased cardiac output, as well as under perfusion of the gut, liver, and pancreas. Intra-abdominal hypertension also decreases total respiratory system compliance which leads to decreased tidal volumes (9). By imposing brief periods of binding, at most 1-2 minutes at a time, we protected against any restrictions in venous return or damage to respiratory, kidney, and intra-abdominal organ function. Furthermore, people wearing commercially available abdominal binders tolerate them well.

#### Pressure Recordings

If any air bubbles were present within the transducer tubing or needle, pressure recordings would be unreliable. Great care and patience was taken to prevent any air bubbles from forming within the system.

### CHAPTER III

### STATISTICS

In order to evaluate the overall contribution of the different treatments across the data set as a whole, a multiple linear regression was performed, analogous to a repeated measures analysis of variance. Dummy variables were used as independent variables to encode treatment effects. Dummy variables are variables that take on a value of 0 or 1 depending on the treatment. Six dummy variables were used to encode each animal and two dummy variables were used to encode for treatments. One of these dummy variables encoded binding of the abdomen and took on the value of 0 for unbound and 1 for bound and the other dummy variable encoded for the location of the binder and took on the value of 0 for the lower abdomen and 1 for the upper abdomen. One regression was performed using pre-tilt intra-abdominal pressure as the independent variable and another regression was performed using the abdominal hydrostatic indifferent point as the independent variable. Pairwise comparisons were made using a modified Bonferroni paired t-test to control for multiple simultaneous comparisons. Significance was accepted at  $p < 0.05$ .

## CHAPTER IV

### RESULTS

Table A1 represents median  $\pm$  standard error, minimum, and maximum anatomical measurement values for the 7 female rats used in this study. The median weight was  $184 \pm 5.4$  g, ranging from 162 – 200 g. The median distance from the xyphoid to the right atrium was  $2.5 \pm 0.2$  cm. The median distance from the xyphoid to the dome of the diaphragm was  $1.3 \pm 0.3$  cm. Lastly, the median distance from the xyphoid to the pelvic floor was  $7.5 \pm 0.6$  cm.

Figure B2 demonstrates the effect of binding the lower abdomen on intra-abdominal pressure for one rat during three sequential abdominal bindings in a single representative rat. As shown, binding the lower abdomen increased intra-abdominal pressure from 1 to 2 cm of viscera in this rat.

Figure B3 shows the median  $\pm$  standard error of the baseline intra-abdominal pressures for all 7 rats in the supine position, which was found to be  $1.0 \pm 0.5$  cm of viscera (Table A2). Binding the lower abdomen significantly raised intra-abdominal pressure to  $2.1 \pm 0.6$  cm of viscera ( $p < 0.05$  compared to control) and binding the upper abdomen significantly raised intra-abdominal pressure to  $3.3 \pm 0.9$  cm of viscera ( $p < 0.05$  compared to control).  $P_{ab}$  was not significantly different between the bound lower and bound upper conditions ( $p > 0.06$ ).

The time course of the response of abdominal pressure to tilting in the unbound and bound lower condition for a single representative rat is shown in Figure B4. In this example, abdominal pressure fell by about 3 cm upon head-up tilt in the two control (unbound) conditions whereas abdominal pressure fell by about 2 cm when the lower abdomen was bound.

The time course of the response of abdominal pressure to tilting in the unbound and bound upper condition for a single representative rat is shown in Figure B5. In this

example, abdominal pressure fell by about 4 cm upon head-up tilt in the two control (unbound) conditions whereas abdominal pressure fell by about 6 cm when the upper abdomen was bound.

Figure B6 shows the median location of the  $HIP_{ab}$  for all 7 rats measured in cm caudal to the xyphoid. In the unbound condition, the  $HIP_{ab}$  was located  $5.2 \pm 0.3$  cm caudal to the xyphoid (Table 2). Binding the lower abdomen significantly raised the location of the  $HIP_{ab}$  to  $3.5 \pm 0.2$  cm caudal to the xyphoid ( $p < 0.05$  compared to the unbound condition). Binding the upper abdomen significantly lowered the location of the  $HIP_{ab}$  to  $7.1 \pm 0.9$  cm caudal to the xyphoid ( $p < 0.05$  compared to bound lower). The location of the  $HIP_{ab}$  was not significantly different between the unbound and bound upper conditions ( $p > 0.06$ ).

## CHAPTER V

### DISCUSSION

The major new findings of the present study are as follows. The abdomen behaves as a closed compartment and has its own hydrostatic indifferent point. The abdominal HIP lies caudally within the compartment. Binding the lower abdomen raises the location of the abdominal HIP and binding the upper abdomen lowers the location of the abdominal HIP. Each of these will be considered in detail below.

#### The Abdomen Behaves as a Closed Compartment

Contrary to Rushmer's simplified model, the abdomen is obviously a closed compartment. In the supine position in anesthetized rats, intra-abdominal pressure was found to be low (~1 cm of viscera) and this finding is in accordance with others (15, 16). In Rushmer's model, upon standing up, pressure remains low at the cranial portion of the compartment, near the diaphragm. While Rushmer never used the term in dealing with his model, the  $HIP_{ab}$  would be located at a point near the diaphragm. In contrast, we found that the abdominal pressure is low when lying down and remains low at the caudal portion of the abdominal compartment. As noted previously, a potential explanation for Rushmer's findings is that he did not get all of the air removed from the abdomen. When he made incisions to insert the balloon-tipped catheter, air probably entered the abdominal cavity and there was no independent verification that all of the air was successfully removed. To the extent to which air was entrapped within the abdominal cavity, this compartment would fail to behave as a fluid filled compartment with the associated hydrostatic pressures which could alter the apparent location of the  $HIP_{ab}$ .

#### The Abdomen has a HIP

Must the abdominal compartment have a HIP? It has been well established that the venous system and cerebral spinal fluid within the subarachnoid space and ventricles



contain hydrostatic indifferent points (3, 12, 20). Wagner first defined the venous hydrostatic indifferent point in 1886 as the “natural reference point of hydrostatic pressure shifts in the circulation” (12). Clark et al. (6) tilted dead dogs and determined the  $HIP_v$  was ~6 cm below the level of the heart. She also tilted anesthetized dogs and found similar results, but that the  $HIP_v$  was closer to 12 cm below the heart. Studies by Gauer and Thron (12) revealed the  $HIP_v$  is 5 to 8 cm below the diaphragm in human subjects. Alternatively, Magnaes (20) studied the effects of body position and cerebrospinal fluid pressure. He reported that in humans, the HIP for the cerebral spinal fluid compartment was located between C-6 and T-5 (20). As mentioned previously, the HIP is determined by the distribution of compliance (12, 3) and changes in volume and size of the components within the compartment may alter the location of these various HIPs.

It is conceivable that there could be circumstances that would render the concept of a HIP for the abdominal compartment moot. For example, in going from the supine position to upright posture any combination of abdominal muscle contraction, diaphragm contraction, and/or the weight of the heart and lungs pushing on the diaphragm might cause pressure throughout the abdomen to be greater than supine levels. That is, there may not be a location where pressure in the upright posture equals the pressure in the supine posture. However, in all animals we were able to identify a hydrostatic indifferent point within the abdominal compartment.

#### The $HIP_{ab}$ Lies Caudally Within the Compartment

Perhaps the most surprising finding was the extent to which the  $HIP_{ab}$  was found to be located so caudally near the pelvis. On average, the  $HIP_{ab}$  was found to be 2.3 cm cranial of the pelvis, but clearly within the abdominal compartment. The expectation was that the  $HIP_{ab}$  would lie near the middle of the abdominal compartment.

An important consequence of a caudally located  $HIP_{ab}$  is the adverse effect this has on hepatic transmural pressure. While measuring intra-abdominal pressure 2 cm below the xyphoid, we saw surprising falls in pressure to quite low values (Table A2). This location is caudal to the liver, meaning pressure outside the liver must have fallen to even lower negative pressures. This is important because the liver has a specific compliance of  $25 \text{ ml kg}^{-1} \text{ mm Hg}^{-1}$ , making it the most compliant of the abdominal organs (21). Twenty-five percent of the cardiac output is dedicated to the liver and the liver contains about 15% of total blood volume (18). Direct electrical stimulation of splanchnic nerves has been shown to dispel up to 50% of liver blood volume (21), thus, the liver is an important blood reservoir. Taken together, it is possible that there is a profound propensity for blood volume to accumulate in the liver owing to the large increase in transmural pressure by the large fall in intra-abdominal (visceral) pressure during head-up tilt.

#### Binding of the Lower Abdomen Raises the Location of the Abdominal HIP

As discussed previously, the abdomen behaves as a closed compartment and with generally constant compliance throughout we would expect the  $HIP_{ab}$  to be located near the middle of the abdomen. Because the location of the HIP is determined by compliance, volume, and size of the compartment, there is potential for altering the  $HIP_{ab}$ 's position. By binding the lower abdomen, we were able to raise intra-abdominal pressure as seen in Figure B2. This alone would improve orthostatic intolerance by reducing abdominal venous transmural pressure. Also as expected, the increase in stiffness in the lower abdomen imposed by binding of the lower abdomen shifted the  $HIP_{ab}$  cranially. The median  $HIP_{ab}$  after binding the lower abdomen was raised by 1.7 cm, compared to the location of the  $HIP_{ab}$  while unbound.

Figure B4 shows tilting and the changes in intra-abdominal pressure with binding the lower abdomen. Binding of the lower abdomen first raised intra-abdominal pressure above baseline, and when tilted, the fall in pressure was less than in unbound tilts. Binding of the lower abdomen and raising the  $HIP_{ab}$  also has further consequences on venous transmural pressure. This is because raising the level of the  $HIP_{ab}$  will lessen the fall in pressure at the level of the liver during head-up tilt. Thus, the overall rise in intra-abdominal pressure imposed by binding of the abdomen (at any location), and the cranial shift of the location of the  $HIP_{ab}$  imposed by binding of the lower abdomen, will work synergistically to protect hepatic venous transmural pressure from dramatic changes and thus shields the liver from taking up a large amount of blood.

These results have implications for treating patients experiencing orthostatic intolerance. Not only does abdominal binding protect the liver from large changes in venous transmural pressure, but it also acts like the skeletal muscle pump in the legs by constricting splanchnic blood vessel diameter and forcing blood back to the heart. The increased venous return and stroke volume will alleviate the fall in cardiac filling that occurs while standing upright (24).

#### Binding the Upper Abdomen Lowers the Location of the Abdominal HIP

Binding of the upper abdomen resulted in a caudal shift in the  $HIP_{ab}$  and this finding provides further evidence that the compartment behaved as proposed. This is shown in Figure B6 with a median  $HIP_{ab}$  7.1 cm caudal to the xyphoid. From Table A1, the median distance from the xyphoid to the pelvic floor is 7.5 cm, thus, the  $HIP_{ab}$  is located near the pelvis, but still within the abdominal compartment. As explained prior, binding the upper abdomen raises intra-abdominal pressure and increases local stiffness, lowering the position of the  $HIP_{ab}$  towards the pelvis.

Binding the upper abdomen is of dubious practical significance and has no applicable use in treating orthostatic intolerance. It does, however, reconfirm the expectations about the abdominal compartment's behavior and demonstrates that the location of the  $HIP_{ab}$  can be driven either cranially or caudally by abdominal binding. Moreover, stiffening the upper abdomen via upper abdominal binding is expected to mimic the effects of an increase in compliance of the lower abdomen which was not attempted in the present study but is expected to occur post-partum.

The foregoing concepts raise the issue of the applicability of the present findings to the phenomenon of postpartum syncope. Grubb et al. (14) reported on 12 women who developed episodes of hypotension resulting in syncope in the immediate postpartum period. Postpartum syncope can be extremely dangerous for the mother, as well as the baby if the mother is holding them at the time of the episode.

During pregnancy, blood volume increases 50% higher than non-pregnant values along with a fall in systemic vascular resistance and blood pressure. While blood volume goes back to normal values quickly after parturition, changes in peripheral blood flow may continue up to 6 weeks following delivery (14). This results in hypotension and potential episodes of syncope, similar to orthostatic intolerance.

The abdominal muscles also go through remarkable changes during pregnancy. Gillear et al. (13) reported a 115% increase in rectus abdominis muscle length at 38 weeks of gestation. It not only stretches and thins, but the rectus abdominis muscles actually separate and the width of the linea alba increases by week 30 of gestation. This width separating the rectus abdominis muscles can be anywhere from 2-4 cm wide to 20 cm wide, most occurring at the level of the umbilicus (7, 13). Coldron et al. (7) reported that most recovery of this separation occurs in the first 8 weeks postpartum and plateaus. By 12 months postpartum, the rectus abdominis changes in thickness, shape, width, and separation width still were not at control values, and it is unknown if they ever reach pre-pregnancy values again. With thin and separated abdominal muscles, one may conclude

that the abdominal wall will have decreased stiffness. As we've discussed, changes in stiffness may alter the location of the  $HIP_{ab}$ . This could potentially exacerbate pressure changes. With a more compliant lower abdomen following parturition, the  $HIP_{ab}$  would shift caudally, leading to even greater negative pressures in the cranial portion of the abdomen. More negative pressures at the cranial portion of the abdomen would potentiate blood accumulation in the liver and thereby further reduce cardiac output and arterial pressure, leading new moms to experience syncope and loss of consciousness.

### Our Model Revisited

Figures B7, B8, and B9 demonstrate the changes in pressure throughout the abdominal compartment of a model rat in the supine position, head-up tilt position, and while binding the lower abdomen during head-up tilt (respectively). The median length of the abdominal compartment, from dome of the diaphragm to pelvic floor, was 8.8 cm (Table A1). The line drawing of the model rat shows this length and depicts the relative location of abdominal contents. Total venous blood pressure includes a dynamic component, due to the pumping action of the heart, and a hydrostatic component, due to gravitational forces. Intra-abdominal pressure is also recorded, and thus, transmural pressure can be calculated. A previous study in our laboratory found that the venous  $HIP$  was 1.5 cm caudal of the dome of the diaphragm where venous pressure was ~1.0 cm of blood in Sprague-Dawley rats (unpublished observations).

The rat in Figure B7 is in the unbound, supine position. The presumed dynamic component of venous pressure has been set at 0.8 cm of blood at the dome of the diaphragm and increases to 1.8 cm of blood at the pelvic floor. Absent gravitational forces, the hydrostatic venous pressure is constant at 0.8 cm of blood. Therefore, the total venous blood pressure rises to 0.0 cm of blood at the caudal end of the abdominal compartment. Intra-abdominal pressure is also constant at 0.8 cm of blood and thus

transmural pressure rises from 0.0 cm of blood near the dome of the diaphragm to 1.0 at the base of pelvis.

In Figure B8 the rat is in the unbound, head-up tilt position. The  $HIP_v$  and  $HIP_{ab}$  are located at 1.5 cm and 6.5 cm respectively from the dome of the diaphragm. Due to gravitational forces, there is now a venous hydrostatic blood pressure and intra-abdominal pressure gradient. Above the  $HIP_{ab}$ , intra-abdominal pressure falls to -5.1 cm of blood at the dome of the diaphragm and below, it rises to 3.1 cm of blood at the pelvic floor. As discussed previously, a consequence of a caudally located  $HIP_{ab}$  is the adverse effects on hepatic transmural pressure. With negative intra-abdominal pressures near the liver and thus large increases in transmural pressure, this may potentiate the propensity of blood to pool in the hepatic veins. For example, in this model transmural pressure at the dome of the diaphragm rose from ~0 cm of blood in the supine posture (Figure B7) to 4.4 cm of blood when upright (Figure B8).

Figure B9 demonstrates how binding the lower abdomen shifts the  $HIP_{ab}$  cranially to 4.8 cm below the dome of the diaphragm. This results in less of a fall in intra-abdominal pressure (-3.7 cm of blood) and less of a rise in transmural pressure (3.0 cm of blood) at the cranial portion of the abdominal compartment, near the liver. Venous blood pressures are presumed to remain the same as in the unbound condition (Figure B7 and B8). Thus, the overall rise in intra-abdominal pressure imposed by binding of the lower abdomen and the cranial shift in location of the  $HIP_{ab}$  will work collectively to protect hepatic venous transmural pressure and lessen the propensity for blood to pool in the liver.

### Technical Considerations Reconsidered

#### Introduction of Air

By employing a minimally invasive approach via inserting the side-hole modified wick intra-abdominal needle system into the abdomen without an incision, we greatly

reduced the likelihood that air entered the abdominal cavity. As represented in Table A2, the intra-abdominal baseline pressure measurements were within expected values (16, 17) and the compartment behaved like a fluid-filled compartment.

#### Location of the Pressure Recordings

As stated previously, intra-rectal pressure recordings were originally attempted but abandoned due to unstable results.

#### Gradients in Abdominal Pressure

Measurements were taken in triplicate and the needle apparatus was removed and/or repositioned between each measurement in order to balance out the inhomogeneous nature of the abdominal contents. By taking the median of the measurements would further moderate the influence of any extreme values.

#### Modified Wick

The modified wick technique was successful in measuring intra-abdominal pressure non-invasively. By using the side-hole modified hydrostatic needle, we were also able to avoid the problem of obstructing the needle tip and thus, sustain a continuous column of fluid required for accurate pressure recordings.

#### Blind Insertion

Postmortem measurements allowed us the opportunity to ensure abdominal organs and blood vessels were intact and had not been damaged during the blind insertion of the needle. There was no evidence to indicate visible damage within the abdominal compartment in any of the rats.

#### Tilting Protocol

There were no visible or evident problems with the tilt-table, the rat, needle, and or transducer tubing slipping or moving that could cause errors in recording. The care

and time taken to secure all components to the tilt-table proved worthy to circumvent the potential problem.

#### Abdominal Binding

Ventilation was monitored while imposing abdominal binding on the rat and binding was limited to a maximum of 1-2 minutes at a time. This protected against a restriction in venous return or damage to respiratory, kidney, and intra-abdominal organ function.

#### Pressure Recordings

As mentioned previously, great care and patience was taken to prevent any air bubbles from forming within the transducer tubing or needle.

#### Limitations

The most obvious limitation to our study is our research subjects. The abdomen of a rat, a small quadruped, may behave differently than the abdomen of a human, a relatively tall biped. However, Brown et al. (2) reported that based on morphology and architecture of the abdominal wall muscles, Sprague-Dawley rats are a valid model for human abdominal wall musculature.

A second limitation to our study is the effects of anesthesia on the rat's abdominal muscle tone. It is likely that the abdominal muscle wall tone would be reduced, which may have exaggerated our findings. Even if this would affect the specific values, it is likely that the general trend would be similar.

#### Future Studies

Future research needs to be focused on human subjects, which would eliminate the possible limitations of the rat model. Studies on pre and post-partum subjects, animal or human, would reveal the contribution of alterations in the location of the  $HIP_{ab}$  on post-partum syncope.



### Conclusion

To summarize, we were able to establish that the abdomen behaves as a closed compartment and has its own hydrostatic indifferent point. The  $HIP_{ab}$  is located caudally within the compartment, on average 2.3 cm cranial of the pelvic floor. Binding of the lower abdomen significantly raises the location of the  $HIP_{ab}$ , while binding of the upper abdomen lowers its location. The cranial shift of the location of the  $HIP_{ab}$  due to binding of the lower abdomen has implications for treatment of patients suffering from orthostatic intolerance because binding of the lower abdomen protects the liver from being exposed to a large increase in local venous transmural pressure during upright posture.

APPENDIX A  
TABLES

Table A1. Subject characteristics.

|   | Median    |
|---|-----------|
| Weight (g)                                | 184 ± 5.4 |
| Xyphoid to the right atrium (cm)          | 2.5 ± 0.2 |
| Xyphoid to the dome of the diaphragm (cm) | 1.3 ± 0.3 |
| Xyphoid to the pelvic floor (cm)          | 7.5 ± 0.6 |

· Values are medians ± SE for n = 7 female rats. Min, minimum; Max, maximum; g, grams; cm, centimeters.

Table A2. The affect of abdominal binding on intra-abdominal pressure and the location of the abdominal hydrostatic indifferent point.

|                  | $P_{ab}$<br>cm of viscera | $HIP_{ab}$<br>cm | Site<br>cm |
|------------------|---------------------------|------------------|------------|
| Unbound          |                           |                  |            |
| Supine           | 1.0 ± 0.5                 |                  |            |
| 90° Head up Tilt | -1.8 ± 0.3                | -5.2 ± 0.3       | -2.0 ± 0.1 |
| Bound Lower      |                           |                  |            |
| Supine           | 2.1 ± 0.6                 |                  |            |
| 90° Head up Tilt | 1.2 ± 0.6                 | -3.5 ± 0.2       | 2.0 ± 0.05 |
| Bound Upper      |                           |                  |            |
| Supine           | 3.3 ± 0.9                 |                  |            |
| 90° Head up Tilt | -0.4 ± 0.5                | -7.1 ± 0.9       | -3.0 ± 0.5 |

Values are medians ± SE for 7 female rats.  $P_{ab}$ , intra-abdominal pressure;  $HIP_{ab}$ , location of the hydrostatic indifferent point of the abdomen relative to the xyphoid; Site, location of the needle and transducer relative to the xyphoid.

APPENDIX B  
FIGURES

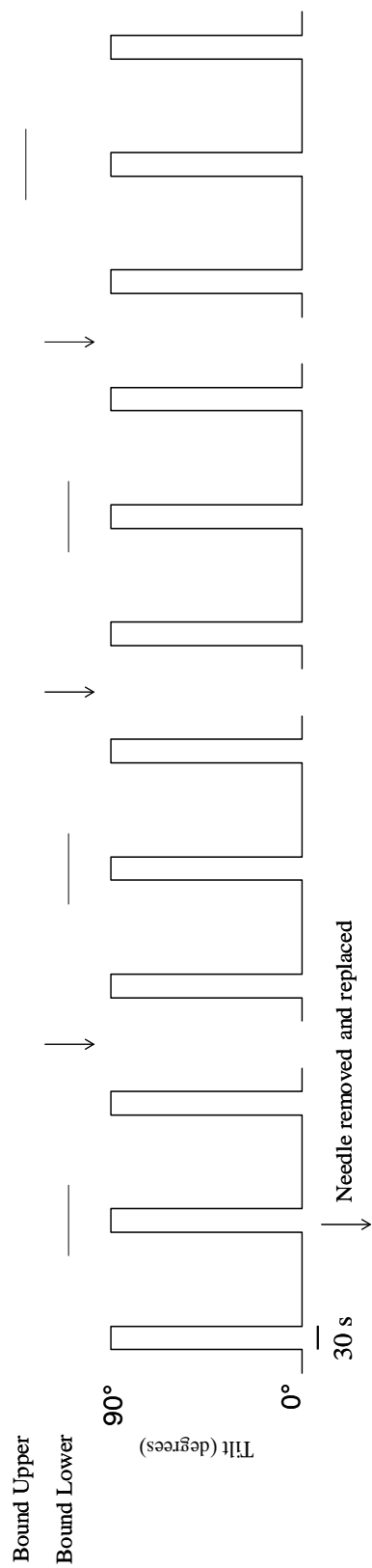


Figure B1. Schematic of experimental tilting and binding protocol

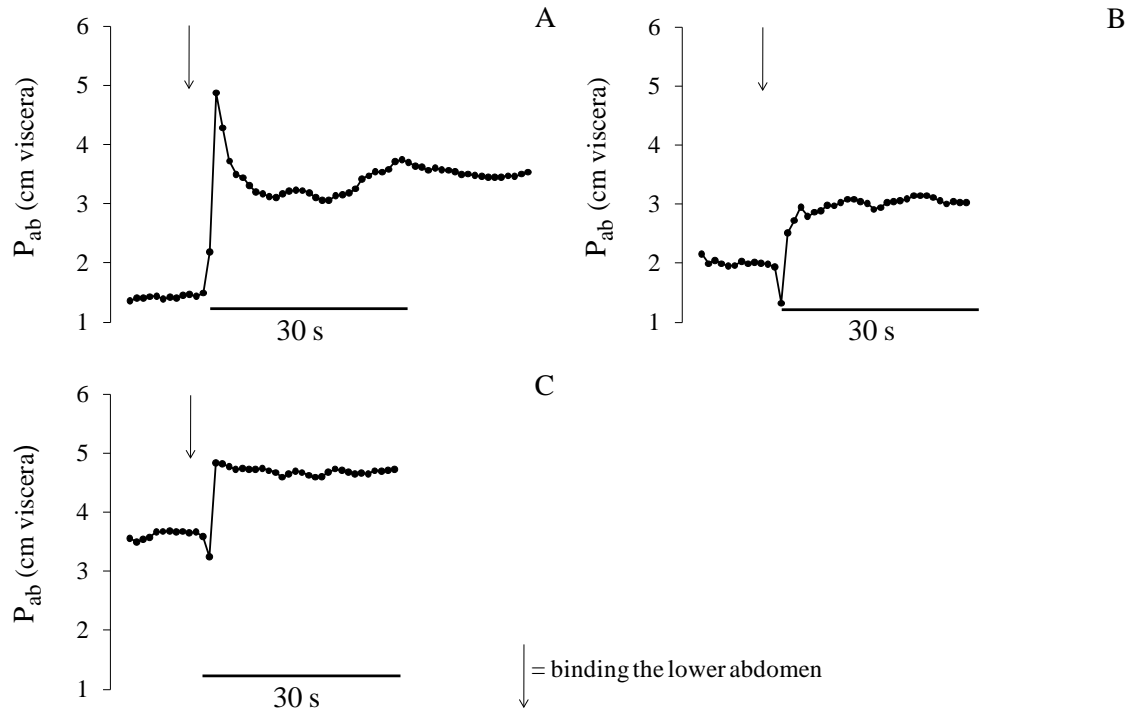


Figure B2. The effect of binding the lower abdomen on intra-abdominal pressure in a single representative rat. Each panel shows intra-abdominal pressure ( $P_{ab}$ ) measured in cm of viscera beginning 10 seconds before binding of the abdomen, which is noted by the vertical arrow, and continuing for at least 30 seconds after binding of the abdomen which was performed in triplicate.

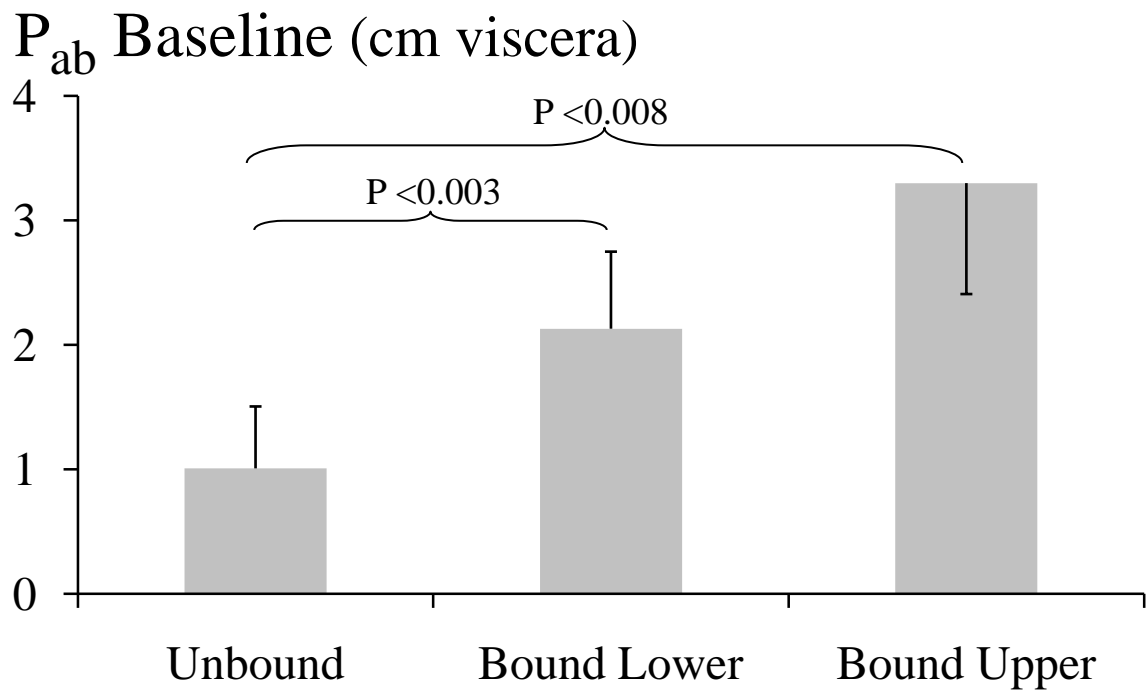


Figure B3. The effect of binding the lower and the upper abdomen on baseline intra-abdominal pressure. Binding of the lower and of the upper abdomen raised intra-abdominal pressure compared to the unbound control condition. Values are medians  $\pm$  SE for  $n=7$  female rats.  $P_{ab}$ , intra-abdominal pressure measured in cm of viscera.

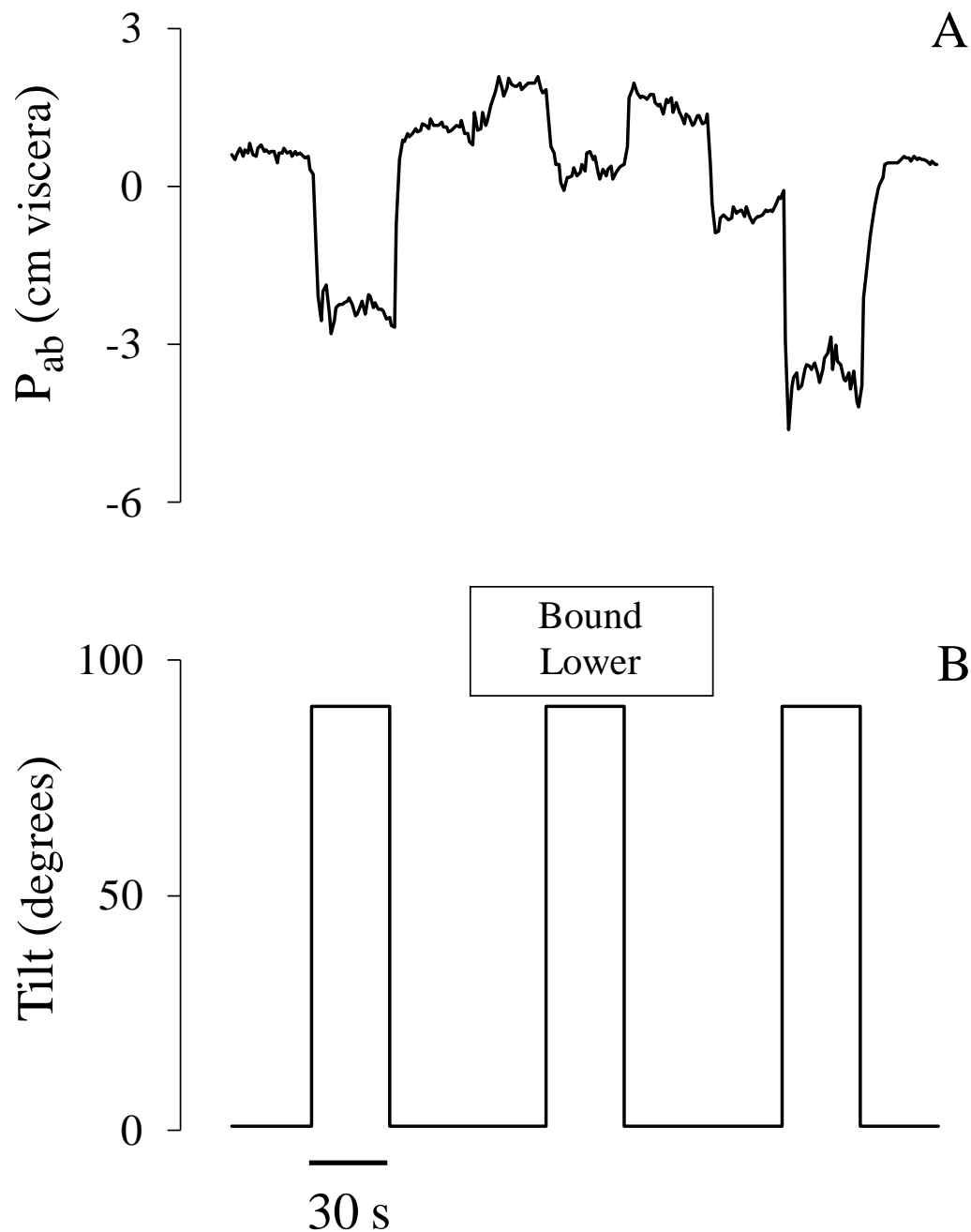


Figure B4. Time course of the effects of tilting and of binding the lower abdomen on intra-abdominal pressure in a single representative rat. (A)  $P_{ab}$ , Intra-abdominal pressure measured in cm of viscera. (B) degrees of the tilt. Each head-up 90 degree tilt was imposed for 30 seconds. Binding of the lower abdomen was imposed beginning 30 s before the onset of the second head-up tilt and was maintained until 30 s after tilt-back to the supine posture. The needle and the transducer were located 2 cm caudal to the xyphoid in this trial.



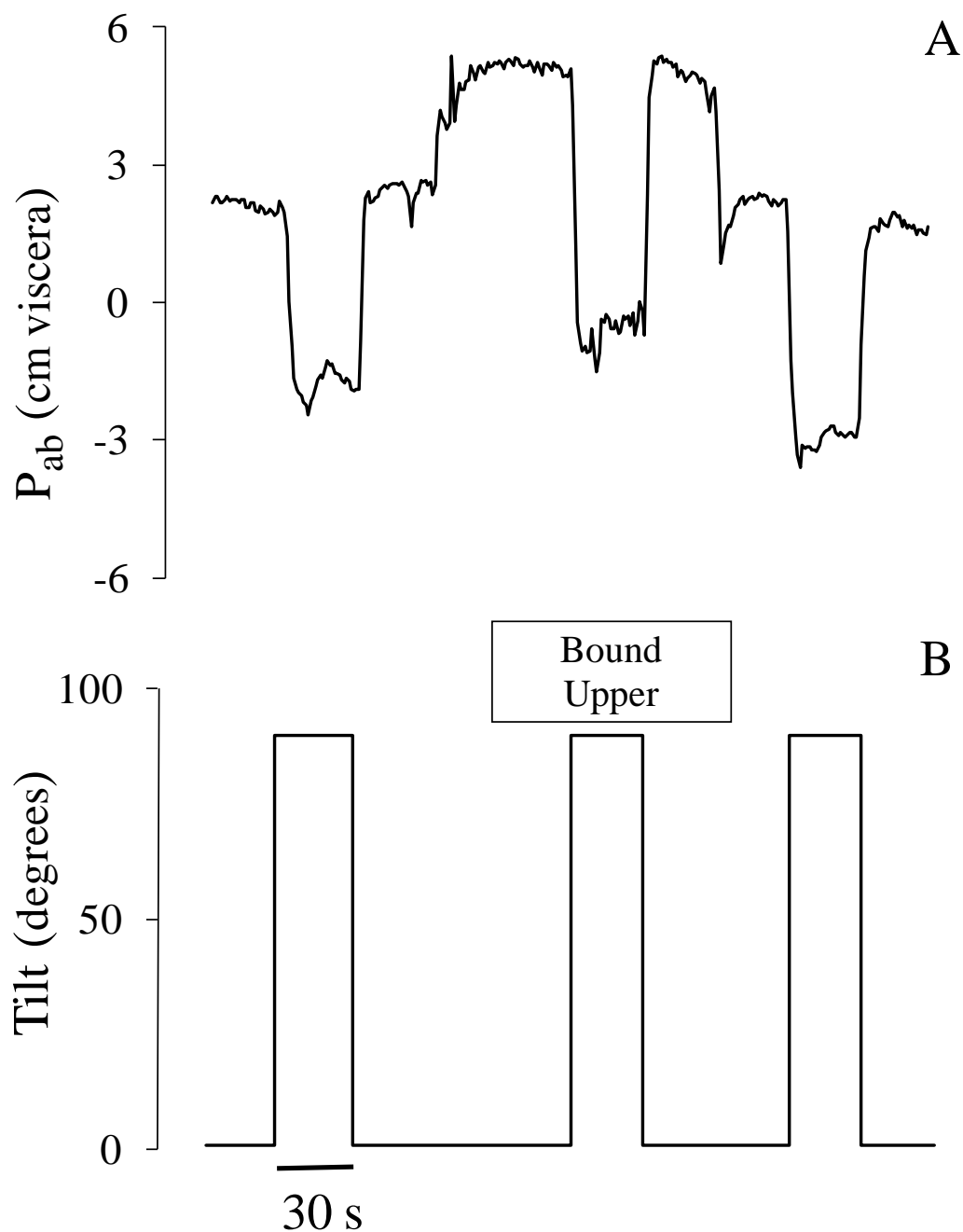


Figure B5. Time course of the effects of tilting and of binding the upper abdomen on intra-abdominal pressure in a single representative rat. (A)  $P_{ab}$ , Intra-abdominal pressure measured in cm of viscera. (B) degrees of the tilt. Each head-up 90 degree tilt was imposed for 30 seconds. Binding of the upper abdomen was imposed beginning 30 s before the onset of the second head-up tilt and was maintained until 30 s after tilt-back to the supine posture. The needle and the transducer were located 4 cm caudal to the xyphoid in this trial.

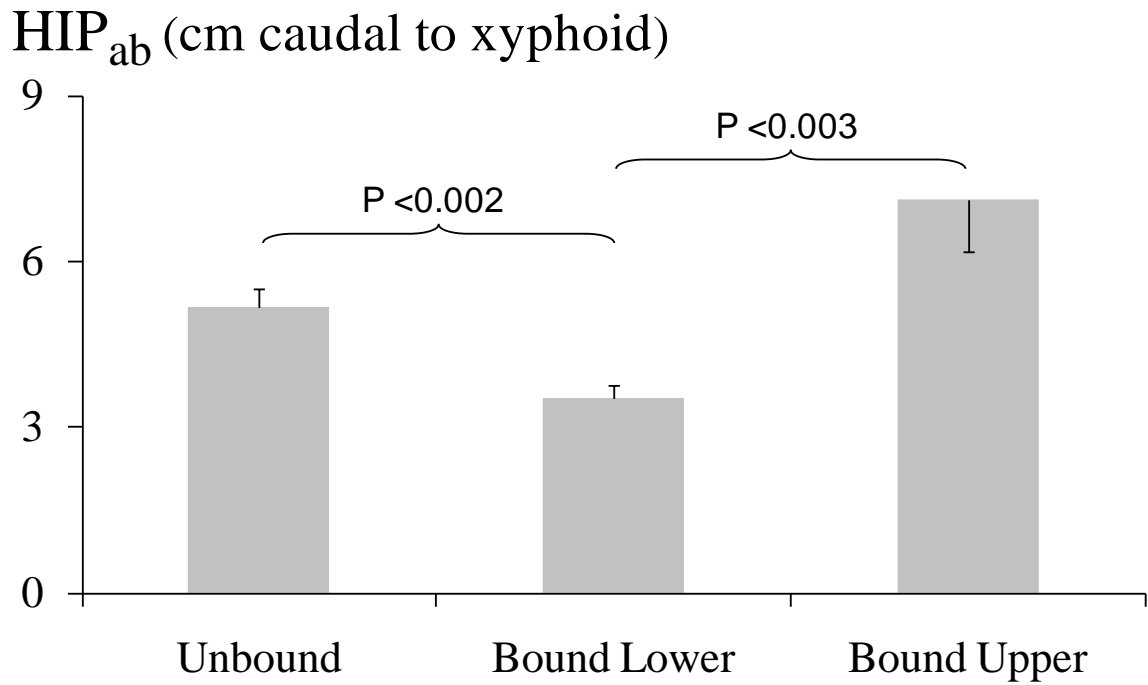
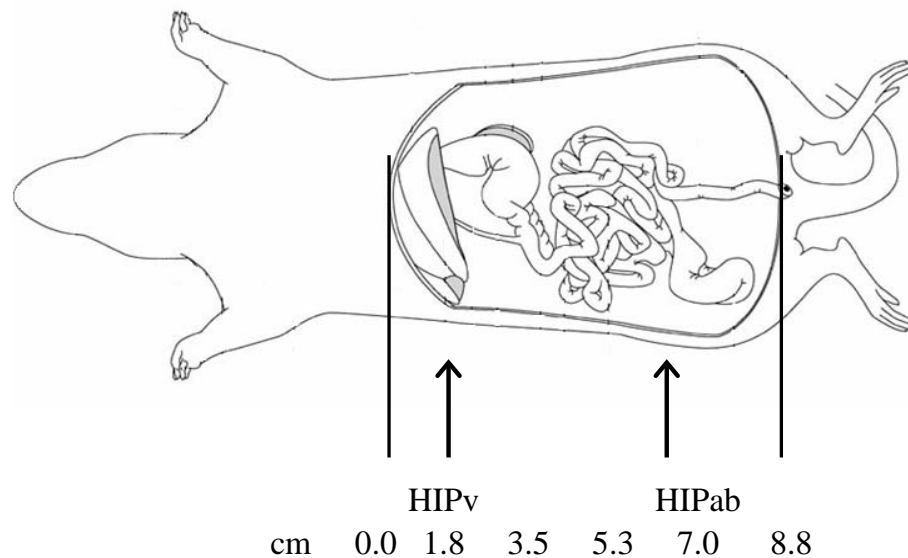
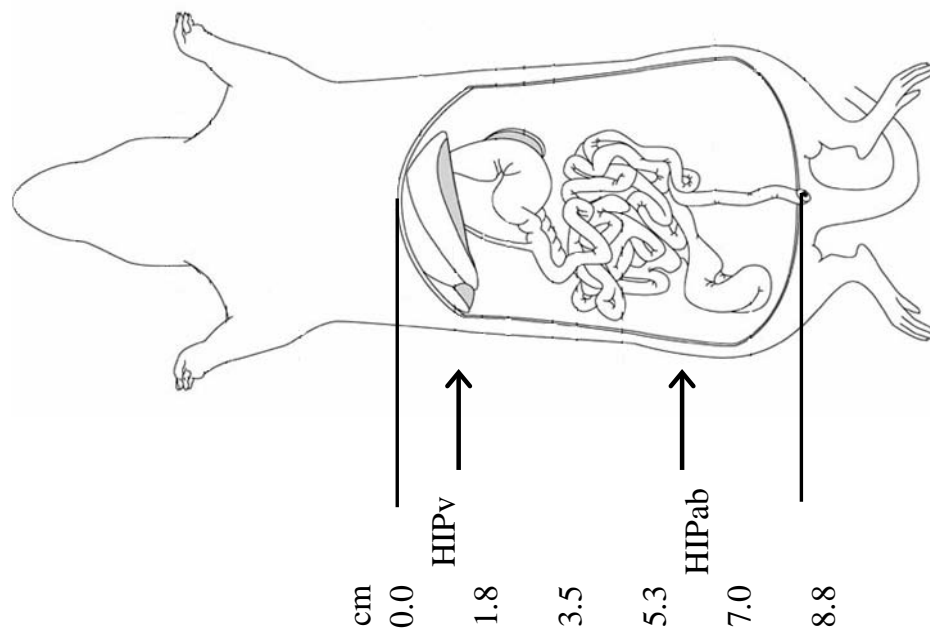


Figure B6. The effect of binding the lower abdomen and of binding the upper abdomen on the location of the abdominal hydrostatic indifferent point. Binding of the lower abdomen shifted the location of the HIP<sub>ab</sub> cranially and binding of the upper abdomen shifted the location of the HIP<sub>ab</sub> caudally. Values are medians  $\pm$  SE for  $n=7$ . HIP<sub>ab</sub>, hydrostatic indifferent point measured in cm caudal to the xyphoid.



| Venous Blood Pressures |             |          | $P_{ab}$ | $P_{tm}$ |
|------------------------|-------------|----------|----------|----------|
| Dynamic                | Hydrostatic | Total    |          |          |
| cm blood               | cm blood    | cm blood | cm blood | cm blood |
| 0.8                    | 0.0         | 0.8      | 0.8      | 0.0      |
| 0.9                    | 0.0         | 0.9      | 0.8      | 0.1      |
| 1.0                    | 0.0         | 1.0      | 0.8      | 0.2      |
| 1.1                    | 0.0         | 1.1      | 0.8      | 0.3      |
| 1.2                    | 0.0         | 1.2      | 0.8      | 0.4      |
| 1.4                    | 0.0         | 1.4      | 0.8      | 0.6      |
| 1.5                    | 0.0         | 1.5      | 0.8      | 0.7      |
| 1.6                    | 0.0         | 1.6      | 0.8      | 0.8      |
| 1.7                    | 0.0         | 1.7      | 0.8      | 0.9      |
| 1.8                    | 0.0         | 1.8      | 0.8      | 1.0      |

Figure B7. Pressures and locations of the  $\text{HIP}_v$  and  $\text{HIP}_{ab}$  in the supine position of a model rat.  $\text{HIP}_v$ , location of the hydrostatic indifferent point of the venous system;  $\text{HIP}_{ab}$ , location of the hydrostatic indifferent point of the abdomen;  $P_{ab}$ , intra-abdominal pressure;  $P_{tm}$ , transmural pressure; cm, centimeters.



| Venous Blood Pressures |          |             | Pab      | Ptm      |
|------------------------|----------|-------------|----------|----------|
| Dynamic                |          | Hydrostatic | Total    |          |
| cm blood               | cm blood | cm blood    | cm blood | cm blood |
| 0.8                    | -1.5     | -0.7        | -5.1     | 4.4      |
| 0.9                    | -0.5     | 0.4         | -4.2     | 4.6      |
| 1.0                    | 0.5      | 1.5         | -3.3     | 4.8      |
| 1.1                    | 1.5      | 2.6         | -2.4     | 5.0      |
| 1.2                    | 2.5      | 3.7         | -1.5     | 5.2      |
| 1.4                    | 3.5      | 4.9         | -0.6     | 5.4      |
| 1.5                    | 4.5      | 6.0         | 0.4      | 5.6      |
| 1.6                    | 5.5      | 7.1         | 1.3      | 5.8      |
| 1.7                    | 6.5      | 8.2         | 2.2      | 6.0      |
| 1.8                    | 7.5      | 9.3         | 3.1      | 6.2      |

Figure B8. Pressures and locations of the  $HIP_v$  and  $HIP_{ab}$  in the head-up tilt position of a model rat.  $HIP_v$ , location of the hydrostatic indifferent point of the venous system;  $HIP_{ab}$ , location of the hydrostatic indifferent point of the abdomen;  $P_{ab}$ , intra-abdominal pressure;  $P_{tm}$ , transmural pressure; cm, centimeters.

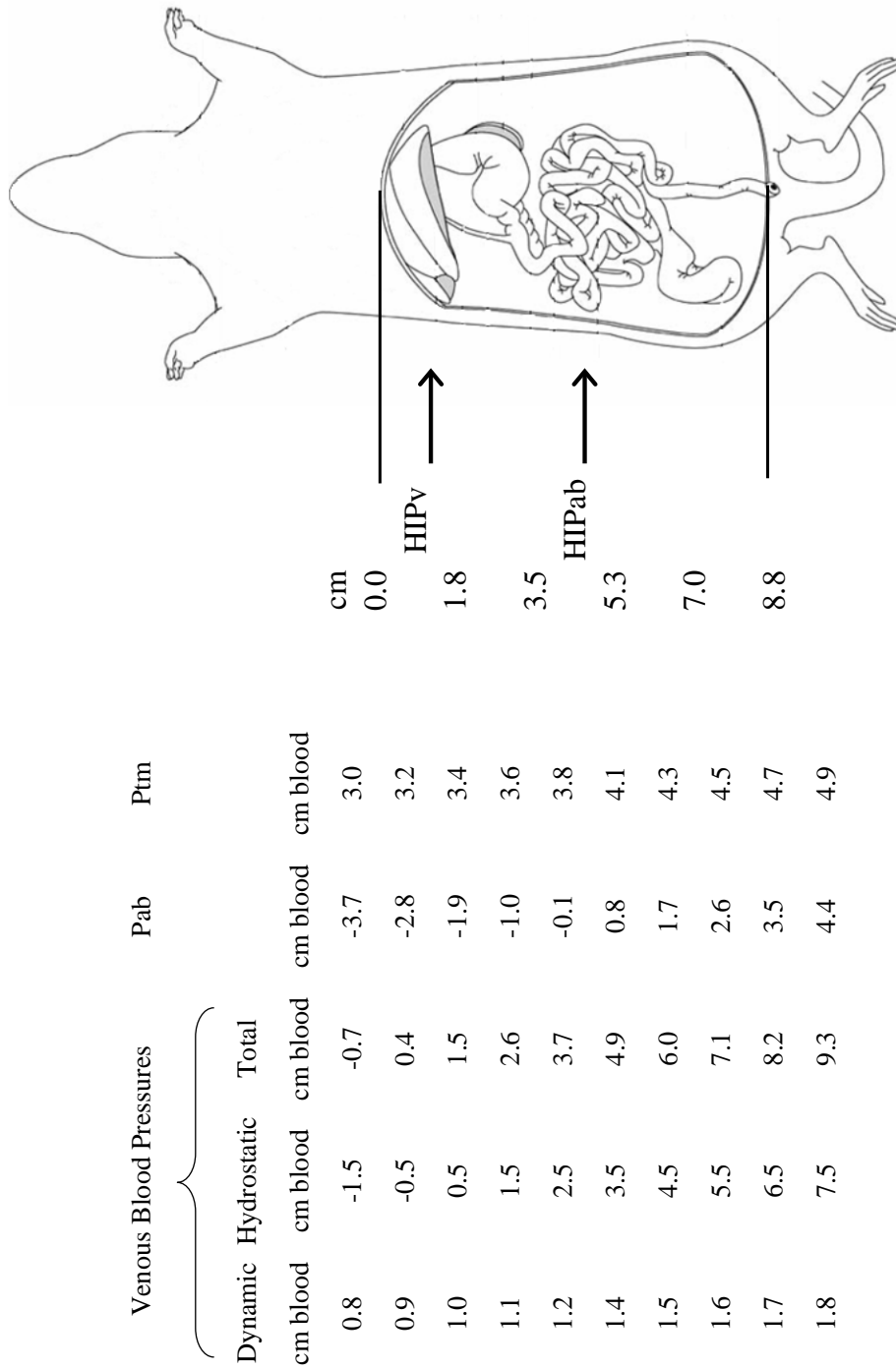


Figure B9. Pressures and locations of the  $HIP_v$  and  $HIP_{ab}$  in the head-up tilt position of a model rat while binding the lower abdomen.  $HIP_v$ , location of the hydrostatic indifferent point of the venous system;  $HIP_{ab}$ , location of the hydrostatic indifferent point of the abdomen;  $P_{ab}$ , intra-abdominal pressure;  $P_{tm}$ , transmural pressure; cm, centimeters.

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