Circulatory Physiology

As a Country Doc

Episode 1

Hemodynamics

Patrick Eggena, M.D.

Novateur Medmedia, LLC.
This Episode is dedicated to Bonnie and

to our children Kendra and Brandon and

to our grandchildren Basia, Anika, and August.
Foreword

This is the first of three episodes in the Circulatory Physiology Series. Each episode starts with a case where the student finds himself or herself in the imaginary world of a Country Doctor who is called upon to manage a clinical problem related to a 50-minute lecture given by the author to First Year Medical Students. Video tapes of these lectures are divided into short segments which are interwoven with relevant chapters of the author's ebook, “Medical Physiology of the Heart-Lung-Kidney.”
About the Author

The author was born in London in 1938. His parents had fled from Germany in 1933 after his father was wrongly accused of burning down the Reichstag in Berlin as Hitler was rising to power. When War broke out, the author’s family was interned on the Isle of Man and, after the War ended, transported back to Germany. There the author grew up on a farm, attended Gymnasium, and emigrated to America at the age of 18.

Shortly after arriving in the US he was drafted into the Army and sent overseas where he served as a Medic. Upon returning to the US he attended Kenyon College and then Medical School at the University of Cincinnati. After serving as a house officer at the Cincinnati General Hospital he started a career in Medical Research, first as an NIH post-doctoral fellow at the Brookhaven National Laboratories and the University of Copenhagen and then as an Established Investigator of the American Heart Association at the Mount Sinai School of Medicine. There he rose through the academic ranks to Professor of Physiology & Biophysics and served for 5 years as Acting Chairman of the Department.

He chaired the Physiology Course for more than 20 years, taught all aspects of Physiology, and participated in the Art and Science of Medicine courses for First and Second Year Medical Students.

After retiring from teaching and research, the author returned to living on a farm with his wife and horses. Once a week he functions as an Emergency Physician in a nearby hospital --alone for the 16-hour night shift -- where he applies his understanding of Physiology to everyday patient care at the bedside.

Students at The Mount Sinai Medical School showed their appreciation for his teaching by awarding him The Excellence in Teaching Award on twelve occasions. Student comments and evaluations relating to the episodes published here are given on the next pages.
Dr. Eggena is the best teacher I have ever had. I always felt secure that he would explain things thoroughly and logically and address our questions effectively. He is so familiar with the material, and its application to clinical practice, that I think he knows how to anticipate students' questions and confusion, and that makes him an excellent teacher. I also thought his text book and the supplemental practice programs online were invaluable resources. I feel that Eggena has given me a very firm grasp of the basics of cardiopulmonary physiology, and I'm very grateful to have had him as a teacher.

I thought Dr. Eggena was great. It was really helpful to have both his book and his computer program to supplement lectures - with 3 ways to learn the same information (and in the same order!) it is hard not to eventually understand each concept. The computer program with quizzes was especially useful. Lectures were clear and well organized.

Dr. Eggena is one of the finest teachers I've yet experienced. His patience and thorough explanations allowed me a deep understanding of the material, while his focus on the practical aspects of each topic left me with a sense of competency that I will remember in the coming years. I enjoyed each of his lectures and have a deep respect for his dedication to providing study materials for students beyond the lectures and his wonderful text book. This has been an exciting and memorable learning experience.

Great lecturer, very clear.

Very clear lectures. Keep up the good work!

Great professor, very knowledgeable, patient, clear, concise.

Dr. Eggena was very thorough and clear in his explanations of cardiovascular and pulmonary physiology. His handouts were very helpful, as were his multimedia programs.
Oh my goodness, where to begin? Dr. Eggena is PHENOMENAL. He is so old-school using his projector and sharpie, drawing schematics and graphs he's obviously done a million times, and has such a story-teller's voice. But that's what makes him GREAT. More professors should realize that maybe the powerpoint isn't the best format to teach, that maybe a less recently available form of technology would be a better teaching aide. More professors should give up trying to find a working dry erase board marker and switch to projectors and sharpies. On top of that, to have created a multimedia program and quizzes that reinforce the material in such an entertaining way! Really I can't think of anything negative to say except that Dr. Eggena's lectures didn't extend to the whole of physiology and that his multimedia program did not have anything on kidneys, endocrine, GI, etc.

I found some of his lectures to be a little too fast paced, and unclear in some points. But he has a definite great rapport with the students, seems to really care about teaching, and his multimedia programs and multitude of practice questions were invaluable.

One of the best professors I have had yet. Very clear explanations, always happy to answer questions. A kind and approachable professor with clear clinical applications.

A truly masterful educator. And physician. excellent

Great instructor!

Eggena is the best. So clear! good

Fantastic teacher.

Once I got the hang of it, his outlines were helpful and it was a change to draw along during class rather than just typing away on a computer. His multimedia programs were also immensely helpful and the only reason I passed.

Dr. Eggena was a phenomenal educator and lecturer. I truly learned a lot from him regarding cardio and respiratory physiology. His online material was very helpful in studying for quizzes and exams. Thanks for a great semester!

Dr. Eggena was great. He went quickly but clearly through the material, and he always pre-
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The Situation

Michelle walks out the front door
The Case

What is the Physiology related to your observation?

Treatment
Kay: “Doc, good that Michelle had a cell phone so she could call us.”

Doc: “Okay, what’s on your mind?”

Kay: “Why was her skin pale and cold and clammy?”

Doc: “Perspiring onto cold skin is called **diaphoresis**. The sweating is due to stimulation of sweat glands by so-called **sympathetic cholinergic nerves**. Acetylcholine released from these nerve endings binds to muscarinic receptors which results in sweating. Her skin was cold because blood vessels are constricted so that blood is diverted from the skin to the coronary arteries and to the brain. Diaphoresis indicated that the Michelle had a decrease in cardiac output — an emergency that required prompt attention!

Kay: “It is norepinephrine that binds to alpha-1-receptors that constricts skin vessels. Right?”

Doc: “Yes, norepinephrine is the mediator for all other sympathetic nerves, and when it binds to alpha-1-adrenergic receptors on smooth muscle of skin arterioles causes constriction of these vessels. Without (or only little) blood flowing to the
skin it looks pale and feels cold. The blood that no longer flows to the skin is diverted to the brain and to the coronary vessels of the heart that need it more in this emergency situation, as we already mentioned."

Kay: “Why did she feel like throwing up?”

Doc: “Increased sympathetic stimulation of the gastrointestinal tract diminished blood flow and slowed digestion and absorption of food and liquids. As peristalsis of her intestines slowed and her sphincters contracted she felt bloated and nauseated and almost vomited.”

Kay: “Why was she confused?”

Doc: “You’re right, Kay. She seemed sort of dazed. She had a small cut on the back of her head. Perhaps she sustained a concussion when she hit her head on the tree stump. With head injuries you always have to worry about a subdural hematoma. It was important to rule that out with a CT scan when she got to the hospital.”

Kay: “It was a relief to see that she could wiggle her toes.”

Doc: “Yes --it suggested that she had not injured her spinal cord --at least not when we first saw her. But she still could have had a fracture.”

Kay: “Is that why you told her not to move until the 911 people arrived?”

Doc: “Yes --and when the EMS came they immediately stabilized her head and neck with a brace as a precaution before putting her on a stretcher and carrying her to the ambulance.”

Kay: “And they also put a splint on her left leg.”

“Yep --she turned out to have a fractured femur with a large hematoma. You can lose a lot of blood into the thigh without noticing it. Have to keep that in mind with leg injuries.”

Kay: “Why was her stomach hard as a board?”

Doc: “That’s called guarding or a surgical abdomen.”

Kay: “Why is it called that?”

Doc: “Because you usually have to call a surgeon to fix it. You see, the abdomen is normally soft when you gently push down on it during a physical examination to feel if the liver or spleen are enlarged. It will give way to your hand. When it doesn’t,
something is irritating the peritoneum -- could be a ruptured appendix, a perforated peptic ulcer, or --as with Michelle -- blood in the abdominal cavity from a ruptured spleen.

Kay: “Why was she contracting her abdominal muscles?”

Doc: “It helps venous return.”

Kay: “How so?”

Doc: “Place your hands on your stomach and take a breath in. What happens?”

Kay: “My stomach moves out -- expands.”

Doc: “Right, because when your diaphragm moves down pressure in the peritoneal cavity increases which pushes on the large veins and milks the blood through one-way valves toward the heart. Therefore tensing up on stomach muscles helps to move blood back towards the heart against the force of gravity.”

Kay: “Why were her neck veins collapsed?”

Doc: “They were relatively empty from loss of blood. The neck veins are normally filled to about 2 or 3 cm above the sternal notch. That’s how you measure the central venous pressure (CVP).

Kay: “I don’t understand why you use the sternal notch as a zero reference point. We learned that the tricuspid valve was the reference.”

Doc: “True -- the tricuspid valve is the zero reference point for all pressures in the circulation, but it is more difficult to locate than the sternal notch. The tricuspid valve is approximately at the level of the 4th intercostal space in the right midaxillary line, which is about 5 cm below the sternal notch. So if you see that the neck veins are distended 2 cm above the sternal notch, the CVP is 7 cm H2O (or about 5 mmHg), which is normal. Now, when you are lying down flat, as Michelle was, the neck veins should be distended, but they were not. So her CVP was much lower than normal.

What did you hear when listening to her heart?”

Kay: “It was beating fast.”

Doc: “Yes -- she had a tachycardia. Her heart rate was >100 beats/min. What do you think may have caused this?”

Kay: “Sympathetic stimulation?”
Doc: “Yes --sympathetic stimulation of the SA node. But also a lack of parasympathetic inhibition.

You know, if you cut the nerves to the SA node --which surgeons due in a heart transplant operation--the isolated heart beats at 100 beats/min. Much faster than normal. This increase in the rhythm of the isolated heart is caused by the absence of tonic parasympathetic inhibition by the vagus nerve.

Now Michelle’s heart was beating at about 120 beats/min. This required additional stimulation of the SA node by sympathetic nerves and circulating epinephrine.”

Kay: “Epinephrine does more than just make the heart beat faster! Doesn’t it?”

Doc: “Oh yes, epinephrine exerts 4 different actions on Michelle’s heart to increase cardiac output -- all mediated by beta-1-adrenergic receptors:

1. **Chronotropic Action**: Increases heart rate by increasing the slope of phase 4 depolarization of the SA nodal action potential.

2. **Dromotropic Action**: Increases AV nodal conduction by increasing the slope of phase 0 depolarization of the AV nodal action potential.

3. **Inotropic Action**: Increases myocardial contractility by increasing the open-time of L-type calcium channels during phase 2 of the myocardial action potential.

4. **Lusitropic Action**: Increases the rate of myocardial relaxation by speeding calcium uptake by the sarcoplasmic reticulum after phosphorylating phospholamban which releases tonic inhibition of the sarcoplasmic calcium pump.

Kay: “Pretty complicated. I’m sorry I asked that question. But I understand that Michelle’s heart is beating faster and stronger to compensate for the decreased blood returning to it. But how did her brain know that it was a good idea to stimulate the heart?”

Doc: “The brain is not only the most vital organ but also the most delicate one. So the brain has surrounded itself with a series of pressure and flow detectors that send out early warning signals when blood flow to the brain is threatened. Such sensors for blood pressure are situated in the walls of the carotid sinuses and in the arch of the aorta; they are called **baroreceptors**
as you have learned in your physiology classes. A fall in blood pressure and wall tension decreases the extent to which these baroreceptors are stretched, and this information is then relayed via the glossopharyngeal nerve from the carotid sinuses and via the vagus nerve from the aortic arch to the medulla. In the medulla the decreased input from baroreceptors is integrated with information from other pressure and flow detectors, and the vasomotor center is activated sending impulses to the heart by nerves and epinephrine to increase its output.

Kay: “I see, but which is more important: The increase in contraction (inotropic effect) or the increase in heart rate (chronotropic effect)?”

Doc: “The bottom line here is that you want to increase cardiac output. Now cardiac output is equal to stroke volume times heart rate. The amount of blood that Michelle can squeeze out of her left ventricle during systole, i.e. the stroke volume, is limited primarily by the end-diastolic volume, i.e., the degree to which her heart fills during diastole. In her case, end-diastolic volume is, of course, way down because venous return is markedly decreased. She will, however, increase her stroke volume a little by ejecting blood more rapidly, so that her end-systolic volume will be decreased. But she won’t come close to doubling her stroke volume.

By contrast she can more than double her heart rate, i.e., from about 60 beats/min to 120 beats/min in her case. So, to answer your question: the chronotropic action of epinephrine contributes more to cardiac output than the inotropic action of epinephrine --at least in this particular situation.

Kay: “Why did you measure her blood pressure by palpation?”

To measure blood pressure by auscultation you have to be able to hear the so-called Korotkoff sounds, as you well know. These sounds depend upon turbulence that is created in the brachial artery as the cuff-pressure on the artery is reduced to a point where blood firsts starts to flow through the partially obstructed vessel. When the stroke volume is reduced --as was in Michelle’s case --the velocity of blood flow is reduced which results in less turbulence and less noise. So I couldn’t hear any sounds to make the blood pressure measurement and I had estimate her blood pressure by palpation. Although I could not hear the pulsations, I could feel the pulse -- it was weak and thready, i.e., pulsus parvus.”
Kay: “So you determined the pressure at which you could no longer feel her pulse as you inflated the blood pressure cuff?”

Doc: “Yes. Her pressure was clearly reduced. It was only about 60 mmHg. And her pulse was also difficult to feel.

Kay: "Her pulse felt weak because less blood was rushing under your fingers?"

Doc: “It’s not the fluid wave under your fingers that you feel on taking a pulse, but the pressure wave that is initiated in the wall of the aorta when the stroke volume is first ejected during systole. This initiates a pressure wave that travels along the wall of the aorta and down to the radial artery where you can feel it. This wave travels much faster than blood. The stiffer the blood vessels the faster the wave travels. It is sort of like putting your ear to the railway to hear the train coming long before you can actually see it.”

Kay: “Never tried that, Doc. “

**So, she was in shock because her blood pressure was less than normal! --Right? What is normal for her anyway?**

Doc: “The average normal adult blood pressure is 120/80 mmHg, where the upper number is the systolic pressure and the lower number the diastolic pressure. The systolic pressure is the highest pressure that blood in large arteries reaches as the heart contracts; the diastolic pressure is the lowest pressure that blood reaches as the heart relaxes. In a young, healthy woman, such as Michelle, a systolic blood pressure of 90-105 mmHg is not uncommon and normally no reason to worry. However, a systolic blood pressure of less than 90 mmHg, together with signs and symptoms of diminished tissue perfusion, is abnormal and a reason for concern.

Kay: "If her blood pressure is decreased and her cardiac output is down -- let’s say by one-half --then all of her organs get only half of what they need?"

Doc: “As Michelle lost blood into her peritoneal cavity and into her left thigh, the volume of blood being returned to her heart each minute, her venous return, was diminished. With less blood flowing into her heart, less was pumped back out and cardiac output fell. When cardiac output is decreased, the autonomic nervous system sets priorities. It channels the limited flow of blood to organs that are most important for immediate survival. So --in the hierarchy of organs --the brain is on top, then comes the heart, and last the kidneys. It is,
therefore, not unusual for a person to survive an episode of hemorrhage only to die several weeks later from renal failure because all the blood from the kidneys had been diverted to the coronaries and to the brain."

Kay: "Is that why she couldn't make any urine, and why she was nauseated and felt cold and clammy?"

Doc: "Yes."

Kay: "But if you clamp down on the vessels carrying blood to the kidneys, gut, and skin, won't you decrease venous return and, therefore, cardiac output?"

Doc: "Yes, you will. But that's the price you have to pay to get the blood pressure up to perfuse the coronaries and get blood to the brain."

Kay: "Doc --I'm getting confused. Didn't you say that blood pressure falls with a fall in cardiac output?"

Doc: "Yes --decreasing the volume of blood flowing from the heart into the large arteries will cause a fall in blood pressure, provided you don't change peripheral resistance. It is the same in a tire: less air means a lower pressure. However, the reduction in blood volume in Michelle's large arteries (where blood pressure is measured) was minimized by constricting arterioles which kept blood from leaving the large arteries. This, in turn, raised blood volume and blood pressure in her large arteries and kept as much blood as possible flowing to the coronaries and to the brain."

Kay: "But aren't the coronary and brain vessels also constricted in circulatory shock?"

Doc: "No --at least not to the extent as are the vessels to her kidneys, gut, skin, and muscles."

Kay: "I see, that's the price she has to pay to keep her heart beating and remain conscious."

Doc: "The decrease in venous return from arteriolar constriction is off-set by tensing up on large veins and mobilizing fluids from interstitial spaces."

Kay: "I can understand how sympathetic stimulation of smooth muscle in the large veins decreases their compliance, makes them stiffer, a smaller compartment, so they hold a smaller volume of blood at a higher pressure which helps to move blood against the force of 21
gravity back to the heart, i.e., increases venous return. We’ve already talked about that.”

Doc: “And there are also reservoirs of blood in the spleen and liver that are mobilized.”

Kay: “Yes--but not too much from the spleen in Michelle’s case.”

Doc: “No, you’re right, of course. But this is actually only the initial, the first response to a fall in blood pressure. When blood pressure starts to fall, the vasomotor center in the medulla sends impulses over sympathetic nerves to the capacitance vessels tensing them up a little and forcing more blood back into the heart to increase the end-diastolic volume. That’s all that is often needed to restore blood pressure. But, if increasing the stroke volume doesn’t restore blood pressure, more intense sympathetic stimuli to arterioles of the kidneys, gut, skin and muscle increase peripheral resistance to keep blood in the large arteries and thereby raise blood pressure.”

Kay: “I see, but what you really need is an increase in total blood volume.”

Doc: “And that is to some extent accomplished by mobilizing fluids from the interstitial spaces of the skin, gut, kidneys, and (primarily) muscle.”

Kay: “You get extra fluids from all the organs where arterioles are constricted?”

Doc: “Yes, because when arterioles are constricted the hydrostatic pressure downstream in the capillaries is reduced. This decreases filtration of fluids from blood to the interstitial spaces around cells and, therefore, tips the balance in favor of reabsorption of interstitial fluids into blood.”

Kay: “The plasma oncotic pressure pulls the fluid from the interstitial spaces into blood! Right?”

Doc: “Yes, the balance between the net hydrostatic pressure favoring filtration and the net plasma oncotic pressure favoring reabsorption of fluids back into blood is altered in circulatory shock.”


Doc: “Right.”

Kay: “We just had that the other night on our last quiz.”

Doc: “When you listened to her heart with your stethoscope. What did you hear?”
Kay: "**Her heart was beating fast --over 100 beats/min. Tachycardia! --and a murmur?**"

Doc: "Yes --was it in systole or diastole?"

Kay: "**It was a systolic murmur --I think!**?"

Doc: "Good --what could have caused it?"

Kay: "**Aortic Stenosis or Mitral Insufficiency.**"

Doc: "And if this is a new murmur --just happened now with her injury?"

Kay: "**You mean a functional or innocent murmur?**"

Doc: "Well, her murmur could be from mitral valve prolapse. It's not functional or innocent, albeit usually harmless."

Kay: "**How could you tell the difference?**"

Doc: "When does a functional murmur develop or become louder and more readily detected?"

Kay: "**In athletes --when they are running --with an increase in venous return. But her venous return is decreased. So not likely here.**"

Doc: "Good. But patients with severe anemia also develop systolic murmurs because the viscosity of their blood decreases and flow becomes turbulent which may be heard as a murmur --a so-called hemic murmur. Is that a possibility here?"

Kay: "**Oh yes, the Poissieulle equation and the Reynold's number! That's so confusing, Doc.**"

Doc: "It is confusing. The nice arrangement in laminar blood flow is disrupted when the lamina fall apart because of a decrease in viscosity and you get turbulence and a hemic murmur. But regardless of the hemodynamics in anemia, was her hematocrit low when we listened to her heart?"

Kay:"**Yes, of course. She had lost a lot of blood. It could be a hemic murmur. Right?**"

Doc: "True, she had lost whole blood, but the concentration of her red blood cells, i.e. her hematocrit (Hct), and therefore her blood viscosity had not changed."

Kay: "**Oh yes, Doc, but the fluid mobilized from her interstitium would have diluted the blood causing a fall in her hematocrit?**"
Doc: ”True, but this mobilization of fluids from the interstitium is a fairly slow process. Her hematocrit would not have dropped when we examined her. Later on in the hospital, yes, but not when we saw her. Had we measured her hematocrit it would have been normal --about 40%.”

Kay: “So a drop in hematocrit is not a useful sign of bleeding?”

Doc: “Chronic blood loss, yes. But not acute bleeding, as in Michelle’s situation.”

Kay: “So you don’t think she had a hemic murmur?”

Doc: “No, I think her murmur is from mitral valve prolapse, a condition not uncommon (and usually harmless) in young women with abnormally long chordae tendinae.”

Kay: “So, if she has mitral valve prolapse, why did the murmur become so much louder after she had lost a lot of blood?”

Doc: ”Her venous return was markedly decreased which, in turn, led to a decreased end-diastolic volume in her left ventricle. This made it more difficult for her abnormally long chordae tendinae to hold the leaflets of the mitral valve shut as the left ventricle contracts during systole. So the mitral valve prolapsed into her left atrium --especially during the later part of systole when the left ventricular chamber got smaller -- and the turbulent back-flow of blood created the murmur which we heard.”

Kay: “That makes sense, Doc. I also listened to her lungs.

Her lungs sounded normal to me, but why was she breathing so fast?”

Doc: “You are right, Kay. Her lung sounds were perfectly normal, but she was tachypneic, i.e., breathing more than 20 breaths/ min. As we mentioned earlier, when you take a breath in as your diaphragm moves down, the increase in intra-abdominal pressure helps to push blood in the large veins toward the heart, i.e., tends to increase venous return. Now, in addition, the partial vacuum that is created in the intra-thoracic space on inspiration tends to distend the large veins in the thorax and suck blood into the right atrium. So inspiration functions as a sort of a push-pull mechanism for enhancing venous return to the heart.”

Kay: “Yes, but what triggered her increase in ventilation?”

Doc: “An increase in ventilation is normally triggered by peripheral chemoreceptors in
the carotid and aortic bodies responding to a decrease in oxygen tension (a fall in PaO₂) or by central chemoreceptors in the medulla responding to an increase in carbon dioxide tension (PaCO₂).”

Kay: “But would her PaO₂ be decreased or her PaCO₂ increased?”

Doc: “No, it would not be! Indeed, had we taken an arterial blood sample and measured the arterial blood gases (ABGs) we would have found quite the opposite. That is, her PaO₂ would have been high (above 100 mmHg) and her PaCO₂ low (below 40 mmHg).”

Kay: “Okay, so what made her hyperventilate?”

Doc: “The chemoreceptor cells in the carotid bodies fire impulses along the glossopharyngeal nerve (N. IX) to increase ventilation when the cytoplasmic oxygen tension falls below a critical level. This oxygen tension is usually determined by the oxygen tension in blood that is perfusing the carotid bodies, as we already mentioned. However, when blood flow in the carotid artery is markedly reduced, as it was in Michelle, the chemoreceptor cells can’t extract sufficient oxygen to meet their basic metabolic needs and, therefore, trigger an increase in ventilation. It is a little like the hyperventilation one sees in cyanide poisoning. Here the PaO₂ in blood is perfectly normal, but the cells are not able to utilize the oxygen because the machinery for utilizing it has been damaged.”

Kay: “But how does the oxygen sensor in the carotid body work?”

Doc: “In the membrane of the sensor cell is a protein, similar in behavior to hemoglobin in that it changes its conformation depending upon the amount of oxygen it binds. This membrane protein is linked to a potassium channel such that when little oxygen is bound to the protein the potassium channel closes, less potassium exits the cell and the membrane potential becomes more positive (that is, less negative than usual).”

Kay: “Oh, I see --and this change in potential then travels along cranial nerve IX?”

Doc: No, no - its much more indirect and complicated. As the membrane potential changes to a less negative value, calcium channels in the membrane open and calcium ions move down their electrochemical gradient into the cell. The rise in intracellular calcium ion concentration now triggers vesicles loaded with a neurotransmit-
ter to fuse with the membrane and release their contents by a process known as **exocytosis**. The neurotransmitter, in turn, binds to its receptors on cranial nerve IX, which triggers sodium entry into the nerve cell and depolarizes its membrane. This then initiates a wave of depolarization which sweeps along the axon of the nerve and triggers the ventilatory response.”

Kay: “**Doc, I have an easier explanation.**”

Doc: “Yes?”

Kay: “**She was hurting pretty badly and when I get hurt, I breathe faster. So I think that is what happened here.**”

Doc: “Good thought, Kay. Pain is a strong stimulus for ventilation.”

Kay: “**Doc, why was Michelle so thirsty? She wasn’t dehydrated or anything like that!**”

Doc: “When less blood returns to the heart, the atria and blood vessels in the lung are not stretched as much as they usually are. This is sensed by stretch receptors in the atria and walls of the large pulmonary vessels and an impulse is initiated which travels in fibers of the tenth cranial nerve (the vagus) to the vasomotor center in the medulla.”

Kay: “**Like the baroreceptors in the carotid sinuses and wall of the aorta?**”

Doc: “Yes, but they are more sensitive, that is, they respond to smaller decreases in blood volume and lesser pressure changes. So these are really blood volume receptors which monitor venous return to the heart. However, the change in blood volume is measured by the associated change in pressure. So these receptors are sometimes referred to as **low pressure baroreceptors**” in contrast to the high pressure baroreceptors found in the carotid sinuses and wall of the aorta. Sympathetic outflow from the vasomotor center initiated by these low pressure baroreceptors tenses the large veins and promotes venous return.”

Kay:”**Doc, you already talked about this when you said that the initial response to a decrease in venous return was a sympathetic outflow to the capacitance vessels and blood reservoirs.**”

Doc: “Yes, even before blood pressure drops. True we talked about this, but there is more to it.”
Sympathetic impulses and increased levels of circulating epinephrine also go to the **Juxta-glomerular (J.G.) apparatus** in the kidney. Acting on beta-1-adrenergic receptors epinephrine and norepinephrine stimulate renin secretion into the circulation.

Kay: **“Yes Doc, we had this in class. The renin then acts on angiotensinogen from the liver to generate angiotensin I. And angiotensin I is converted in the lung to angiotensin II by an angiotensin converting enzyme (ACE).**

But. Doc, you are not answering my question. **What does this have to do with thirst?”**

Doc: “Well, angiotensin II stimulates thirst center in the lateral hypothalamus. That is why Michelle was very thirsty and wanted water.”

Kay: **“Why didn’t you give her any water?”**

Doc: “Angiotensin II not only generates thirst (it is a so-called dipsinogen) but it also stimulates the release of aldosterone from the adrenal cortex and vasopressin from the posterior pituitary. Aldosterone, in turn, retains salt from the forming urine in the renal collecting ducts while vasopressin holds onto water.”

Kay: **“So --? Isn’t that good? Don’t we want to increase her plasma volume?”**

Doc: “Yes, we do. But if we give her water without salt, her plasma will be diluted --its osmolality will decrease below the normal value of about 300 mOsm/L.”

Kay: **“Yes, but now her heart will be able to pump more blood and blood pressure will increase and organs and tissues will be better perfused. So what’s wrong with that?”**

Doc: “When the plasma becomes too dilute and sodium concentration falls from 140 to about 110 meq/L along with the decrease in osmolality, brain cells swell resulting in seizures. Thus Michelle could have suffered from water intoxication had we allowed her to quench her thirst by drinking water.”

Kay: **“Is that why we gave her isotonic (0.9%) saline?”**

Doc: “Yes. And we gave it intravenously because absorption from the intestines is diminished in circulatory shock and also she was going to be anesthetized for surgery and we wanted to keep her stomach as
empty as possible so she wouldn’t vomit and aspirate stomach content during the operation.”

Kay: “So why did we give her morphine. I know its good for pain which she had but won’t it depress her ventilatory drive and also dilate her capacitance vessels which will decrease venous return?”

Doc: “What you say about morphine is true --it will decrease venous return, but we gave it anyhow to decrease her pain --make her feel more comfortable.”

Kay: “But, Doc, we said earlier that pain raises blood pressure. So why take a chance?”

Doc: “You are right, Kay. Acute pain raises blood pressure, but prolonged intense pain causes neurogenic shock. In neurogenic shock the vasomotor center seems to shut down completely. No sympathetic outflow anywhere and blood pressure drops to about 50 mmHg as vessels become flabby. That is why we gave the morphine in addition to elevating her suffering.”

Kay: “I see Doc. Pain also triggers vasopressin secretion. Is this why she couldn’t make any urine in the hospital?”

Doc: “No Kay --with high concentrations of vasopressin you still make some urine. Her kidneys were completely shut down. She wasn’t filtering any fluid at the glomeruli. If nothing is filtered, nothing comes out as urine. She was anuric. She wasn’t getting rid of any waste products. Her kidneys weren’t functioning at all --not doing their job.”

Kay: “How much urine do you have to make to be sure that your kidneys are working?”

Doc: “About 500 ml per day.”

Kay: “Why not 250 ml or 1000 ml urine/day?”

Doc: “A healthy person with functioning kidneys can make urine as concentrated as 1200 mOsm/L. This requires high circulating concentrations of vasopressin to render the collecting ducts freely permeable to water, and you need to collect enough salt and urea in the renal medulla to attract water from the forming urine.”

Kay: “During my internship as a nurse they taught us to call the doctor if a patient makes less than 500 ml of urine
per day. What's so magic about this urine volume?"

Doc: “A patient making less than 500 ml per day is said to be oliguric, which means that not all waste products of metabolism are being filtered at the glomeruli and excreted in urine.

Now on a normal, average diet a person will produce about 600 mOsm/day of waste products -- extra sodium, chloride, potassium, urea, creatinine etc.. To get rid of these 600 mOsm/day of solutes you need at least 500 ml of water -- provided you can concentrate urine to its maximum of about 1200 mOsm/L. That is why you have to make at least 500 ml of urine each day, and if you don’t, you will retain urea and creatinine and other waste products and will be said to have azotemia. That is why urea and creatinine are useful plasma markers for kidney function. So if the kidneys are not functioning properly, plasma creatinine and plasma urea values will be elevated.”

Kay: “Why can’t we make urine more concentrated than 1200 mOsm/L?”

Doc: “Desert rats can, but they have much longer loops of Henle.”

Kay: “Why is this so?”

Doc: “In order to make urine more concentrated than blood you need to deposit a lot of salt and urea in the renal medulla. The amount of sodium chloride deposited there depends upon countercurrent multiplication and countercurrent exchange.

Kay: “This is so complicated. We did have it in class.”

Doc: “True, it’s confusing. Basically, a 200 mOsm/L gradient is established by salt pumps in the thick ascending limb of Henle and this gradient is then multiplied by the number of these pumps arranged in series along the length of the tubule. So the longer the loop of Henle, the steeper the osmotic gradient between tubular fluid and blood. That’s why the desert rat can generate such high gradients.”

Kay: “But how about countercurrent exchange?”

Doc: “The peculiar arrangement of blood flow in the vasa recta prevents the osmotic gradient established by countercurrent multiplication from being washed away.”

Kay: “What do you mean by “washed away”?”
Doc: “As blood flowing to the renal medulla picks up salts and urea, these solutes would be flushed out and the medullary solute stores would be rapidly depleted. But this doesn’t happen, because blood leaves the medulla in vessels right next to vessels entering the medulla. Therefore, the solutes diffuse out of the ascending vasa recta and right into the descending vasa recta and are carried back to the medulla in this way. So the concentration of solutes remains high in the medulla.”

Kay: “Like a hot water heater?”

Doc: “I’m not sure. I think Flamingoes have blood flowing to their feet in this sort of arrangement.”

Kay: “I know that you need vasopressin to make a concentrated urine, but does vasopressin have anything to do with this gradient of medullary hypertonicity?”

Doc: “Yes it does. Vasopressin increases the action of the salt pumps in the ascending Limb of Henle -- along with aldosterone. In this way countercurrent multiplication is increased.”

Kay: “How about countercurrent exchange?”

Doc: “This is also made more effective by vasopressin because it constricts the vasa recta and diminishes blood flow to the renal medulla so that solutes are not washed away as rapidly. Vasopressin preserves the osmotic gradient.”

Kay: “The osmotic gradient that is essential for reabsorbing water from the forming urine in the renal collecting ducts!? Right?”

Doc: “Yes --in the presence of vasopressin the permeability to water of the collecting ducts is increased, allowing water to be returned to blood.”

Kay: “We learned that most of the nephrons are actually in the renal cortex and have short loops of Henle that don’t even reach down into the medulla. So can they make a concentrated urine?”

Doc: “They don’t participate in generating the osmotic gradient. You are correct. But the distal convoluted tubules from the cortical nephrons and juxta-medullary nephrons all feed into a common collecting duct that passes through the medulla where water is reabsorbed.”
Kay: “The cortical nephrons can still concentrate the urine up to the osmolarity of blood by themselves, can’t they?”

Doc: “Yes, vasopressin also increases the permeability to water of the distal convoluted tubule which will raise urine osmolarity to about 300 mOsm/L, the osmolarity of blood. You also have to bare in mind that blood flow to these different populations of nephrons is not fixed, but it changes.”

Kay: “What will do that?”

Doc: “In Michelle’s situation sympathetic stimulation will shift blood flow from cortical to juxta-medullary nephrons --the ones best suited for reabsorbing water and concentrating the urine.”

Kay: “Doc, you said that urea was also involved in making a concentrated urine. I thought that you wanted to get rid of urea, not hang onto it?”

Doc: “True, urea is a waste product that needs to be excreted, but you need to keep some in the renal medulla --actually quite a bit, about 600 mOsm/L. It’s been known for a long time that people who make little urea on a low protein diet cannot concentrate their urine to the normal value of about 1,200 mOsm/L.”

Kay: “But how does urea get into the renal medulla in the first place? It’s not actively transported across the thick ascending limb of Henle like salts?”

Doc: “The high urea concentration in the renal medulla is established by passive diffusion of urea in the thin ascending limb of Henle and in the bottom part of the collecting duct by the renal papilla --but only in the presence of vasopressin.”

Kay: “So vasopressin increases permeability also to urea?”

Doc: “Yes -- vasopressin increases urea permeability of the luminal membrane of so-called principal cells in the lower collecting ducts.”

Kay: “Why only in the lower part of the collecting ducts?”

Doc: “That’s where urea concentration is high enough to diffuse down it’s concentration gradient into the medulla. Higher up in the collecting duct vasopressin increases permeability only to water.”

Kay: “And as water is reabsorbed the urea is left behind in the collecting duct and becomes more concentrated?”
Doc: “Yes, Kay --a clever system. The so-called Staverman Reflection Coefficient for urea changes along the length of the collecting duct. High up in the collecting duct the coefficient is 1.0 and lower down somewhere around 0.5.”

Kay: “What is this Staverman Coefficient?”

Doc: “When the coefficient is 1.0, the membrane is completely impermeable to the solute and it will, therefore, exert a maximal effect in pulling water towards it. This happens in most of the collecting duct. That’s why urea is stored in the medullary interstitium. That’s it’s function, it’s purpose for being there.”

Kay: “And when the coefficient is less than 1.0 down by the papilla?”

Doc: “When the coefficient is less than 1.0, the membrane is somewhat permeable to urea. That happens when vasopressin is present, but only low down in the collecting duct. So now urea does not exert as much of a pull on water. It is not as effective in reclaiming water from the collecting duct as it is higher up.”

Kay: “So what good is the low urea Reflection coefficient?”

Doc: “You need to replenish the urea stores in the renal interstitium. Also, as urea moves down its concentration gradient across the lower collecting duct water will move along with it --a solute-linked water flux, so to speak.”

Kay: “Are you saying that you can move water without an osmotic gradient?”

Doc: “Yes --a solute, like urea, moving down its concentration gradient across the collecting duct will pull water along with it.”

Kay: “So this movement of urea in the collecting duct would not change the osmolarity of urine, but it would decrease urine volume. Wouldn’t it?”

Doc: “Yes --I believe this to be so.”

Kay: “Doc, you said that people on a low protein diet cannot make a maximally concentrated urine. Do other people have this problem as well?”

Doc: “Patients with Diabetes Insipidus or Psychogenic Polydipsia -- compulsive water drinkers -- produce many gallons a day of dilute urine and when you withhold water or give them an injection of vasopressin they still cannot form urine with an osmolarity of 1,200 mOsm/L. Perhaps 400
mOsm/L or so, and it takes several days before they can fully concentrate their urine.

Kay: “And why is this?”

Doc: ”It’s because in the absence of vasopressin they have washed out much of the urea and salt in their renal medulla and it takes time to re-establish the medullary solute stores.”

Kay: “The kidney is so confusing, isn’t it Doc?”

Doc: “It is Kay.”

Kay: “Thanks --it’s getting late, I’ll see you tomorrow.”

Doc: “Okay Kay --good night.”
Overview of Michelle’s adjustments to internal hemorrhage

1. Hemorrhage

2. Decreased ventricular filling and decreased left ventricular stroke volume.

3. Decreased stretch of carotid sinus and aortic arch

4. Increased vasomotor center (VMC) activity

5. Decreased parasympathetic impulses to the sinoatrial (SA) node.

6. Increases sympathetic impulses and epinephrine from adrenal gland.

7. Increased heart rate, increased myocardial contractility; constriction of arterioles to skin, gut, kidneys, muscles; contraction of venous blood reservoirs.

Fig 1-1. P. Eggena. The Physiological Basis of Primary Care. Novateur Medmedia.
Please draw cardiac output/venous return curves as a function of time for Michelle (a) before she falls from her horse, (b) shortly after her accident, (c) following compensation, and (d) after treatment.
Structure and Function of the Cardiovascular System
1. Overview of the Cardiovascular System

1. The Chambers of the Heart

The heart is made of four chambers, two atria and two ventricles (Figure 6-1).

Venous blood from the peripheral organs and tissues enters the right atrium through the superior and inferior vena.
Figure 6-1. Overview of the Heart and Circulatory System. Un-oxygenated blood is returned via the superior and inferior vena cava to the right atrium and flows through the tricuspid valve into the right ventricle. Blood is pumped by the right ventricle through the pulmonic valve into the pulmonary artery and through the capillary beds of the right and left lungs. Arterialized blood drains via the pulmonary veins into the left atrium and enters the left ventricle via the mitral valve. The left ventricle then pumps the arterIALIZED blood through the aortic valve into the aorta, which supplies blood to the various peripheral organs and muscles.
The heart is made of four chambers, two atria and two ventricles (Fig.6-1). Venous blood from the peripheral organs and tissues enters the right atrium through the superior and inferior vena cava and then flows through the tricuspid valve into the right ventricle; from there it is pumped through the pulmonary valve into the pulmonary artery and distributed to the capillary beds of the right and left lungs. Here oxygen is added and carbon dioxide removed, that is, venous blood is arterialized. Arterialized blood collects in pulmonary veins, flows into the left atrium, then enters the left ventricle through the mitral valve and is ejected through the aortic valve to be distributed to the organs and tissues of the body.

The left ventricle is a powerful muscle shaped into a chamber that functions as a pump when it contracts. Because the left ventricle must generate great pressure to move blood to the head, arms, legs, and to all the visceral organs (i.e., the kidneys, gut, liver, pancreas, and spleen), the wall of the left ventricle bulges with muscle. The wall of the right ventricle is much thinner because much less pressure is needed to force blood through the vessels in the lungs. Compared to the ventricles, the walls of the atria are flabby because there is normally little resistance as blood flows unimpeded across the tricuspid or mitral valves into the ventricles. Of course, the atrial walls do contain muscle that contracts to fill the ventricles with about one-third more blood than they would otherwise contain. But contraction of the atria is usually not essential, because when they fail to contract in a coordinated and effective way - as seen commonly in patients with atrial fibrillation - the heart still delivers sufficient blood to adequately perfuse the tissues, at least at rest. As we have discussed previously, the electrical potentials - which are generated by the heart and can be measured with electrodes at the surface of the body (i.e., by electrocardiography) - are proportional to the amount of muscle in the walls of the various heart chambers, so that the electrical signals generated by the atria (the P waves) are weak compared to the signals coming from the ventricles (the QRS waves).
2. The Blood Vessels
As mentioned above, the muscle mass of the two ventricles differs considerably. The right ventricle pumps blood through the lungs where resistance to blood flow is low, so that the right ventricular wall requires relatively little muscle. In contrast, the left ventricle has a much greater muscle mass because it must force blood against the much higher resistance of the peripheral circulation. The aorta must withstand the high blood pressures generated by the left ventricle; its walls are reinforced by strands of elastic fibers and bands of smooth muscle. As the aorta gives rise to its major arteries and these, in turn, divide and subdivide to form arterioles, elastic tissue decreases progressively, and more smooth muscle now takes its place in the vessel wall. Thus, the walls of arterioles are almost entirely smooth muscle. Because this muscle contracts or relaxes in response to an increase or decrease in sympathetic stimulation which alters resistance to blood flow, the arterioles are sometimes referred to as resistance vessels. It is here that the total peripheral resistance, which we will discuss a little later, is primarily regulated.

Each arteriole gives rise to many capillaries. Blood flow into the capillaries is controlled by smooth muscle in the walls of terminal arterioles. In some tissues (i.e., the mesenteries), a cuff of smooth muscle on terminal arterioles forms a sphincter (a precapillary sphincter) that constricts or relaxes depending upon the metabolic needs of the tissue. When one looks at a capillary bed (in live tissue) under a microscope, one notices red blood cells lined up in columns which are either stagnant or moving rapidly through capillaries across the visual field. It appears that constriction of the precapillary vessels does not just slow movement, but brings all movement to a complete halt. Then, just as suddenly as the movement had stopped, it starts up again as precapillary vessels relax. This constriction and relaxation of precapillary vessels, which had caused sudden movements of red blood cells, are referred to as vasomotion. In the resting state only a fraction of all capillaries are open. This is especially true for skeletal muscle. The capillary walls have neither elastic tissue nor muscle - just a single layer of endothelial cells. This permits rapid transfer of gases, fluids, and nutrients between blood
and interstitial fluid; for this reason capillaries are called **exchange vessels**.

Blood leaving capillaries enters **venules**, the larger **veins**, the **vena cava** and then flows into the right atrium. Valves in the larger veins create relatively short hydrostatic columns of blood and allow blood to move in only one direction - toward the heart, instead of flowing backward with the pull of gravity. Veins are much less muscular than are arteries, and their walls also have less elastic tissue. Veins are, therefore, more compliant than arteries, which gives veins a greater capacity for storing blood at lower pressures. The larger veins are, therefore, sometimes referred to as **capacitance vessels**. The smooth muscle in the walls of these capacitance vessels is innervated by sympathetic nerves. When these nerves are stimulated, as they are, for example, in exercise or hemorrhage, the veins become less compliant and cannot hold the usual amount of blood. This, in turn, shifts blood from these venous reservoirs toward the heart, from where it is pumped into the large arteries to sustain blood pressure.
Distribution of Blood
Distribution of Blood Volume

Lecture 1-2: Distribution of Blood Volume
An average person weighing 75 kg has a **plasma volume** of about 3 liters and a **blood volume** of about 5 liters, considering that **whole blood** is about 60% plasma and 40% red blood cells. Most of this blood (about 65%) is on the venous side of the circulation in the peripheral veins and the venous reservoirs in the spleen and liver. About 15% is in arteries and arterioles, and another 15% is in the heart and pulmonary vessels (see Fig.6-2). Only 5% of the blood volume is in capillaries because they are very short (only a few millimeters) and, therefore, hold relatively little blood despite their large numbers.

A normal **cardiac output** at rest is about 5 liters/minute, so that the entire blood volume of 5 liters is moved through the circulation once every minute. About 15% of the cardiac output perfuses the brain, 25% the gastrointestinal system (including spleen and liver), 20% the kidneys, 4% the coronaries, and the rest goes to the musculoskeletal system and skin (see Fig.6-2). During exercise cardiac output increases to 15 liters/minute or more, and a much greater fraction of the cardiac output now goes to skeletal muscle and a significantly lesser fraction to the kidneys and gastrointestinal tract.
Distribution of Cardiac Output

Lecture 1-3: Distribution of Cardiac Output
Velocity of Blood Flow
Velocity of Blood Flow

Lecture 1-4: Velocity of Blood Flow
It is important to keep in mind that the heart can only pump the amount of blood that is returned to it from the various organs and tissues. In other words, venous return must equal cardiac output. Therefore, when the cardiac output is 5 liters/min, 5 liters of blood will pass through the aorta, the arterioles, the capillaries, the veins, and enter the right atrium within the span of one minute. Although the same volume of blood flows each minute through the various sections of the circuit (measured in liters/min), blood will flow at different linear velocities in each section (measured in meters/second).

The **linear velocity of blood flow** is inversely related to the mean cross-sectional area of the vessels through which blood is moving (see Fig. 6-3, A and B). The cross-sectional area of the vascular system increases from the aorta to the capillary bed because as arteries and arterioles branch they give rise to a greater number of smaller blood vessels. Let us pretend that we could focus on a single red blood cell (RBC) as it moves through the circulation. When the RBC is first ejected by the left ventricle into the aorta, its linear velocity will be maximal because the aorta has the smallest total cross-sectional area (about 3 cm²). As the RBC leaves the aorta and moves through the arteries and arterioles to enter the capillaries, its velocity decreases progressively and reaches minimum speed in the capillaries where the mean cross-sectional area is greatest (about 3,000 cm²). Slow flow of blood through the capillaries is essential to allow enough time for gases and nutrients to diffuse across the capillary wall. As the RBC leaves the capillaries, its velocity increases
again in the venules and veins as the cross-sectional area progressively decreases to about 9 cm$^2$ in the vena cava.
Pressures in the Circulation
Pressures in the Circulation
Let us next take a look at pressures in different parts of the circulation (see Fig.6-3,C). Left ventricular pressure rises to about 120 mmHg during systole and falls to between 5 and 10 mmHg during diastole. As intraventricular pressure rises during systole and exceeds aortic pressure, the aortic valve opens and blood is ejected into the aorta. Because the aortic valve normally offers little resistance to blood flow, the pressure in the aorta is only slightly lower than it is in the left ventricle in early systole. In late systole pressure in the aorta is slightly higher than in the left ventricle as a result of kinetic energy imparted to the blood during rapid ejection. During diastole, however, aortic pressure is substantially higher than intraventricular pressure.

During systole the left ventricle forces its stroke volume of roughly 80 ml (at rest) into the aorta. Because of the viscosity of blood and the resistance to flow in the periphery, the stroke volume is not instantaneously forced through the circuit. Only part of the stroke volume moves out of the aorta and the major arteries to the muscles and various organs during systole - perhaps one-third. The remainder is stored in the aorta and large arteries, and these structures, of course, expand to accommodate the increased volume. During diastole the elastic fibers, which have been stretched in systole, recoil and gradually push the rest of the stroke volume through the circuit. As blood runs off into capillaries during diastole, pressure in the large arteries declines toward zero mmHg. However, long before this level is reached, the left ventricle contracts again and forces a new stroke volume into the arteries. The lowest pressure that is reached before the next ventricular contraction occurs is, of course, the diastolic blood pressure.

The difference between the peak (or systolic) blood pressure and the diastolic blood pressure is called the pulse pressure. This pulse pressure increases slightly as one proceeds from aorta to the large muscular arteries, but then declines to a very low value in the capillaries (see Fig.6-3,C). The reason for the slight increase in pulse (and systolic) pressure in the large arteries is that the pressure wave is reflected in the periphery and combines with waves spreading toward the periphery. This summation is thought to be similar to the formation of larger waves observed when waves reflected from a pond's edge meet those spreading toward it.

A steady, nonpulsatile flow is seen in capillaries when pressures have been damp-
ened by arteriolar constriction. When arteri-oles are dilated, however, or when the pulse pressure in the aorta is abnormally high - as it is, for instance, in aortic insufficiency or in severe anemia (case 6), the pulse wave will be transmitted all the way to the capillary bed, which can be seen on physical examination. If you apply pressure on the end of a fingernail, you will see that the outer part of the nail bed blanches while the inner part remains red. Now look at the borderline between white and red and you can see that the borderline moves with each heart beat, illustrating pulsatile flow in these capillaries.

Despite differences in pulse (and systolic) pressure, the mean blood pressure in the aorta is very similar to what it is in the brachial artery, where blood pressure is usually measured (see Fig.6-3,C). The mean arterial pressure is not the average pressure between the systolic and diastolic pressure, but rather an average value under the pressure curve throughout systole and diastole. This mean pressure value can be approximated by adding one-third of the pulse pressure to the diastolic pressure (note that the pressure during diastole is weighted more heavily because diastole is usually much longer than systole). Thus, for a person with a systolic pressure of 120 mmHg and a diastolic pressure of 80 mmHg, the pulse pressure is 40 mmHg, and the mean arterial pressure is 93 mmHg.

The mean pressure in arterioles is between 40 and 60 mmHg and declines in capillaries to between 20 and 40 mmHg. Capillary pressures will depend on the pressure transmitted through arterioles, on whether the precapillary vessels are constricted or relaxed, and on pressures in the postcapillary venules. An increase in venous pressure is readily transmitted backward to the capillaries because postcapillary venules do not constrict. Indeed, this is why the patient in case 6 had peripheral edema.

The pressure in the peripheral veins is about 10 mmHg and decreases to about 5 mmHg in the vena cava and the right atrium. The central venous pressure (CVP) can be estimated on physical examination in the following manner: With the patient in a semi-recumbent position look for a distended external jugular vein. Adjust the patient's position so that the meniscus of the blood column falls between the clavicle and angle of the jaw. Measure the vertical distance between the meniscus and the tricuspid valve, which serves as a zero reference point and is located at the fourth intercostal space in the midaxillary line. The CVP, measured in cm H$_2$O, can be con-
verted to mmHg by dividing by the specific gravity for mercury, which is 13.5 g/ml.
Types of Blood Flow
Types of Blood Flow
The movement of blood through the circulatory system is essentially of two types: 
(1) laminar flow or (2) turbulent flow (Fig.6-4). In laminar flow, the thin layer (or lamina) of water molecules in direct contact with the vessel wall is stationary. But as second, third, and fourth, etc. concentric layers of water slide over each other (by breaking hydrogen bonds between water molecules), movement increases progressively toward the center of the blood vessel so that water moves as a spike through a tube. In turbulent flow, on the other hand, the lamina fall apart and small aberrant currents form as the fluid travels as a front, rather than a spike, through the vessel.

Laminar flow is the most efficient type of flow in the sense that the least amount of driving pressure yields the most volume flux. Laminar flow is also referred to as Newtonian flow and is characterized by Poiseuille's equation,

\[ Q = \frac{(\Delta P \times \pi r^4)}{(8 \times l \times \eta)} \]

where \( Q \) is the amount of fluid flowing through a tube in liters/min, \( \Delta P \) is the driving pressure across the tube, \( r \) is the radius of the tube, \( l \) is the length of the tube, and \( \eta \) is the viscosity. This equation predicts, for instance, that doubling the tube length will decrease flow by one-half, but that halving the radius of the tube will decrease flow by a factor of 16! Thus, relatively minor changes in the diameter of vessels (e.g., constriction or relaxation of arterioles) can lead to profound changes in blood flow. In case 6 in response to anemia, autoregulation dilated resistance vessels, increasing blood flow by the fourth power of the radius. The decrease in hematocrit from 45% to 20% reduced viscosity

Fig.6-4. Laminar and turbulent flow. Laminar flow occurs in straight, smooth vessels in accordance with Poiseuille’s equation. Laminar flow deteriorates into turbulent flow when Reynold’s number exceeds a value of approximately 2,000. Turbulent flow is less efficient than laminar flow and cannot be calculated by using Poiseuille’s equation.
by almost one-half, which should have increased flow almost twofold, according to the Poiseuille equation.

The circulatory system, however, does not behave exactly as water flowing through the straight glass tubes on which Poiseuille based his conclusions about laminar flow. Laminar flow is seen only in small, straight tubes where flow is slow, as in the arterioles and capillaries. In these vessels we would expect to see a fall in resistance and enhanced flow in the man in case 6. Where velocity is high, where tubes are large, or where there are irregularities in the tube, blood flow is turbulent (see Fig. 6-4).

In the larger vessels, and particularly in the chambers of the heart, a decrease in blood viscosity actually increases resistance and tends to slow blood flow. When flow occurs at a high velocity (as it does in the heart and large vessels) a decrease in viscosity changes blood flow from laminar to turbulent flow, which is much less efficient and no longer obeys the Poiseuille equation. Therefore, we cannot predict changes in total peripheral resistance from viscosity measurements of blood alone.

In turbulent flow energy is wasted in the form of heat and sound. The sound waves generated by turbulent flow around a plaque or constricted artery are called bruits. Heart murmurs are caused by turbulent blood flow through stenotic or incompetent valves. A functional or hemic murmur is caused by a decrease in viscosity and/or an increase in velocity of blood flow in an otherwise normal heart (as in case 6). Functional murmurs are loudest during the early part of systole when ejection of blood is rapid. They are never heard in diastole when blood flow is slow. The functional murmur of anemia disappears following blood transfusion, as it did for the man in case 6 after 2 units of blood from which most plasma had been removed (i.e., packed red blood cells), had been given.

The tendency for flow to become turbulent is given by Reynolds number (R). This is a dimensionless number that takes into account all the factors that contribute to turbulent flow:

\[ R = \frac{\text{velocity} \times \text{diameter} \times \text{density}}{\text{viscosity}} \]

When Reynolds number exceeds a value of 2,000, laminar flow will deteriorate into turbulent flow even in a straight, smooth vessel. However, in the presence of irregularities in the vessel wall or at points where the vessel branches, turbulence will be
seen at much lower values than 2,000. This equation predicts, for instance, that turbulent flow is more likely in the aorta, where the velocity of blood flow is high and the vessel diameter is great, than in a capillary, where the velocity is low and the diameter small. Moreover, the equation helps explain why severe anemia often causes functional heart murmurs from reduced blood viscosity and increased velocity of flow from high output.
Blood Viscosity
Effects of Hematocrit on Blood Viscosity
Newton was first to measure viscosity of liquids. He studied the slippage of concentric layers of liquids as he stirred them in a drum with a central rotor. He observed that the layer closest to the rotor moved fastest with a progressive decline in circular motion as the wall of the drum was approached. We now know that this slippage between portions of water is due to rupture of hydrogen bonds and, in deed, the strength of the hydrogen bond has been estimated from measurements concerning temperature-dependent changes in water viscosity.

**Effects of Hematocrit and Protein Concentration on Blood Viscosity**

The relationship between hematocrit (Hct) and blood viscosity is shown in Figure 6-5. Plasma is about twice as viscous as water, and whole blood, in turn, is about twice as viscous as plasma. The Hct in healthy men and women ranges between 40% and 50%, with women tending toward the lower end of the range. Viscosity rises sharply when the Hct rises above 50% and is about twice normal at an Hct between 60% and 70%.

Individuals with such abnormally high concentrations of red blood cells are said to have **polycythemia**. To keep the flow of blood constant with twice normal viscosity would require twice the normal driving pressure, according to Poiseuille's equation, if there were no compensatory change in the diameter of resistance vessels. Thus, one might expect patients with polycythemia to have systemic blood pressures in excess of 200 mmHg. However, on physical examination most patients with polycythemia are found to have only...
slightly elevated blood pressure because arterioles compensate for the increased blood viscosity by dilating and, moreover, blood flow to tissues is reduced.

Polycythemia may be caused by a primary abnormality in red cell proliferation (e.g., polycythemia vera or excessive erythropoietin production by a renal tumor) or it may be caused by a secondary (adaptive) response to hypoxemia that is seen in people who live at high altitudes (e.g., in the mountains of Peru or Nepal) or in patients with chronic heart or lung conditions. In individuals with secondary polycythemia, the increase in oxygen carrying capacity is a useful compensatory response to diminished oxygen loading of blood in the lungs - but only up to an Hct value of about 60%. Above this value, blood simply becomes too viscous (tending to clump and form rouleaux (stacks of donut-shaped red blood cells, see Fig. 6-6). However, changes in protein concentration are much less important than changes in Hct in altering blood viscosity.

Marked elevations in plasma protein concentration (e.g., multiple myeloma) will also increase blood viscosity. The increased viscosity is not only due to the increased concentration of protein molecules per se, but also due to the tendency of proteins (especially fibrinogens) to adhere to red blood cells and increase their stickiness so that they tend to clump and form rouleaux (stacks of donut-shaped red blood cells, see Fig. 6-6). However, changes in protein concentration are much less important than changes in Hct in altering blood viscosity.
Flow-dependent Changes in Blood Viscosity
Flow Dependent Changes in Blood Viscosity

The viscosity of blood changes not only with the hematocrit and protein concentration, but also as a function of the velocity of blood flow and the geometry of the vessels through which blood is flowing. These flow-dependent changes are not real changes in blood viscosity - they cannot be measured with a viscosity meter in a test tube - so they are categorized as apparent changes in viscosity. These apparent changes in viscosity are primarily due to the fact that blood does not behave as a Newtonian fluid, such as water, because of suspended particles and their changing distribution during flow.

As blood flows at high velocity, red cells take on streamlined, bullet-like, shapes and accumulate in the center of the stream to form an axial core. This greatly diminishes frictional resistance between blood and the vessel wall which now interacts essentially with the plasma portion of blood. When flow is sluggish, as it is in the postcapillary venules, red blood cells leave the axial core, form rouleaux, and increase viscosity (Fig. 6-6). This increase in blood viscosity due to sludging of red blood cells is a major determinant of resistance and rate of blood flow in the immediate postcapillary region of the circulation.

The increase in the apparent viscosity of blood in the postcapillary region is offset by a decrease in the apparent viscosity of blood in the precapillary region. When blood flows through arterioles with diameters less than 0.5 mm (but greater than the diameter of a red blood cell), blood behaves as if it were thinner, i.e., flow is greater than expected for a given driving pressure. This phenomenon, the Fahraeus-Lindqvist effect, is thought to result from a flow-dependent decrease in the Hct in microvessels (Fig. 6-6). What apparently happens is this: The red blood cells line up in the axial core of the stream and, therefore, move more rapidly than the plasma in the outer lamina close to the vessel wall. Thus, blood leaving the capillaries would have a higher Hct, were it not for the fact that the spacing between individual red blood cells increases as blood flows through small arterioles and capillaries. This preserves the normal ratio of blood cells to plasma as blood leaves the microcirculation; yet, at any one point in a small vessel, the Hct is lower than normal (e.g., one-half normal in Fig. 6-6) and viscosity is accordingly reduced.
Flow-Dependent Changes in Blood Viscosity

Fig. 6-6. Flow-dependent changes in blood viscosity. The flow of blood from arterioles via the capillaries into venules is shown. The apparent viscosity of blood in small (less than 0.5 mm diameter) arterioles and capillaries is decreased (Fahraeus-Lindqvist Effect) due to increased spacing between red blood cells as they move at higher velocity in the axial core. Note that red blood cells also become more bullet-shaped in small vessels. In the postcapillary venules the apparent viscosity of blood increases due to sludging and formation of rouleaux.
Radius of Vessel
Radius of Vessels
1. Driving and Distending Pressures in Vessels

According to Poiseuille’s equation resistance to blood flow changes with the fourth power of the radius, so that increasing or decreasing the radius of an arteriole by altering sympathetic tone to vascular smooth muscle will have marked effects on blood flow through the arteriole (Fig. 6-7,A). For example, if the radius is reduced by a factor of 2, flow will diminish by a factor of 16. Moreover, for any given radius, flow increases in direct proportion to the increase in driving pressure. This is illustrated in Figure 6-7,B for a lead pipe. However, arterioles are different from rigid lead pipes or glass tubes in that changes in the driving pressure are associated with changes in the radius.

We have a tendency to think of blood pressure as providing a driving force that is applied only to moving blood through the circulation and forget that this same pressure also pushes the vessel wall out and keeps the vessel distended (as described by the Laplace equation, Fig. 6-7,A). Flow and driving pressure in arterioles are, therefore, not related linearly (see Fig.6-7,B).

2. Aneurysms

The relationship between vessel radius, the distending pressure, and the wall ten-
sion is given by the Laplace equation, which states that wall tension (T) equals pressure (P) times radius (r):

\[ T = P \times r \]

One can predict from this relationship that wall tension (measured in dynes/cm) is much greater in a large vessel, such as the aorta, than in a small vessel, such as a capillary - not only because of the higher pressure (measured in dynes/cm²) in the aorta, but primarily because of its much larger radius (measured in cm). Indeed, the wall tension in the aorta is about a ten thousand-fold greater than in a capillary. To prevent this increase in tension (the linear force exerted on muscle strands and elastic fibers) from rupturing the vessel wall, the aorta needs considerable elastic and muscle fiber support. In contrast, the capillary wall can withstand the considerably lower tension without any extra collagen fibers or muscle, so its wall consists of only a single layer of endothelial cells.

Let us briefly consider the series of events that take place in the aorta when the wall cannot withstand the arterial pressure generated by the left ventricle. When the wall of the aorta has been weakened - perhaps by calcific plaques in atherosclerosis or by clogging the vasa recta by chronic inflammation in tertiary syphilis - the wall bulges outward in the area of damage (see Fig.6-8). This, in turn, increases the radius of the vessel at that point. Assuming that blood pressure remains constant, this increase in radius leads to an increase in wall tension which, in turn, leads to further expansion of the aneurysm by a positive feedback mechanism, eventually resulting in a blow out.

![Aortic Aneurism](image)
bulging of the wall at that point with a further increase in the radius, etc. This **positive feedback** loop rapidly terminates in a blow-out, just as a tire first bulges and then ruptures at a point where the rubber has worn thin. Such abnormal dilations in vessels are called **aneurysms**.

Aortic aneurysms are usually due to atherosclerosis and are most common in the lower aorta below the origins of the renal arteries. Such aneurysms are seldom painful although they may produce a pounding sensation in the abdomen. On physical examination a pulsatile mass is palpated and its size is measured by ultrasound or x-ray techniques. The risk of rupture and sudden death from an abdominal aneurysm of the aorta is considerable when its diameter exceeds 6 cm or when it is found to be expanding on serial examinations, in which case surgical excision with graft replacement is usually recommended.
9

Resistance to Blood Flow
Resistance to Blood Flow
1. Total Peripheral Resistance

The overall resistance of blood as it flows from the left ventricle through the peripheral organs and tissues and returns again to the right ventricle is called the total peripheral resistance. The total peripheral resistance is equal to the pressure gradient between the aorta and the vena cava, divided by the amount of blood that flows in response to that gradient, which is the cardiac output:

\[ \text{TPR} = \frac{\text{MSAP} - \text{CVP}}{\text{CO}} \]

For example, if the mean systemic arterial pressure (MSAP) is 93 mmHg, the central venous pressure (CVP) is 3 mmHg, and the cardiac output (CO) is 5 liters/min, the total peripheral resistance (TPR) will equal 18 mmHg/L/min. The units for TPR are often converted from mmHg/L/min to dynes x sec x cm\(^{-5}\) by multiplying by 80, i.e., 18 mmHg/L/min x 80 (dynes x sec x cm\(^{-5}\))/ (mmHg/L/min) = 1,440 dynes x sec x cm\(^{-5}\).

Because it is now possible to measure all of the above variables simultaneously on patients in intensive care units, this information is important for making decisions on the use of agents that increase CO or reduce TPR. For clinical purposes, TPR is a good estimate of the afterload of the left ventricle. For example, patients with congestive heart failure and markedly elevated values for TPR often respond to vasodilator treatment with an increase in cardiac output and increased tissue perfusion (see case 5).

2. Parallel and Series Resistances

The total peripheral resistance is the sum of all the individual resistances in different parts of the circulation. These resistances are arranged either in series (for example, the resistances of arteries, arterioles, capillaries, venules, veins) or in parallel circuits (for example, the resistances of the kidneys, the gastrointestinal tract, muscles, skin, brain, etc.). The total resistance \(R_{\text{total}}\) of three individual resistances \(R_1, R_2,\) and \(R_3\) arranged in series is simply the sum of the individual resistances, i.e., \(R_{\text{total}} = R_1 + R_2 + R_3\) (Fig. 6-9,A). The total resistance of individual resistances arranged in parallel circuits is obtained by adding conductances, where the conductance equals 1/resistance. Thus, the total conductance or \(1/R_{\text{total}}\) equals \(1/R_1 + 1/R_2 + 1/R_3\) (Fig. 6-9,B).

When circuits are arranged in series, the individual resistances are always less than the total resistance. However, when cir-
circuits are arranged in parallel, the individual resistances are always greater than the total resistance. Consider, for example, the resistance to the kidneys. The pressure gradient across the kidneys (between renal artery and renal vein) is about 90 mmHg, and about 1 L/min of blood flows through the kidneys (20% of cardiac output), so that the renal resistance is 90 mmHg/L/min, which is five times greater than the total peripheral resistance. The obvious advantage of this arrangement is that the resistance to any one organ can be increased by selective arteriolar constriction without increasing the TPR and, thereby, the work load of the left ventricle.

Not all organs are arranged in parallel circuits. The pulmonary circulation is arranged in series with the peripheral circulation. Were it not for the right ventricle that pumps blood only through the lungs, the pulmonary circulation would place an inordinate strain on the left ventricle. Consider for a moment what would happen if the booster function of the right ventricle were lost: the pressure in the central veins would now have to be high enough to force blood through the pulmonary vasculature. In other words, central venous pressure (CVP) would have to rise to the level of the pulmonary artery pressure (about 20 mmHg), and the capillary pressure in the peripheral tissues would have to be even higher for blood to flow towards the heart. This high capillary pressure would, in turn, cause peripheral edema. We normally do not have these high venous pressures and peripheral edema because the right ventri-

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**Fig. 6-9.** Series and parallel resistances. A. Resistances in series that blood encounters as it flows (Q) from arteries (R1) into arterioles (R2) and into capillaries (R3) along its pressure gradient (P1 thru P3). The total resistance of these three resistances (R1 thru R3) in series is given by their sum, \( R_{total} = R1 + R2 + R3 \). B. Resistances in parallel that blood encounters as it flows (Q) from the aorta along its pressure gradient (P1-P2) through the gastrointestinal system (R1), the kidney (R2), or skeletal muscle (R3). Resistances in parallel circuits are added as individual conductances, which are the inverse of the resistances, i.e., \( 1/R_{total} = 1/R1 + 1/R2 + 1/R3 \).
cle keeps the CVP much lower than the pulmonary artery pressure. But when the right ventricle fails to pump normally, we do observe an increase in CVP and the characteristic symptoms of peripheral edema.
Measurement of Blood Pressure
Measuring Blood Pressure
Everyone has had their blood pressure taken at one time or another. A cuff is placed around the upper arm and inflated to a pressure well beyond the systolic pressure, i.e., 30-40 mmHg above the expected systolic pressure (Fig. 6-10). You then listen over the brachial artery with a stethoscope for Korotkoff’s sounds, which are heard when the brachial artery under the cuff is partially obstructed so that blood flow becomes turbulent distal to the cuff. When the cuff pressure is above the systolic pressure in the brachial artery, the artery is completely occluded, no blood flows distally in the artery and, therefore, no sounds are heard on auscultation. As the cuff is now gradually deflated, a pressure is reached where some blood rushes through the brachial artery during the peak of systole and hits the column of stagnant blood distal to the cuff and produces a sound. The pressure reading when the sound is first heard is the systolic blood pressure. As the cuff pressure is gradually lowered further the intensity and duration of the sound increases and then becomes muffled and fades away when a pressure is reached at which the brachial artery under the cuff is always open, during systole as well as during diastole. The pressure at which the sound first becomes muffled is usually taken as measurement of the diastolic blood pressure (see Fig. 6-10). Measuring blood pressure with the sphygmomanometer by auscultation and palpation. A cuff is placed around the arm and pumped to a pressure of 160 mmHg, in this example. At this point the brachial artery under the cuff is completely occluded, no blood flows distally, and no sounds are heard. As the cuff pressure is gradually lowered (by opening the valve to the cuff), a pressure is reached where a small jet of blood rushes under the cuff at the peak of systole and creates turbulence distal to the cuff where it can be heard by auscultation with a stethoscope (Korotkoff’s sounds) or palpated as a small pulse wave. This is the systolic pressure. Sounds are heard at increasing intensity as cuff pressure is lowered below systolic pressure. Sounds then become muffled and disappear when cuff pressure reaches diastolic blood pressure, at which time the brachial artery is no longer occluded and blood flow again becomes laminar.
When blood pressure is low - as it is, for instance, in patients in circulatory shock - turbulence is minimal and Korotkoff's sounds may not be heard. In such situations, the systolic (but not the diastolic) blood pressure can usually be estimated by palpating the pulse in the brachial artery and then noting the pressure at which the pulse disappears when the cuff is gradually inflated.

Blood pressure can also be measured at the ankles. In the supine position, ankle and arm blood pressures are normally similar. A significant reduction in ankle blood pressure relative to pressure in the arms suggests obstruction of blood flow in the aorta, iliacs, and/or femoral arteries, most commonly due to the presence of atheromatous plaques. Such patients are at increased risk for having a heart attack or a stroke, and are likely to benefit from preventive measures, e.g., aspirin, exercise, weight reduction, and lowering blood cholesterol with diet and drugs.

Automated blood pressure machines are now in common use, especially by patients with hypertension which allows them to monitor the response to (or need for) treatment by themselves at home.
Determinants of Blood Pressure
Determinants of Blood Pressure

Lecture 1-9: Determinants of Blood Pressure
Blood pressure, in clinical usage, refers to pressure in the brachial artery. This pressure is similar in value to pressures in the other major arteries, including the aorta, assuming that all pressure readings are taken at the same level to avoid differences due to gravity. For instance, when a person is standing, blood pressure in the femoral artery will be greater than in the brachial artery. Blood pressure depends upon two variables: (1) the volume of blood in the large arteries and (2) the compliance of large arteries. Unfortunately, neither of these variables can be measured in life.

The volume of blood in the large arteries depends upon how much flows in and how much flows out. In other words, the volume and pressure (P) in the large arteries depend upon (1) the cardiac output (CO) and (2) the total peripheral resistance (TPR). \( P = TPR \times CO \), which is the same relationship discussed earlier for the measurement of total peripheral resistance. Accordingly, blood pressure will increase when the total peripheral resistance increases and/or when cardiac output increases. Although we can measure CO, TPR, and P, we cannot measure the volume of blood in the large arteries nor the elastic properties of these vessels, which are responsible for the observed blood pressure.

The compliances of large arteries (such as the aorta) have been measured at autopsy by filling the vessels with various volumes of fluid and measuring the associated pressure changes (see Fig. 6-11). The slope of the volume-pressure curve (\( \Delta V/\Delta P \)) is the compliance. The compliance of large arter-
ies decreases with advancing age and/or with atherosclerosis. This is sometimes referred to as **hardening of the arteries**. Because the arteries of older people are stiffer than normal, they can hold a normal volume of blood only at a higher than normal pressure and this accounts, in part, for the increased blood pressure so often seen with advancing age.

The compliance of large arteries is also slightly diminished by sympathetic constriction of vascular smooth muscle, which tends to raise blood pressure. Much more important is that sympathetic constriction increases peripheral resistance so that less blood flows out of the aorta and large arteries into arterioles and capillaries. This leaves a greater blood volume in the large arteries and increases blood pressure even without any change in large vessel compliance.

The compliance of large vessels in a given individual (young or old) is not a constant value, but decreases as pressure rises (see Fig. 6-11). This is presumably due to an elastic limit that is reached by fibers in the vessel wall as they uncoil and become excessively stretched. Therefore, a person with hypertension and a high diastolic blood pressure will experience a greater rise in blood pressure (i.e., a greater pulse pressure) than a person with a normal diastolic blood pressure for the same left ventricular stroke volume.
Pulse Pressure
Pulse Pressure

Lecture 1-10: Pulse Pressure
The compliance of the aorta and large arteries and the volume of blood in these vessels cause the changes in blood pressure that are measured in the brachial artery. There are many volumes and many pressures during the cardiac cycle. The peak pressure, the systolic pressure, is seen only for the short moment when the large arteries reach a peak volume during the period of rapid ejection (see Fig. 6-12). As blood runs off through the arterioles and volume in the large arteries declines, pressure falls. The pressure associated with the smallest volume in the large arteries is the diastolic pressure. The difference between the systolic and diastolic pressures is the pulse pressure.

Although we can measure systolic and diastolic pressures, the blood volumes and vessel compliance responsible for these pressure changes cannot be measured. Nevertheless, there is some minimal (unmeasured) volume in the large arteries (Vd) when diastolic blood pressure (Pd) is measured (see Fig. 6-12). As the left ventricle ejects its stroke volume into the large arteries during systole, their volume increases to a maximum volume (Vs), which is associated with a maximum pressure (Ps). The pulse pressure, Ps - Pd, will therefore depend upon the compliance and the maximum volume changes in the large arteries.

![Pulse Pressure and Vessel Compliance](image)

**Fig. 6-12.** Relationship between pulse pressure and large artery compliance. The relative volume of blood contained within the aorta and large arteries of a normal subject (a) and a patient with atherosclerosis (b, low compliance) is plotted as a function of pressure within these vessels. The pressures associated with minimal volumes are the diastolic pressures (Pd), whereas the pressures associated with maximum volumes are the systolic pressures (Ps). The pulse pressure (PP) is the difference between systolic and diastolic pressures. In this graph, the assumption has been made that both subjects (a) and (b) have the same diastolic blood pressure of 75 mmHg and that the aorta and large arteries are filled with the same volume of blood during systole (i.e., approximately equal stroke volumes). The systolic blood pressure of (b) will rise to a much higher value (175 mmHg) than it will in (a) (125 mmHg), so that the pulse pressure (PP) in (b) is 50 mmHg higher than it is in (a). Accordingly, pulse pressure is proportional to stroke volume divided by aortic and large vessel compliance.
Vs-Vd. The difference between Vd and Vs depends on the stroke volume, the velocity of left ventricular ejection (ΔP/Δt\text{max}), and the total peripheral resistance. When the total peripheral resistance and velocity of ejection are constant, the pulse pressure (PP) is proportional to the stroke volume (SV) divided by large vessel compliance (C): 

\[ \text{PP} \sim \frac{\text{SV}}{\text{C}} \]

Thus, the pulse pressure increases as arterial compliance decreases. This is seen with advancing age or in patients with atherosclerosis. As mentioned earlier, patients with hypertension also have high pulse pressures because compliance (even of normal arteries) is decreased in the high pressure ranges. The pulse pressure also increases with an increase in the stroke volume. One sees this frequently in individuals with bradycardia or in patients with aortic regurgitation, for example.

The pulse pressure is closely related to the pulse you feel at the patient's wrist on physical examination. You do not sense the actual flow of blood through the radial artery but rather a pulse wave that is initiated by radial stretch of the aorta during ejection of the stroke volume. This wave travels about 100 times faster along the arteries than blood actually flows. The velocity of the pulse wave is inversely related to the compliance of the arterial tree. Therefore, the pulse wave travels faster along noncompliant, atherosclerotic vessels than along normal, flexible arteries.

Taking a person's pulse is an important part of the physical examination. The radial pulse not only provides useful information about cardiac and circulatory function but also communicates your concern for the patient's well-being. Therefore, you must not rush when taking a pulse. Place the three middle fingers along the radial artery and sense the amplitude of the pulse wave, its force, its velocity, its rhythm and its rate, and note any changes during inspiration and expiration. A weak and thready pulse, which one may encounter in a patient who is in circulatory shock (see case 1), is called pulsus parvus. A sluggish, biphasic pulse of low velocity, which one may encounter in left ventricular outflow obstruction, is called a bifid pulse or pulsus tardus. A bounding, strong pulse is seen with high pulse pressures in anemia (see case 6) or in aortic insufficiency and is called a water hammer or Corrigan pulse.

In a patient with cardiac tamponade the intensity of the pulse decreases substantially
during inspiration (see Fig. 6-13). This is called **pulsus paradoxus**. Pulsus paradoxus is said to exist when the systolic blood pressure falls by more than 10% on inspiration. The mechanism for pulsus paradoxus is as follows: During inspiration more blood is returned to the right ventricle. The right ventricle normally accommodates the increased volume by bulging outward into the pericardial space. However, when the pericardial space is filled with fluid (**cardiac tamponade**) the right ventricle cannot expand outward and, instead, bulges into the left ventricular chamber, diminishing left ventricular filling. The resulting decrease in left ventricular stroke volume, in turn, decreases systolic blood pressure, which can be palpated at the patient’s wrist when the decrease is excessive. Cardiac tamponade is a medical emergency requiring rapid removal of fluid from the pericardial space.

The intensity of the pulse may vary from one beat to the next (Fig. 6-14,A). This is called **pulsus alternans**. It is a sign that the left ventricle is unable to eject similar stroke volumes from one beat to the next and usually signifies severe left ventricular failure.

An irregular pulse may be due to an **ectopic beat** (e.g., a premature ventricular contraction [PVC]). This beat may occur prematurely at a time when the left ventricle has not had sufficient time to fill, so
that the stroke volume may be insufficient to induce a pulse wave that can be felt at the wrist in the radial artery (Fig. 6-14, B). However, the contraction of the ventricle and closing of heart valves will be heard with the stethoscope. The difference in beats/min heard at the heart and beats/min felt at the wrist is called the **pulse deficit**. It is a measure of the number of ectopic beats per minute. Such ectopic beats are quite common in young medical students and are no cause for alarm. They are often caused by a lack of sleep, smoking, drinking coffee, or anxiety before or after an examination. However, in a patient with a history of coronary artery disease, ectopic beats take on special significance.

**Fig. 6-14. Dropped beats and pulsus alternans.** A. In pulsus alternans a large pulse wave alternates with a small pulse wave. This phenomenon is characteristic of severe left ventricular failure. B. The ECG is compared with a tracing of arterial pressures in the brachial artery. An early premature ventricular contraction (PVC) causes only a small increase in brachial artery pressure which may not be palpated but is heard on auscultation, resulting in a dropped beat (or pulse deficit). The PVC is followed by a compensatory pause during which left ventricular filling is augmented, so that the next QRS complex triggers a larger than usual pulse wave (postectopic potentiation).
Review
Interactive Questions
93

Pale, cold, clammy skin.

My stomach hurts. I feel like throwing up. Her abdomen is hard as a board.

Neck veins are collapsed.

How are you going to treat her?

Heart rate: 120 bpm, new late systolic murmur.

Water, water please!

Pain and large bruise.

Deep breaths at 25/min.

BP 60 mmHg by palpation.

Weak, thready pulse.
Case: Essay/Small Group Questions
1. When you first saw Michelle after falling off her horse her skin was pale and cold and clammy. What is this called? What does it suggest? What causes it?

2. Her stomach was hard as a board and painful when you palpated her abdomen. What does this suggest?

3. Why did she feel like throwing up?

4. Why were her neck veins collapsed?

5. Why was her heart beating fast?

6. How do you measure blood pressure?

7. How can you measure blood pressure if you cannot hear Korotkoff’s sounds?

8. She had mitral valve prolapse, why is this murmur louder at this time when she is in circulatory shock?

9. Please make a graph of her ventricular, aortic, and atrial pressures during a cardiac cycle and indicate where you hear the murmur of mitral valve prolapse.

10. Name and explain the four effects of epinephrine on the heart.

11. Draw cardiac output and venous return curves for Michelle before and just after she first fell off her horse. Next add the curves and discuss how she compensated on her own and was eventually helped by an infusion of isotonic saline.

12. Why was she thirsty?

13. Why was she not given water to quench her thirst?

14. Why did the substantial blood loss increase her ventilation?

15. How do the oxygen sensors in the carotid body work?

16. How might ventilation enhance cardiac output?

17. How does the distribution of cardiac output change in circulatory shock?

18. Why was she initially anuric and later oliguric?

19. What causes azotemia?

20. Explain the time course of changes in hematocrit following acute internal bleeding.

21. How are fluids mobilized from the interstitial spaces of muscles when the plasma volume is reduced?

22. What determines the size of the extracellular fluid compartment?
23. What are the benefits and potential harmful effects of giving morphine to Michelle?
Lecture: Essay/Small Group Questions
Anatomy

1. Name the structures through which a red blood cell passes as it leaves the right ventricle and returns to the right atrium.

2. Why is the wall of the right ventricle thinner than the wall of the left ventricle?

3. Appreciate the relative amounts of muscle and elastic tissues in different vessels of the circulation and the reasons for these differences.

Blood volume

4. How is the volume of blood distributed in various parts of the circulation?

5. When and how will this distribution change?

Blood flow

6. What determines cardiac output?

7. Roughly how much blood flows to the various organs of the body at rest?

8. Which organs and tissues receive relatively less blood in circulatory shock?

9. What is the velocity of blood flow in capillaries compared to flow in the aorta and vena cava?

Laminar flow

10. What are the characteristics of laminar flow?

11. How would laminar flow change if you were to (a) double the length of the vessel, (b) double the driving pressure, (c) double the viscosity of the fluid, and (d) double the radius of the vessel?

Turbulent flow

12. What are the characteristics of turbulent flow?

13. How could you detect turbulent blood flow on physical examination?

14. Why do some people develop a functional heart murmur when they become anemic?

Measuring the total peripheral resistance

15. A patient has a brachial artery pressure of 140/80 mmHg, a central venous pressure of 10 mmHg, and a cardiac output of 5 L/min. What is her total peripheral resistance?
**Blood pressure measurement**

16. What are “Korotkoff’s” sounds?

**Determinants of blood pressure**

17. How do changes in arterial compliance, stroke volume, and total peripheral resistance affect blood pressure?

**Pulse pressure**

18. Give examples of situations in which the pulse pressure is increased or decreased.

**Pulsus paradoxus**

20. What causes “pulsus paradoxus”?
True/False Quiz
Directions: An answer is “True” (A) when the complete statement(s) is (are) correct. Otherwise the answer is “False” (B).

**Question 1 of 10**
The velocity of blood flow is higher in the aorta than in the vena cava.

A.

B.
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