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Ten Things All Physicians Should Know About Cardiovascular Disease

Moderated by **William C. Roberts, MD**[1]

Discussants: **Joseph S. Alpert, MD**[2]**; L. David Hillis, MD**[3]

DR. ROBERTS: I am Bill Roberts and it's my privilege to moderate this session. With me is Dr. Joseph Alpert who was born in New Haven, graduated from Yale University and from Harvard Medical School, did his postgraduate training in Boston, and then moved to Worcester, Massachusetts, where he was head of cardiology. He then went to Tucson, Arizona, to be chairman of medicine and he is still there. He has made numerous contributions to our knowledge of cardiovascular disease. Also with me is Dr. David Hillis, presently chairman of the department of medicine at the University of Texas, San Antonio. David was born in Tyler, Texas, and went to Columbia University and then to Columbia College of Physicians and Surgeons. His internship and residency was at Parkland Hospital at the University of Texas Southwestern. He was head of the cardiac catheterization laboratory there for many years and also associate director of the department of medicine. Recently, he moved to San Antonio to be chairman of the Department of Medicine.

Each participant was asked before the roundtable to list 10 facts every non-cardiologist should know about heart disease. Dr. Alpert, could you give your 10 facts?

DR. ALPERT: Bill, I've written editorials about this for *The American Journal of Medicine*. First, common things occur frequently. Therefore, look first for the common things; not the rare things.

Second, quoted from Voltaire, common sense occurs uncommonly. Instead of a logical, simple, straightforward, common sense approach to patients, too often a much more complex, and usually, not very valuable approach is taken.

Third, what I call one of "Alpert's Laws": the less a procedure is indicated, the more likely will it be accompanied by complications." I have seen this many times. Then, of course, you always feel horrible afterwards because you shouldn't have done the procedure in the first place.

Fourth, listen between the lines. That is, sometimes, you meet with the patient, everything sounds fine, and then, just as they're about to go out the door, they say, "Oh, by the way, this is probably not important...." You know that the next thing you're going to hear is the most important thing you're going to hear and you bring the patient back in and go after it.

Fifth, deal with insufficient time provided to see patients. There have been some studies that report that the average physician-outpatient visit is 7 minutes. That's way too little time. I don't do that. I take whatever time it takes to be with a patient, even though I know I'm not getting paid for it.

Sixth, no individual has a monopoly on truth. Every time I round with the house staff I learn something. You can't keep up with everything in this gigantically expanding universe of medical knowledge. I learn particularly from residents who are going into non-cardiology specialties. I also learn from curb-stone consults with my colleagues in other specialties.

Seven, obtaining informed consent from the patient for a procedure can

ABSTRACT

The discussion focused primarily on: 1) Important facts for general internists; 2) cardiovascular facts for non-cardiologists; 3) misconceptions on bypass surgery and percutaneous coronary interventions; 4) what causes atherosclerosis; 5) cholesterol and atherosclerosis; 6) requisites for healthy living. *Med Roundtable Gen Med Ed.* 2012;1(2):145–151.

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help or hurt the situation. Depending on how it's presented, you can markedly increase the patient's anxiety, thereby increasing the likelihood of complications for the procedure. I learned that from Bernard Lown when I was a resident.

Eighth, physicians need to take care of themselves first. If you're telling the patient to stop smoking or lose weight or exercise regularly and you're doing none of them, it's highly unlikely that the patient is going to listen to what you're saying. They'll think you're a hypocrite.

Ninth, respect your fellow healthcare workers. These days, more and more of what we do is a healthcare team thing. The nurses and PharmDs come with us on rounds. There is constant interaction. Every time this happens, something comes out that's better for the patient. Although healthcare providers get so used to the hospital, particularly the intensive care units, lay people often find hospitals terrifying. We need to take that into account when talking to them.

Tenth, the enemy of good is perfect. Sometimes when pushing for a diagnostic or a therapeutic approach and things are going well, we press harder to make them perfect and end up with complications because we push too hard.

DR. ROBERTS: Joe, thank you. David, do you have a list?

DR. HILLIS: I'm going to change the focus somewhat to cardiovascular things that a non-cardiologist should know. The one thing that I deal with almost every day is the misconception on many physicians' parts about the indications for coronary bypass surgery or for percutaneous coronary interventions. What can these procedures do effectively and what can't they do? There is a widespread perception that these procedures prevent myocardial infarctions (MIs). They do not. They're a pretty good way of causing them, but they're not a very good way of preventing them. Lots of patients have these procedures performed, not for symptom relief or for prolongation of life. If I ask patients why they had the particular cardiovascular procedure, most answer "to prevent the big one." I deal with that every day, not only with non-cardiologists, who oftentimes espouse that, but with many cardiology colleagues. The data, however, don't support that.

> ***"Atherosclerosis is a systemic disease, not a regional disease. If one has plaques in the coronary arteries, they also have plaques in the peripheral arteries including the carotid arteries."***
>
> **William C. Roberts**

DR. ALPERT: Bill, I was recently on a roundtable exactly focused on this topic and it came to the same conclusion. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE)[1] and other trials have not supported the idea that we're going to save somebody's life by doing percutaneous coronary angioplasty.

DR. ROBERTS: Does coronary angioplasty plus stents prolong life?

DR. HILLIS:: It is not that these procedures are so poor but that medical therapy is so incredibly good these days. On medical therapy, people with coronary artery disease live a long time. Basically, you cannot make their prognosis better by doing a procedure on them.

DR. ROBERTS: I've got a list of "10 facts" every physician (cardiologist, non-cardiologist) should know. One, the cause of atherosclerosis is an elevated cholesterol level, specifically an elevated low-density lipoprotein (LDL) cholesterol level. Therefore, I don't consider an elevated cholesterol level as a risk factor. I consider it the cause of atherosclerosis. That does not mean, of course, that systemic hypertension, cigarette smoking, diabetes mellitus, obesity, inactivity, stress, inflammation, aging, or genes are not important, but none of them by themselves cause atherosclerotic plaques. To develop atherosclerotic plaques the LDL-cholesterol level in serum or plasma must be elevated.

Two, knowing the arguments supporting the view that cholesterol causes atherosclerosis is helpful when talking to patients. If one gives large amounts of cholesterol or saturated fat to herbivores, atherosclerotic plaques similar to those occurring in human beings are produced. The resulting plaques do not occur in 1 of 10 animals; they occur in every one of them. Indeed, atherosclerosis is the second easiest disease to produce experimentally (The first is an endocrine deficiency by excising an endocrine gland.) Atherosclerosis occurs only in herbivores. Cholesterol is seen in the plaques. The epidemiologic evidence is strong.

The best study in my view is the Seven Countries Studyby Ancel Keys and his colleagues.[2] They compared a large group of people with elevated cholesterol levels with those with much lower cholesterol levels and showed that the frequency of atherosclerotic events and the frequency of dying from those events were much greater in the group with elevated levels than in those with lower levels. Subsequently, it has been shown that the quantity (burden) of atherosclerotic plaques is much greater in those with higher cholesterol levels versus those with lower levels. And finally, lipid-lowering therapy by lowering the LDL-cholesterol level decreases the frequency of atherosclerotic events.

Three, atherosclerosis is a systemic disease, not a regional disease. If one has plaques in the coronary arteries, they are also in the peripheral arteries including the carotid arteries. The involvement in any region is diffuse, that is, there is plaque in every 5-mm segment of those arteries.

Four, knowing the time it takes to heal an acute MI makes management easier. My father (1978-1941) was in bed for a year after he had an acute MI. It was shown in 1939, two years after he had his first one, that it takes 6 to 8 weeks to heal an acute MI.

Five, most (90%) patients with heart failure have had preexisting systemic hypertension. Thus, preventing high blood pressure is a major preventive measure of heart failure.[3]

Six, angiography underestimates the quantity of atherosclerotic plaque in any arterial system because the process is diffuse and an area of maximal narrowing is simply compared with an area less narrowed, and not normal. The angiogram, of course, is a luminogram.

DR. HILLIS:: I would add to that, Bill. There is little appreciation, especially for physicians who don't do angiography, of how crude and rough the estimates are of the severity of the narrowing. The inexperienced physician hears that the patient has a 70% stenosis and thinks that number came from something remotely scientific or accurate, and nothing could be further from the truth. It's a shoot-from-the-hip estimate made from about 5 feet away in about 2 milliseconds. That's especially true for stenoses that are of intermediate severity. That is, there is a huge amount of variability in what observers call those stenoses.

DR. ALPERT: What supports what you both said is that when you do these Doppler wire studies, you discover that the atherosclerosis is diffuse and all you're seeing with angiography are the high-grade lesions, perhaps, one area that's particularly bad, but, usually, the whole artery is involved.

DR. ROBERTS: Some studies that I've been involved with show that the quantity of plaque in all 3 major coronary arteries in people with atherosclerotic events is very similar. The same cholesterol level flows down all of the arteries. Why the internal mammary is different, I don't know.

DR. HILLIS: So do you think the circumflex is different?

DR. ROBERTS: No.

DR. HILLIS: It's not?

DR. ROBERTS: Correct.

DR. HILLIS: The mammary, for some reason, seems to be protected, and I've never understood why.

DR. ROBERTS: Me either. We all need more mammary arteries.

STUDIES DISCUSSED:

COURAGE
Framingham Heart Study
Seven Countries Study

COMPOUND DISCUSSED:

orlistat

DR. ALPERT: What is a "normal" cholesterol level? Early in my career it was <300 mg/dL, then <250 mg/dL, and then, <200. The place to look for the normal, of course, is not in the United States or even Asia, but in the hunter-gatherer societies where people were well nourished and led a Neolithic-time lifestyle, not eating a great deal of meat or fowl, but lots of vegetables, fruits, and berries. Their total cholesterol levels were <100 mg/dL and their LDL cholesterol level, about 30 mg/dL. I often ask house officers, "What do you consider normal cholesterol?" Essentially, everyone in the United States has an elevated cholesterol level and every single person in this country has some atherosclerosis!

DR. ROBERTS: I agree. The numbers you quote are what we have at birth.

DR. ALPERT: One hundred years ago, Native Americans didn't have atherosclerotic disease. There weren't heart attacks or sudden death from heart disease. People died from trauma or infectious diseases. These days, particularly here in the southwest, there is an epidemic of coronary disease, renal failure, and diabetes mellitus in Native Americans. It is due to a change in diet.[4-6]

DR. ROBERTS: Let me give a couple more of my 10. The dominant component of atherosclerotic plaques, at least in the coronary arteries, is fibrous tissue. It's about 70% of the plaque. It's not lipid or calcium or mucoid material—it's fibrous tissue!

The common school of thought is that rupture of a plaque is the cause of acute MI, sudden cardiac death, and the change from stable to unstable angina pectoris, and if rupture of the plaque could be prevented the events would be prevented. In my experience, ruptured plaque occurs only in acute MI. There is no evidence, in my view, that the first episode of angina pectoris or the switch from stable to unstable angina is due to rupture of a plaque. Furthermore, there is no evidence that sudden death from a cardiac standpoint is due to rupture of a plaque. I'm against that school of thought. I consider the *quantity* of plaque to be the major problem, not whether a plaque is vulnerable or not.

DR. HILLIS: Do you think that patients are constantly rupturing minor plaques?

DR. ROBERTS: Probably so.

DR. HILLIS:: And remodeling them at that point? In other words, they are not having an acute event?

DR. ROBERTS: Correct.

DR. ALPERT: About 25 years ago, Henri Cuenoud called me to the autopsy room (at the University of Massachusetts) to see a heart. The patient had died from a non-cardiac condition. The coronary arteries had been opened longitudinally. There must have been 50 different ulcerated plaques, some with little clots, some without, all throughout the coronary tree. Yes, we are rupturing plaques all the time, and the new plaques are integrated into the sum total of the fibrous tissue that eventually blocks the artery.

DR. ROBERTS: Yes, they heal.

DR. HILLIS: Exactly, and you never know it.

DR. ALPERT: This hunt for the vulnerable plaque is a hunt for the Holy Grail.

DR. ROBERTS: I agree with that view. I've got a couple more. It's important for all of us to realize that humans, basically, are herbivores, not carnivores. Although we have some sharp teeth in the front of our mouths, most of our teeth are flat (for grinding vegetables and fruits); carnivores have very sharp teeth. Our intestinal tract is quite long; about 12 times body length, whereas the carnivores' intestines are about 3 times body length. They get rid of it quickly. The carnivores cool their bodies by panting. They have no capacity to sweat. We can pant, too, but we sweat. When we drink fluids, we do it by sipping; the carnivores do it by lapping. The carnivores make their own vitamin C; we obtain it from our diets. The carnivores have claws as appendages; we have hands or hooves. Although many of us eat flesh, our bodies were not made for that type of food.

> ***"When you do these Doppler wire studies in arteries, you discover that the atherosclerosis is diffuse and all you're seeing with angiography are the high-grade lesions, perhaps, one area that's particularly bad, but, usually, the whole artery is involved."***
>
> **Joseph S. Alpert**

DR. ALPERT: Right.

DR. ROBERTS: Lastly, I have a few requisites for healthy living. I agree with Joe that an atherosclerotic preventive is an LDL cholesterol of <50 mg/dL. Additionally our blood pressure needs to be <120/75 mm Hg, our body mass index <25 kg/m2, and we need an empty colon. (I like orlistat, but only once a day [120 mg], not 3 times a day as recommended by its initial producer.) Along with not smoking, limited alcohol intake, vegetarian and fruit diet, we also need a bit of luck.

DR. ALPERT: Bill, I would add one to that list: "You only need to exercise on the days that you eat." E.O. Wilson, probably the greatest living evolutionary biologist, wrote a book called The Social Conquest of the Earth.[7] He wrote about how everybody thinks natural selection is a simple thing. If you're bigger and stronger; you're going to pass those genes on. He writes about how cooperation in human groups is something that enhances the passing of the DNA to the next generation. He writes a lot about our primate relatives, who ate mostly fruits and vegetables, and a small amount of meat. He also wrote about the sudden increase in brain size in the human evolutionary line that correlated with when people started hunting and eating a lot of meat. The whole thing about eating flesh is a complex issue. These people all died in their 30s and 40s, so atherosclerosis was probably not a major problem at that time.

DR. ROBERTS: The animal muscle they ate were in animals running in the wild. These animals were not put in feed lots their last 6 months of life or so and fattened up from 700 to 1100 pounds. The wild animals had very little fat in their muscles, but the amount of cholesterol in them was the same as today.

DR. ALPERT: A very good point.

DR. ROBERTS: I have one last fact all should know. Morphologic studies at autopsy or in explanted hearts after transplantation frequently discover or unearth an important finding not observed clinically. So despite these wonderful clinical "instruments of precision," there are a lot of "clinical misses" discovered only by morphologic examination.

DR. ALPERT: Yes, I'm sure that's true. We're better at diagnosis now however, than ever before. The imaging modalities have made things more accurate, but there is still a lot of room for looking at the tissues.

> *"The inexperienced physician hears that the patient has a 70% stenosis and thinks that that number came from something remotely scientific or accurate, and nothing could be further from the truth."*
>
> **L. David Hillis**

DR. HILLIS: Yes, absolutely. I will mention a couple of specific ones, ones that I deal with on a daily basis in our intensive care unit. Number one is how dyssynergic heart muscle can be after it has recently been ischemic. After an episode of myocardial ischemia, the muscle that becomes hypokinetic or akinetic or even dyskinetic, stays that way hours to days. It is hard to convince our house staff not to perform echocardiography in people 24 to 48 hours after an acute MI, when there is plenty of stunned muscle in that same region as the infarcted muscle. Some of the non-moving muscle will move at a later time–a week or 2. Too many management decisions are based on echocardiograms done at a time when there is plenty of dysfunctional but not dead muscle that in another week or two will look much better.

Physicians have little understanding of pulmonary hypertension in patients with elevated left-sided filling pressures. Patients with chronic heart failure with an elevated left atrial pressure develop an elevated pulmonary artery pressure. If you make the left atrial pressure return to normal, the pulmonary hypertension will melt away. Too many physicians get bent out of shape about seeking pulmonary hypertension. It does not make sense to give nitrous oxide to see what happens to the pulmonary hypertension in this circumstance. James Dalen in 1967 in the *New England Journal of Medicine* in five patients with mitral stenosis and pulmonary artery systolic pressures of 130, 140, and 150 mm Hg demonstrated that when Dwight Harken relieved their mitral stenosis, their pulmonary hypertension melted away.[8]

DR. ROBERTS: We also saw a lot of that at the National Institutes of Health (NIH).

DR. HILLIS: Yes, and Braunwald and colleagues published an article at about the same time of 31 patients with either mitral stenosis or mitral regurgitation in whom they showed exactly the same thing. When the mitral obstruction was relieved, the pulmonary hypertension disappeared.[9]

DR. ROBERTS: The opposite of that is the patient who has a hugely dilated left atrium and severe mitral regurgitation and the pressure in the left atrium is entirely normal, and then the pulmonary arterial systolic pressure is also normal.

DR. HILLIS: Yes, right.

DR. ALPERT: Don't you think, David, that one of the things that is fueling that view (and fear) is the fact that we now have a number of products that can, more or less, selectively lower the pressure in the pulmonary circuit?

DR. HILLIS: Yes.

DR. ALPERT: We now can offer those few patients with primary pulmonary hypertension a real chance of improved function and probably also longer survival.

DR. HILLIS: I agree.

DR. ALPERT: But, you can't translate what happens to that little group of patients with primary pulmonary hypertension to the huge number of people with secondary pulmonary hypertension due to increased left-sided cardiac filling pressures.

DR. HILLIS: The pulmonary arterioles are morphologically very different in these three settings. I call one simply "passive back pressure"; that is, pulmonary hypertension is due to an elevated left atrial pressure for whatever reason. Number two is primary pulmonary hypertension, and number three—probably the most extreme example at the other end—is the Eisenmenger's physiology, with which the morphology of the arterioles is very different and that doesn't go away.

DR. ROBERTS: Pulmonary hypertension secondary to left-sided problems is entirely reversible. There are no plexiform lesions in the lungs, and no matter how high that pulmonary artery pressure gets in patients with

pulmonary hypertension, secondary to left-sided problems, plexiform lesions do not occur. In contrast, in patients with primary pulmonary hypertension or the Eisenmenger syndrome, plexiform lesions are present and the pulmonary hypertension is irreversible.

DR. HILLIS: Dr. Dexter called this the "second stenosis." When patients with mitral stenosis developed pulmonary hypertension, it was as if they had developed a second site of stenosis in their pulmonary arterioles.

DR. ALPERT: Another topic to discuss might be the whole genomic revolution. About a year ago, *Science* had a series of articles called "Has the Genomic Revolution Failed?" When in medical school, it was sickle cell anemia which received the genetic attention. One gene is abnormal, one amino acid is abnormal, and there is the disease. The conclusion was that all diseases were going to be like that.

Subsequently, we have learned that it is about 1 trillion times more complicated. About 60% of the DNA does not make proteins. It's controlling factors that turn on or turn off various protein synthetic activities. Now we know that environment makes a huge influence (epigenetic). It helps to turn on or turn off some of the protein syntheses. What I learned in medical school is like going to the piano and hitting middle C repeatedly. That's sickle cell anemia. Today, it's like 5 orchestras in one room playing 5 different Bach cantatas at the same time.

DR. HILLIS: Another truism has nothing to do with genomics. Of the thousands of medical articles published each year, about half of them will prove to be wrong. The problem right now is we don't know which half.

DR. ALPERT: I agree.

DR. ROBERTS: About genes. I've asked a number of audiences what's the most important "atherosclerotic risk factor" and the answer has most often been "family history." But, as shown by Brown and Goldstein, the atherosclerotic gene occurs in only 1 in 500 of us.[10]

DR. HILLIS: Exactly.

DR. ROBERTS: Atherosclerotic events are common in families because, in my view, family members eat the same food. One doesn't have a 20-ounce steak eater sitting next to a pure vegetarian-fruit eater in many families. So families eat the same food and they get the same diseases.

One other thing: in my view, the statin drug is the greatest cardiovascular drug ever created and we shouldn't be afraid of it.

DR. HILLIS: I agree completely. Although myalgias are extremely common, most of the time they are manageable. Oftentimes, I make the snide remark that statins ought to be in the drinking water.

DR. ALPERT: I say the same thing.

DR. ROBERTS: In the 5-year controlled statin trials, the myalgia frequency was about the same in the placebo group as it was in the drug treatment group.

Clinical Implications

- **Coronary bypass surgery or percutaneous coronary interventions cannot prevent myocardial infarctions.**
- **An elevated cholesterol level causes atherosclerosis. Specifically an elevated low-density lipoprotein (LDL) cholesterol level.**
- **Knowing the arguments supporting the view that cholesterol causes atherosclerosis is helpful when talking to patients.**
- **Atherosclerosis is a systemic disease; therefore if a patient has plaques in the coronary arteries, they may also have plaques in the peripheral arteries including the carotid arteries.**
- **Preventing high blood pressure is a major preventative measure for heart failure.**
- **Angiography underestimates the quantity of atherosclerotic plaque in any arterial system because the process is diffuse and an area of maximal narrowing is simply compared with an area less narrowed, and not normal.**
- **The dominant component of atherosclerotic plaques, at least in the coronary arteries, is fibrous tissue.**
- **Morphologic studies at autopsy or in explanted hearts after transplantation frequently discover or unearth an important finding not observed clinically.**
- **Physicians have little understanding of pulmonary hypertension in patients with elevated left-sided filling pressures.**

DR. HILLIS: You're absolutely right, yes.

DR. ALPERT: In the large MI intervention trials, not including ST-elevation MI, the greatest reduction in events over the next 5 years was with statins—better than beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and aspirin. Statins are the major players.

DR. ROBERTS: It seems foolish to me to buy life insurance and not take a statin drug. That's the best life insurance we have.

DR. HILLIS: Absolutely.

DR. ROBERTS: Would you Joe or David like to add any final comments?

DR. ALPERT: I'm a fan of collecting aphorisms—the little pithy sayings. The one that I love the most is by Winston Churchill. He said, "Americans will always pick the right solution after they've tried all the wrong ones," and he also said that "Democracy is the worst form of government except all the others that have been tried." Although these particular ones do not apply to medicine, others do, such as "only exercise on the days that you eat." Another, "the older you get, the harder you have to work." I've certainly discovered that. Another, from Judah Folkman, who discovered the angiogenesis factor, was on a little sign outside his operating room: "The only substitute for brilliance is experience." The older I've gotten, the more I realize its truth. It's been written that 10,000 hours of education or practice are needed to be an expert. Experience is critical.

DR. ROBERTS: David, do you have final comments?

DR. HILLIS: I'll just add one more aphorism used by Denton Cooley: "The harder I work, the luckier I get." (Gary Player, the golfer, used that one also.)

DR. ALPERT: Michael DeBakey was asked after doing 100 abdominal aortic aneurysm resections without a death: "How could you do a hundred without a death?" He said, "Well, from just good clinical judgment." And the reporter then asked: "How did you get good clinical judgment?" DeBakey replied, "From having bad clinical judgment." The message of course is that we learn more from our mistakes than from our successes.

DR. ROBERTS: Thank you Joe and David.

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