What You Don't Know about Coronary Artery Disease May be Killing You

Statistics: The Big Picture

Let's BEGIN by taking a closer look at current situations our world is facing…

According to the U.S. Bureau of the Census, the resident population of the United States, projected to 04/02/11 is 311,091,090.

According to *Circulation*, a Journal of the American Heart Association 2011 Update - Coronary heart disease mortality in 2007 was 406,351. Each year, an estimated 785, 000 Americans will have a new coronary attack, and 470, 000 will have a recurrent attack. It is estimated that an additional 195, 000 silent first myocardial infarctions occur each year. Approximately every 25 seconds, an American will have a coronary event, and approximately every minute, someone will die of one.

USA Health Statistics

- 1 in 2 will die from heart disease.
- 1 in 2 will develop some form of cancer.
- 1 in 3 will develop diabetes.
- 1 in 3 women are clinically depressed.
- 1 in 6 couples are infertile.
- 1 in 6 kids have a neurological condition.
- 1 in 8 have an auto-immune disease
- 1 in 8 women have a thyroid problem
- These are all "CHRONIC DISEASES"

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Leading Causes of Death (Data are for the U.S. 2007)

- Heart disease: 616,067
- Cancer: 562,875
- Stroke (cerebrovascular diseases): 135,952
- Chronic lower respiratory diseases: 127,924
- Accidents (unintentional injuries): 123,706
- Alzheimer's disease: 74,632
- Diabetes: 71,382
- Influenza and Pneumonia: 52,717
- Nephritis, nephrotic syndrome, and nephrosis: 46,448
- Septicemia: 34,828
- Source: Deaths: Final Data for 2007, table B

The Ohio Study

"The Ohio State Study" ~ Source: Dr. Joe McCord, PhD, Scientific Advisory Board, LifeVantage.

Caveat: Consumers and distributors of health related products should have some degree of understanding of the science behind the product they are either consuming or distributing.

This study has a lot to do about heart disease and heart surgery. Most of us are fairly familiar with heart surgery because we have had friends or family members who have had heart surgery.

Most people are familiar with the term coronary artery bypass surgery (CABS), or coronary artery bypass graft, or carotid endarterectomy, angioplasty with stent insertion to keep the coronary arteries open and the blood flowing.

All of this has become a big part of all of our lives in the last two or three decades. And this study relates very strongly to what is going on in the realm of cardiovascular disease.

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Original Contribution

Protandim attenuates intimal hyperplasia in human saphenous veins cultured ex vivo via a catalase-dependent pathway

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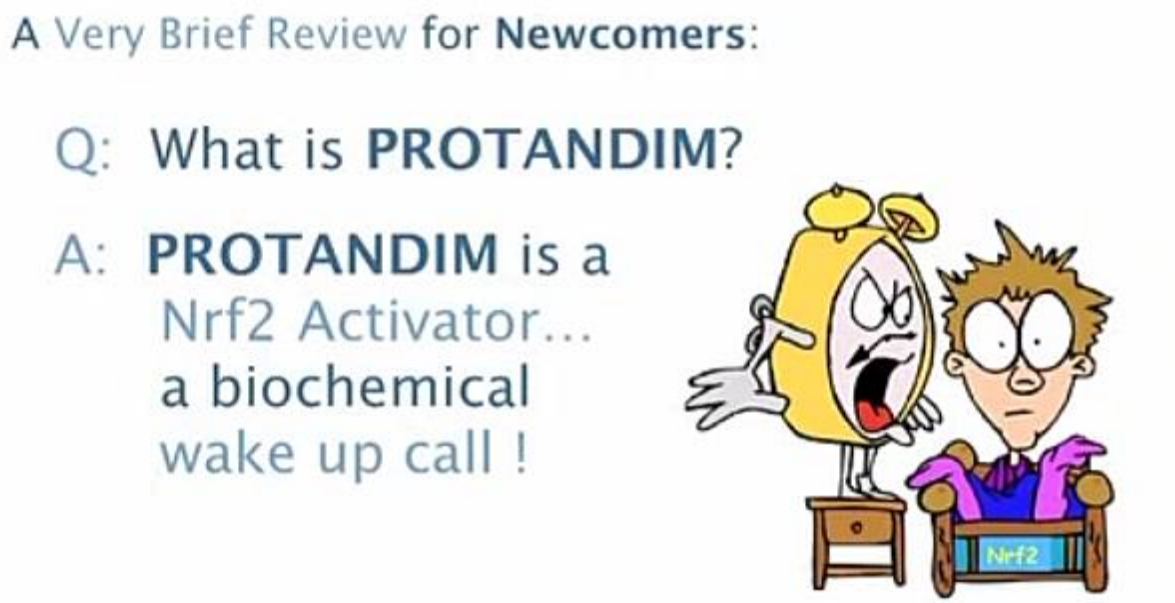
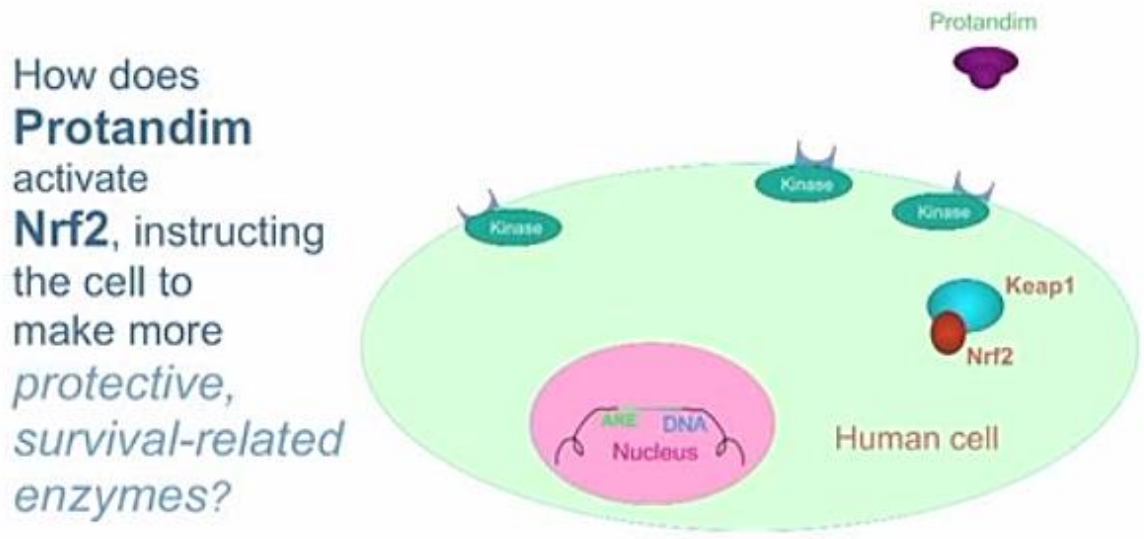
The title reads: "Protandim attenuates intimal hyperplasia in human saphenous veins cultured ex vivo via a Catalase-dependent pathway."

If you understand that, you can go to the back of the room and get your PhD degree right now. By the end of this treatise, you will have some grasp of what this study is about.



Biochemically, Protandim is a Nft2 Activator. A Nrf2 activator is something that delivers a biochemical wake up call to every cell in your body.



The big green oval cell represents one of the several trillion cells in your body.

In the upper right corner you see the little purple mushroom looking object. That represents one of the five elements in Protandim. When you take a Protandim pill, every cell in your body will be bathed in those molecules that make up Protandim

The first thing that Protandim does is it binds to a receptor on a cell.

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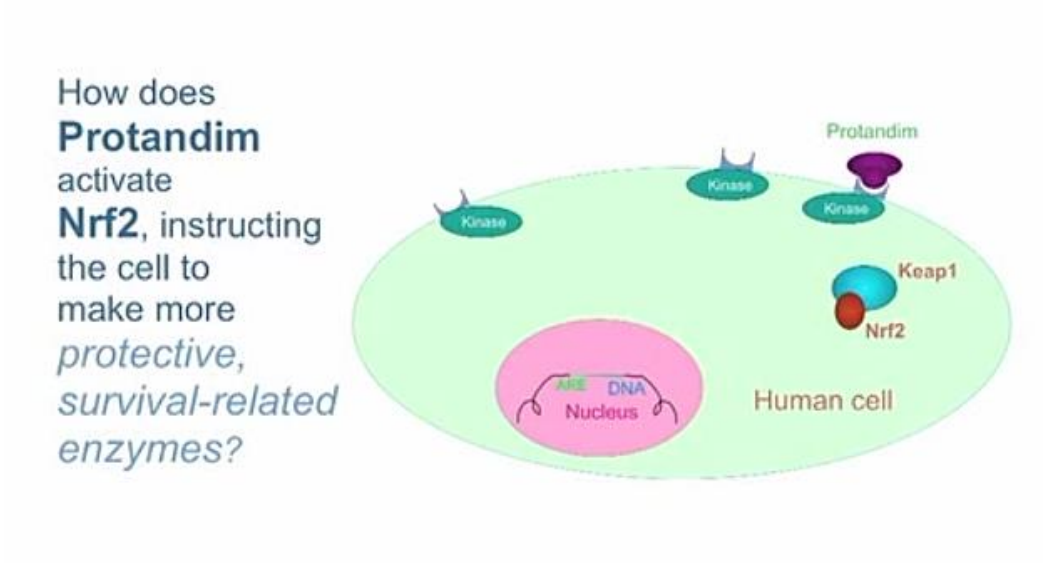
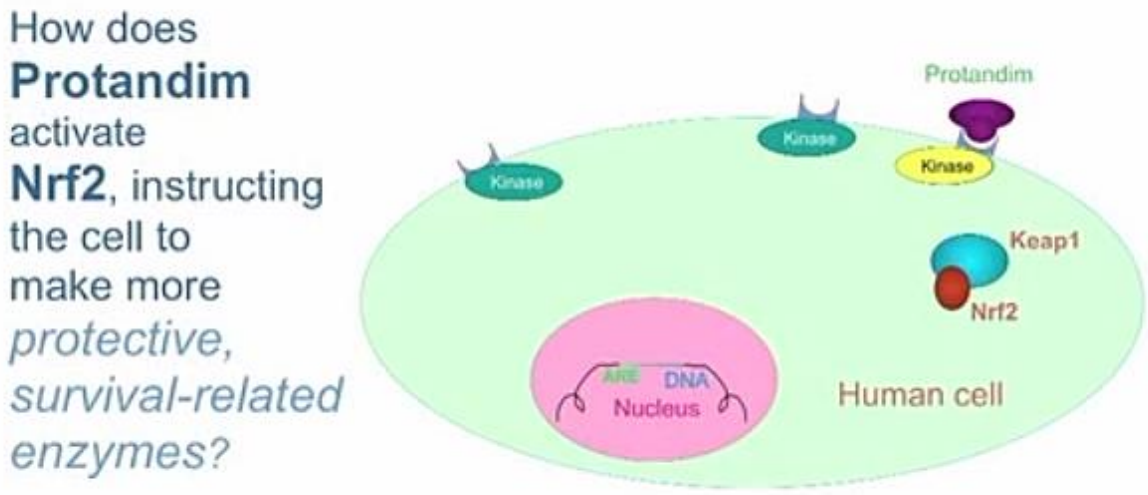


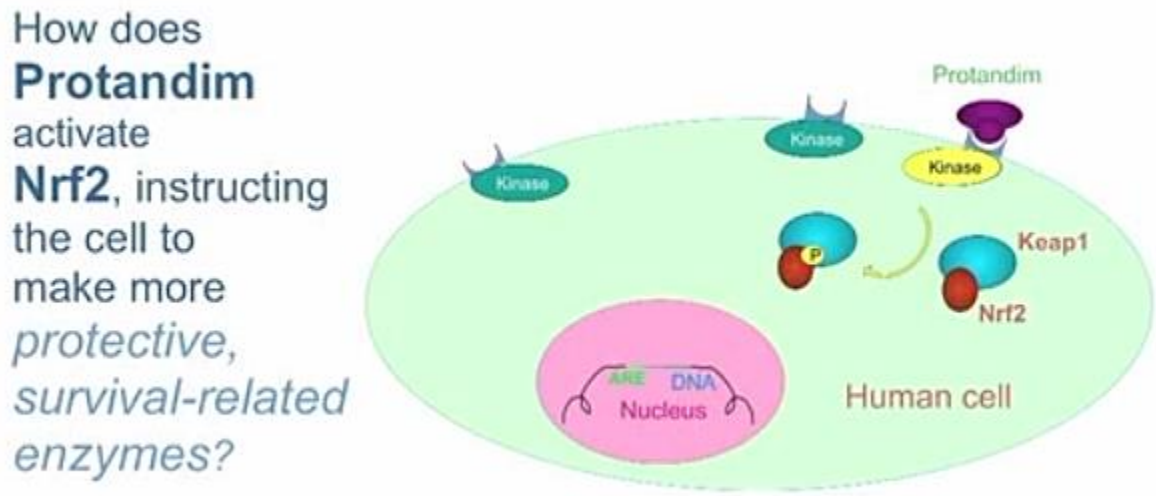
If your cell is your house, what Protandim just did is step on your front porch and it rang your doorbell. That is how the cell interprets that. When that happens at your home, things happen inside your house. You may get up off the couch and walk to the door to see who is there. When Protandim rings the doorbell of the cell, something happens inside. That oval labeled Kinase is a protein that catalyzes a particular metabolic reaction.



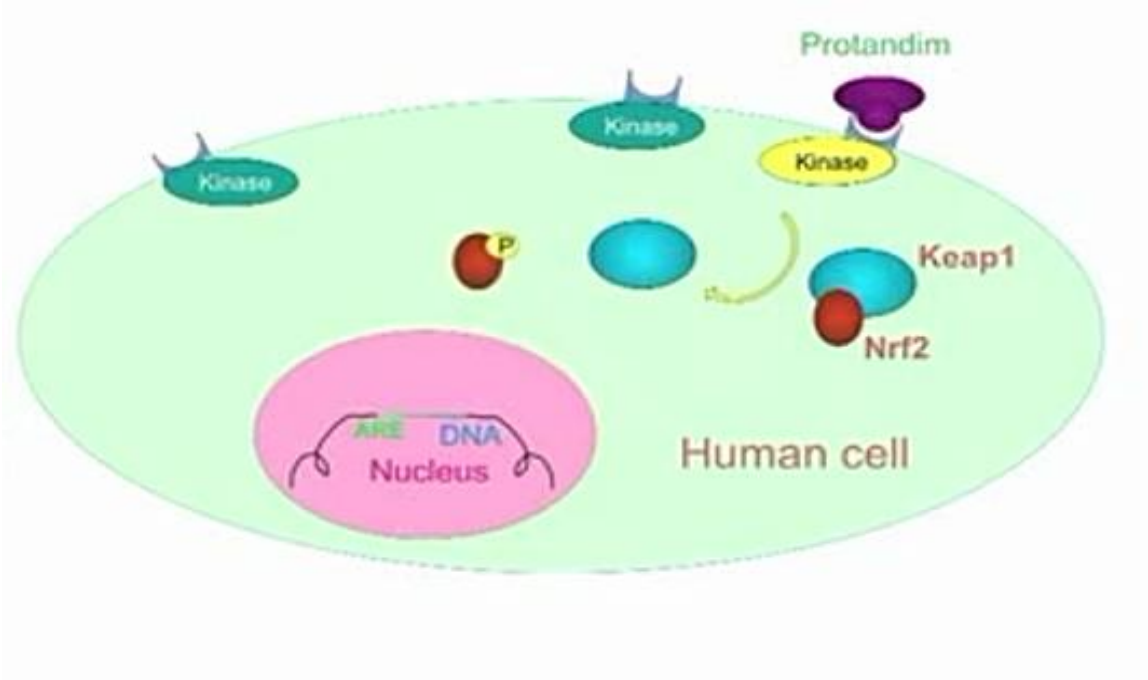
It is activated just like the chimes inside your house are activated when Protandim or someone steps on your front porch and rings the doorbell. Something happens inside. That particular enzyme, the one that is yellow, modifies a protein inside the cell. The protein that is modified is the red oval labeled Nrf2.

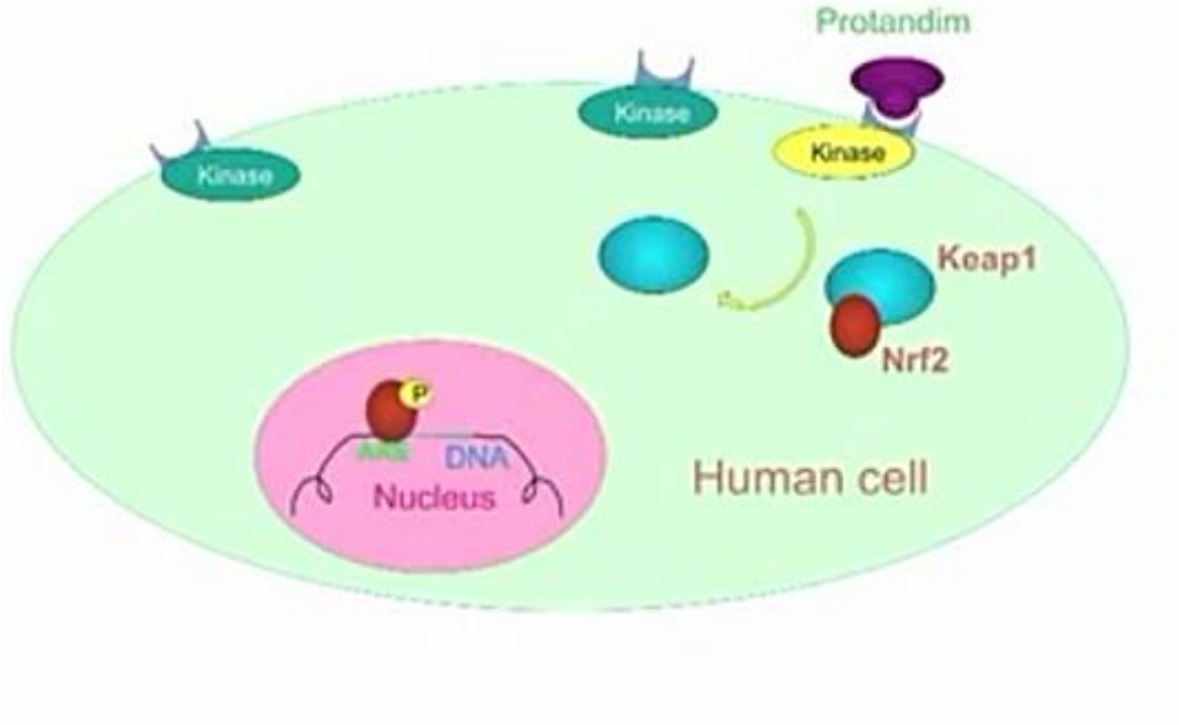
Nrf2 is what biochemists call a "second messenger". To go back to the doorbell analogy, maybe your four year old goes to the door, opens the door and turns around and runs to the kitchen and says 'mommy, Mrs. Smith is at the front door'.

That is the second message. So Mrs. Smith rings the doorbell. Something happens inside your house. Protandim does exactly the same thing. If you look at this red protein, it now has a little yellow circle with a P on it. That P is a phosphate group.



So, the red protein has been modified chemically. It has been held in the cytosol, the main space of this cell, by a blue protein called Keap 1 that is preventing it, if you will, from running into the kitchen or the family room. Once it has been modified, as a result of Protandim ringing the doorbell, that modified Nrf2, that second messenger, is now free. It leaves the blue protein that cytosol has been holding it in and it finds its way to the DNA library of the cell.


Protandim
Kinase
Kinase
Kinase
P
Keap1
Nrf2
ARE
DNA
Nucleus
Human cell


Protandim
Kinase
Kinase
Kinase
Keap1
Nrf2
P
ARE
DNA
Nucleus
Human cell

The DNA is really the central blueprint that controls everything you are, everything your body can produce. And Nrf2, chemically modified, released and running to the room where the DNA is stored (like your 4 year old running into the kitchen) delivers a message to the blue print that really runs this cellular household.

The DNA is comprised of 25,000 genes and they are blue prints that make every protein in your body, every enzyme in your body. This second messenger, Nrf2, has been called the "master regulator" of survival genes. Survival genes are stress response genes. They enable the cells to get through tough times. Some of them are antioxidant enzymes. When Protandim started, what we thought it would do is up-regulate (make more) of two specific enzymes, Superoxide Dismutase (SOD) and catalase.

Protandim upregulates at least 400, maybe closer to 6 or 800 enzymes, not just the two we were originally interested in. Among those enzymes are survival genes of all kinds, not just helping you to survive oxidative stress but helping you to survive traumatic stress. Cells get injured – they respond. Organs get injured – blood vessels get injured.

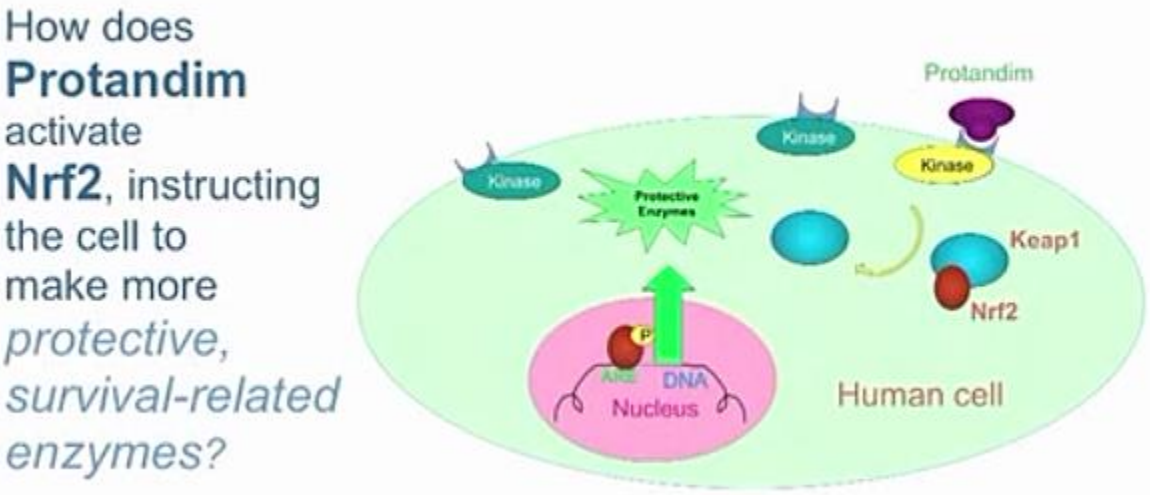
What Happens When Blood Vessels are Injured?

The subject of this treatise is about what happens when blood vessels are injured. And they can be injured by well intentioned surgeons and physicians. And they respond in ways that can create problems for us. Problems not related to the original disease but problems related to what happens next.

When this messenger gets to the DNA it finds every gene in the nucleus that is regulated by a certain kind of switch. Here it is labeled ARE (Antioxidant Response Elements). That's a switch; every gene has a switch, just like every light fixture in your house has a switch. And the genes are expressed; their products are produced as that switch is turned up or turned down. It acts like a dimmer switch: as you turn it up you get more production, as you turn it down you get less production from that particular blue print.

So, Protandim ringing the doorbell results in a re-shuffling of those 25,000 blue prints in the nucleus of the cell. Hundreds of new gene products are produced or more of them are produced. For another couple hundred, they are turned down.

Some of those are pro-inflammatory genes: they promote the inflammatory process. Some are pro-fibrotic genes: they cause scar tissue to form. So, it's really normalization in many cases, a readjustment of all the instructions being sent to that cell. That is what Protandim does. That is how it works. The result is the up-regulation or the increased production of all these protective enzymes called survival genes.



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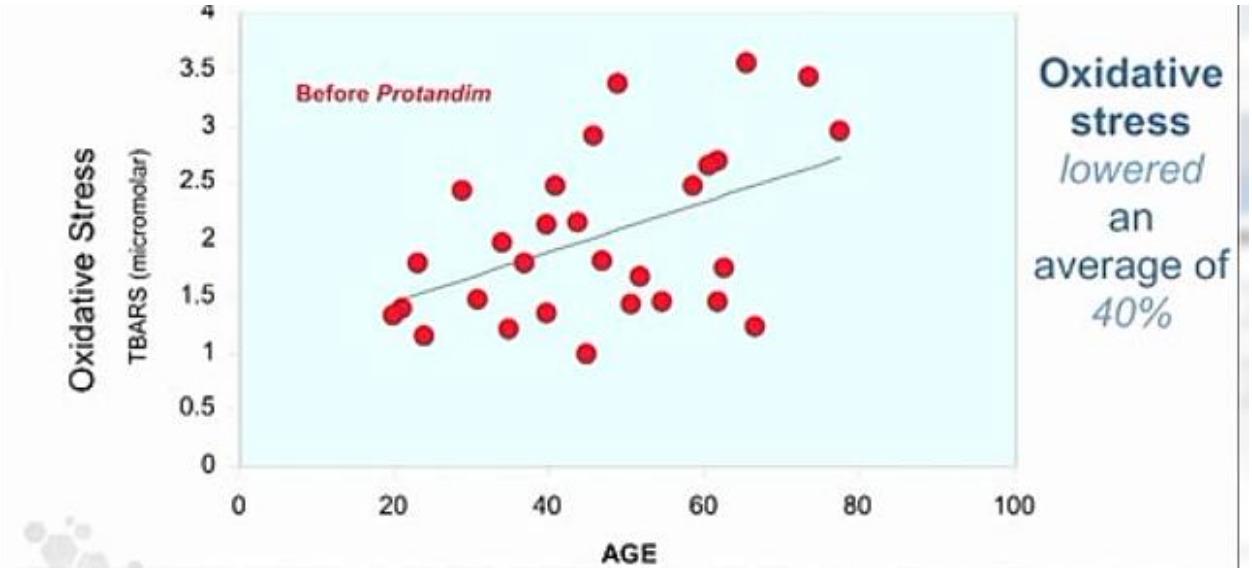

This is a figure from the very first paper published on Protandim. I'm coming back to this because it also relates to what I am going to tell you today about heart disease. Here we are looking at a marker of oxidative stress. One of the most sensitive kinds of molecules in your body to oxidation is polyunsaturated fatty acids: those are the things that make butter. It's a fat. It makes the membranes that hold your cells together. And if you leave a stick of butter on the table for a few days, it becomes rancid. It is interacting with oxygen. It's oxidized by oxygen. And the same thing happens to the polyunsaturated fatty acids throughout your body when faced with oxidants, free radicals.

Here we are measuring that marker of oxidative stress in the blood of healthy people ranging in age from 20 to 78 years old. And they are scattered all around that line. The line is a mathematical linear regression line of the average thing that happens there. And what you see is that it goes higher and higher as you go from age 20 to age 80. And some individuals in the middle ages, in particular, are very different from others. Some of us sit on a couch and eat potato chips and watch TV. Others are training for marathons and it shows in your levels of oxidative stress. Some of us take good care of our bodies and some of us don't; that's why they are scattered.

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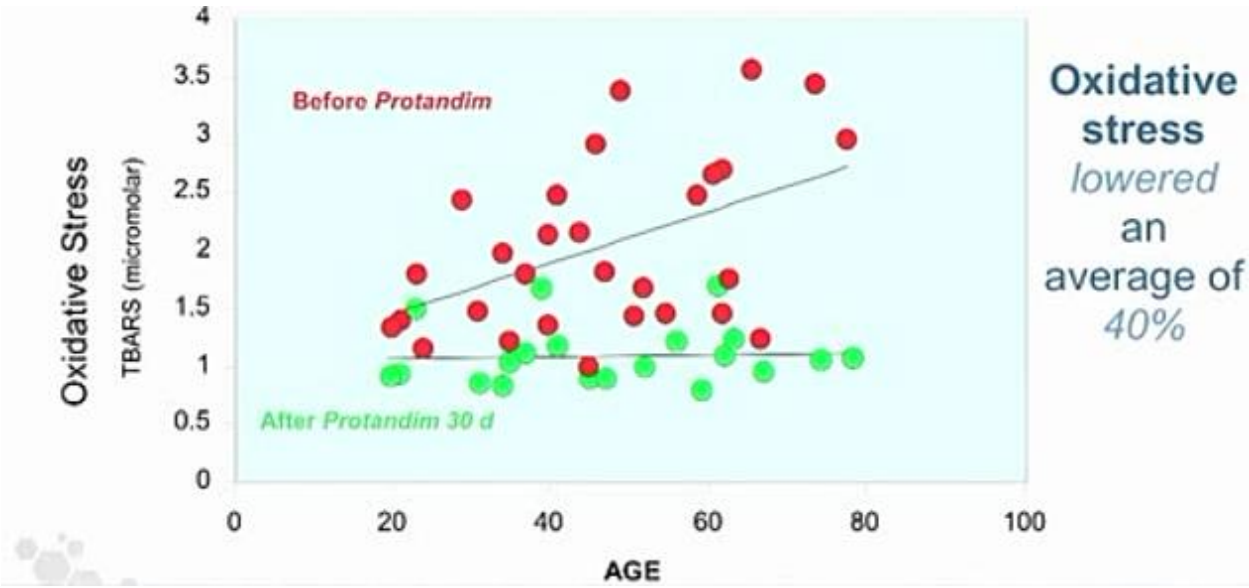
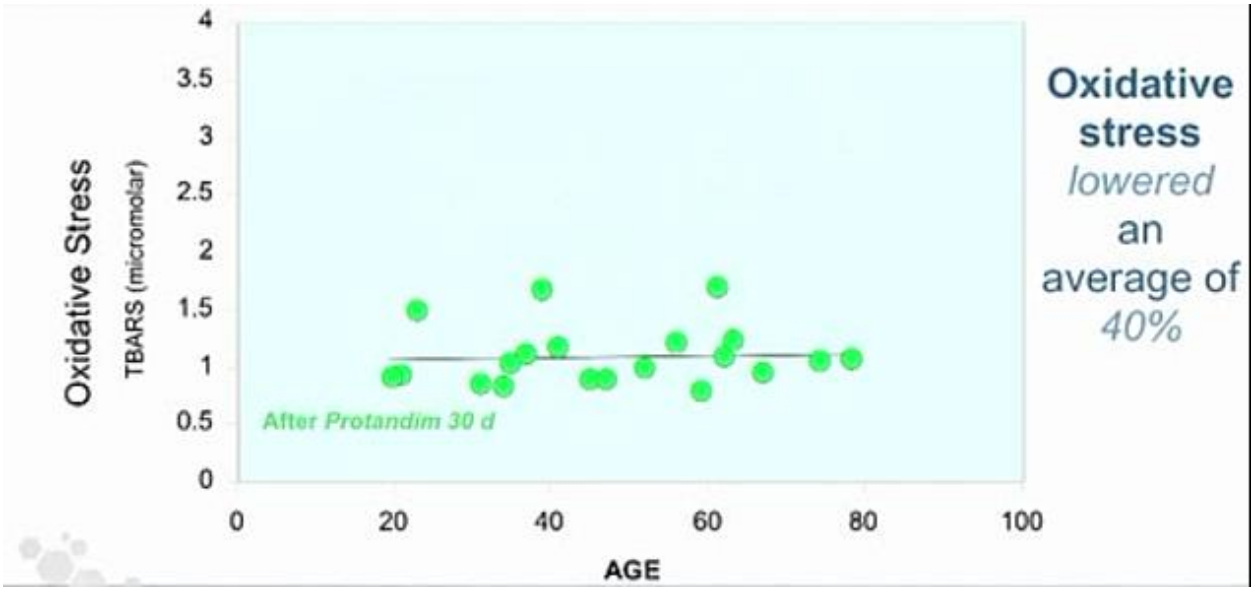
These people all took Protandim for 30 days and what happened is the levels of oxidative stress went from the red dots to the green dots.



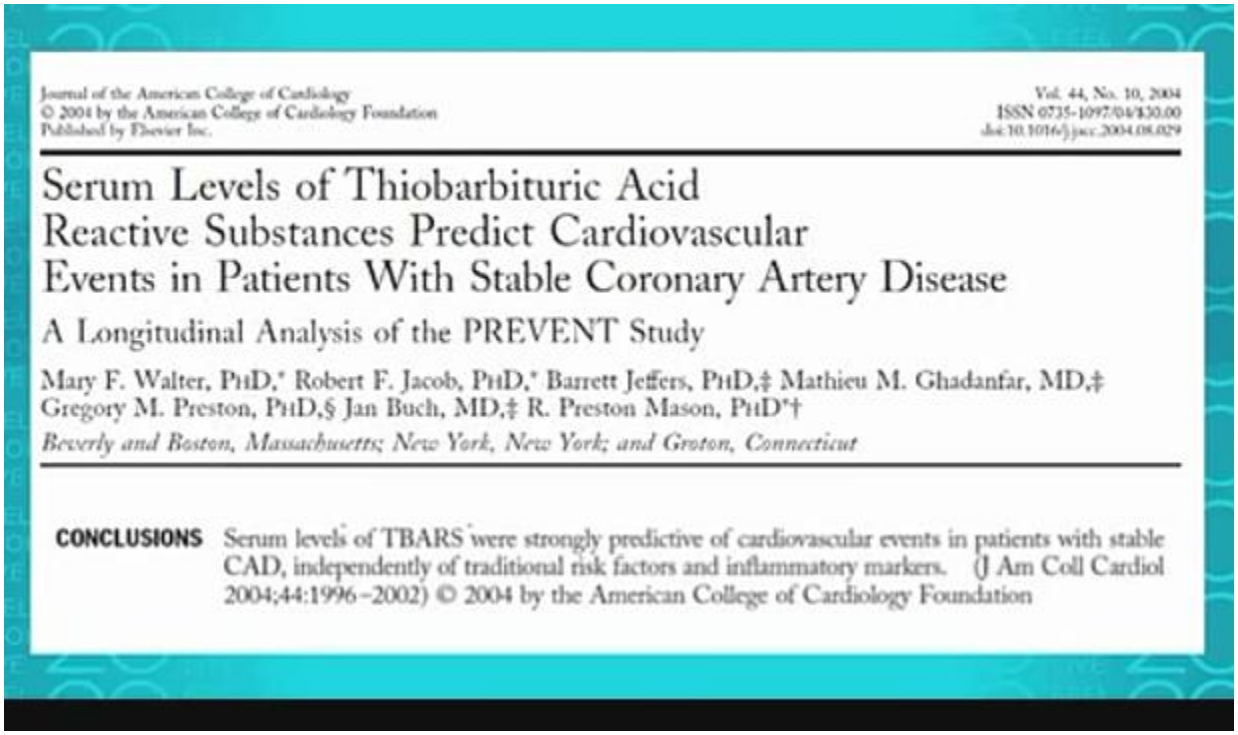
And if you look at just the green dots, you now can't really tell the 80 year olds from the 20 year olds. Everybody fell to that same low level of oxidative stress and that is what we have been saying now for 6 years.



And in this study, oxidative stress was lowered an average of 40%. If you were 78 years old, it went down about 70%. If you were 20 years old, it only went down 20% because you were starting at a better place.

What Was It That Was Actually Measured?

What was measured here is called TBARS: that's an acronym for Thiobarbituric Acid Reactive Substances. These are the chunks of oxidized polyunsaturated acids.



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Serum Levels of Thiobarbituric Acid Reactive Substances Predict Cardiovascular Events in Patients With Stable Coronary Artery Disease

A Longitudinal Analysis of the PREVENT Study

Mary F. Walter, PhD,* Robert F. Jacob, PhD,* Barrett Jeffers, PhD,† Mathieu M. Ghadanfar, MD,† Gregory M. Preston, PhD,§ Jan Buch, MD,† R. Preston Mason, PhD*†

Beverly and Boston, Massachusetts; New York, New York; and Groton, Connecticut

CONCLUSIONS Serum levels of TBARS were strongly predictive of cardiovascular events in patients with stable CAD, independently of traditional risk factors and inflammatory markers. (J Am Coll Cardiol 2004;44:1996–2002) © 2004 by the American College of Cardiology Foundation

So, is that relevant? Does TBARS mean anything? This paper was published in 2004 and it says serum levels, blood levels of TBARS predict cardiovascular events in patients with stable coronary artery disease.

The CONCLUSIONS found that it was an independent marker and actually a better predictor of a cardiovascular event. That is not an event you want to attend. A cardiovascular event may be an attack of angina (chest pain) upon exertion; maybe a myocardial infarct that takes you to your knees that may be fatal.

So there are a number of kinds of cardiovascular events. The important thing is: the higher the TBARS, the more likely a cardiovascular event may occur.

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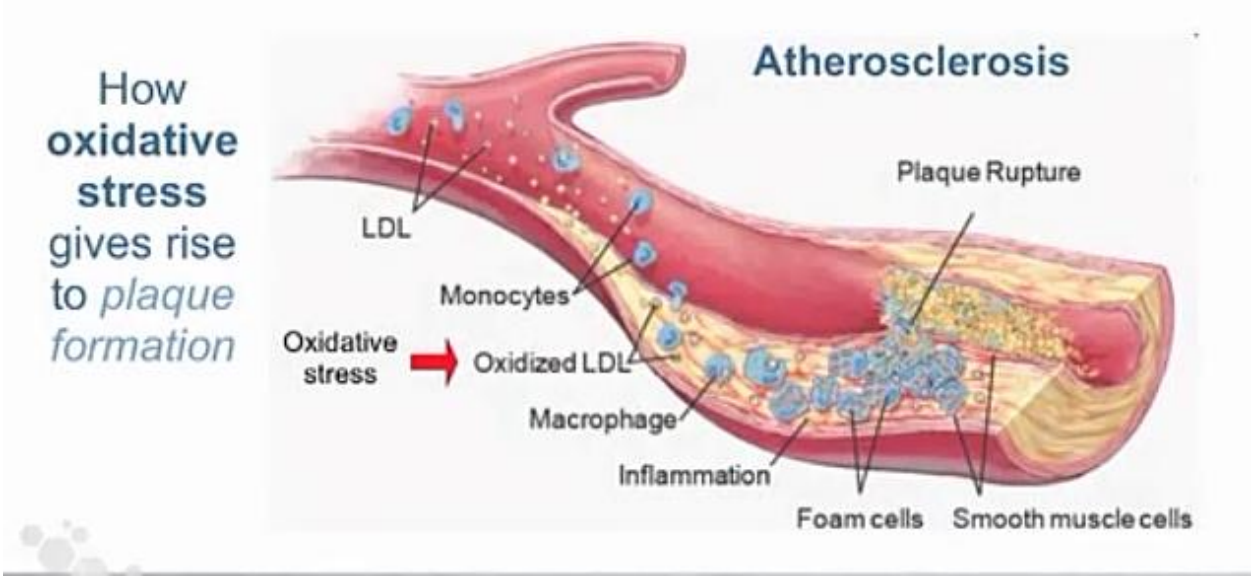
Oxidative stress is hypothesized to give rise to atherosclerosis or hardening of the arteries and plague formation. Plaque is the goop that accumulates in an artery and eventually may clog it.



So you get into trouble if that happens. The heart muscle depends on oxygen. If it doesn't get enough oxygen that muscle has a hard time doing its job: namely pumping the blood. So this figure, if you look at it from left to right is kind of a time line. If you look at the beginning part of this figure (far left) it represents the beginning of an artery in your heart. You see the first thing there is LDL cholesterol. That is a protein that binds cholesterol. We are all obsessed with what our LDL levels are. But LDL is perfectly normal; in fact you die if you don't have any LDL.

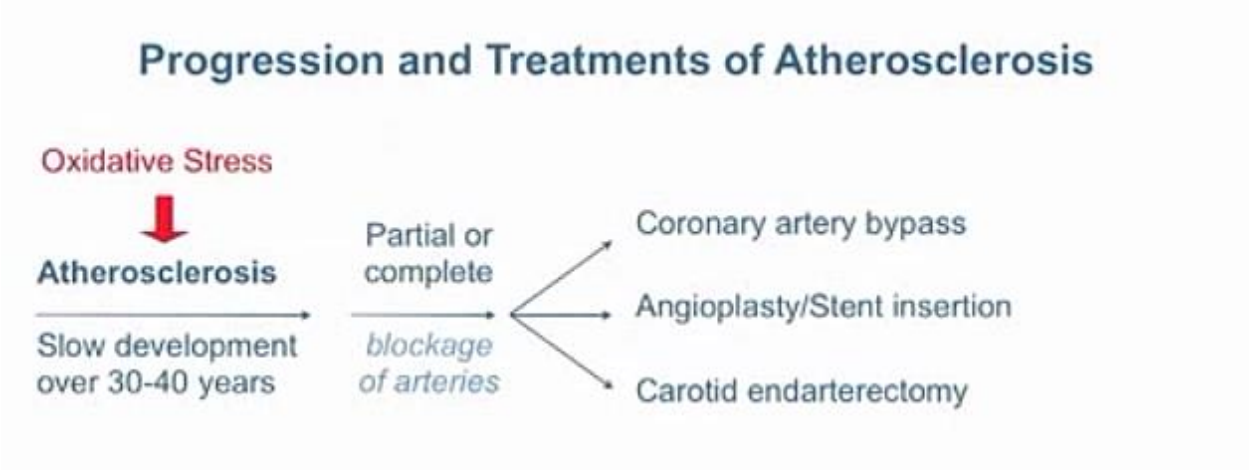
What is important is to keep it low. And why is that important? It is because if oxidative stress enters the picture it leads to oxidized LDL. And that is what many cardiologists believe is the real trigger to atherosclerosis. Also, early on, you see those blue cells labeled Monocytes. These are normal immune cells that can become inflammatory cells and those monocytes recognize the oxidized LDL. So, if free radicals are high, free radicals attack LDL and oxidize it. The monocytes eat that oxidized LDL.

They actually fill up with little globules of it and they become activated inflammatory cells at which point the histologists call them "foam cells" which you see later in the sequence. They look foamy because if you look at them under a microscope there are all these little bubbles of oxidized LDL inside the cells. And those foam cells deposit in

the vessel wall and you see there are now these thickening yellow, ugly deposits that contain foam cells, oxidized LDL and it slowly starts to occlude (close in) the lumen of the artery. The lumen is the part of a pipe that is open in the middle – where the water flows through. If the lumen closes down because there are deposits on the walls of the pipe, then that vessel becomes compromised.

The real problem, the event that may be fatal, is when this deposition of this ugly yellow plaque in the vessel wall breaks through that layer of Teflon that keeps blood from clotting, called a plaque rupture. If that layer of cells is breached and plaque rupture occurs you will get an instant thrombosis: a blood clot that forms right at that spot and that big blood clot will completely occlude the artery and it may be fatal.

So that is the progression of atherosclerosis. We have talked before about how oxidative stress is involved in the early part of that process. But it is also involved in the later part of the process and that is where this Ohio State Study comes in.



So let's assume, going from left to right here that oxidative stress leads to atherosclerosis. It is a slow process developing over 30-40 years.

An alarming part of this is that atherosclerosis begins with something called fatty streaks in the wall of an artery. They are now being seen in children as young as 10 or 12 years old. So they can begin in the first decade of life. The process builds and builds and by the time a person reaches 40, 50, 60 years old there is almost certainly evidence of atherosclerosis. It is a time bomb. Lifestyle can help prevent it. Good

diet, exercise, all the things you hear about will help slow it down. It doesn't have to be the thing that does you in at the end. But it is a process. Like if you build a new house, 20 years later the pipes will be rusty and there will be some corrosion and some deposits. They might be still fully functional but the process is ongoing.

If atherosclerosis leads to partial or complete blockage of arteries, you go to a doctor because you are having chest pains for one reason or another and if it is bad enough there are three common surgical interventions that can occur.

1. One is a Coronary Artery Bypass, an extraordinarily common surgery that most people have heard about.
2. Another procedure done by a cardiologist without so much invasive surgery is angioplasty. That is threading a balloon into that blockage in the artery, inflating a balloon, opening it up. Initially just a balloon was used to stretch the clogged artery open but within a month or two it starts to close down again: not surprisingly. Now what's done is a stent is inserted once the artery is opened up to keep it opened up. It also has consequences: medical problems produced by the surgery itself.
3. Carotid endarterectomy refers to the carotid artery. These big arteries in your neck carry blood to the brain, and are obviously very important. They too get clogged with plaque. And so you may know family members or friends that have had carotid endarterectomy. What the surgeon does there is he literally temporarily bypasses the clogged part of the artery, opens it up and scrapes out the gunk.

All 3 of these procedures have failure rates. They are not complete permanent solutions to the problem. And if you look at the 10 year failure rate – 10 years is a long time for a surgical procedure to improve your quality of life. But with CABS, after 10 years, 50% of the graphs have failed.

They are either almost completely blocked again or, they have been completely blocked and so often CABS has to be repeated. Sometimes one of the other procedures mentioned above can help. Coronary artery bypass graft (CABG) surgery is one of the most common surgical procedures performed in the United States. In appropriately selected patients, CABG surgery results in improved survival, relief of angina, and improved quality of life. Despite frequent use of artery grafts, vein grafts remain the most frequently used conduit. The long-term patency (duration of remaining open) of

vein grafts is limited and graft failure has consequences similar to those of coronary artery disease: recurrent angina, myocardial infarction (MI), additional revascularization procedures, and premature death.

With stents and angioplasty, they don't even last that long. A new approach to inhibiting neointimal hyperplasia and preventing graft failure involves using edifoligide, which was developed to work via gene therapy to inhibit cell proliferation. For this study, scientists took each patient's harvested vein (that would be used for the graft) prior to CABG and treated the vein for 10 minutes with a pressure-mediated delivery system with either edifoligide or saline placebo.

The scientists found that edifoligide had no effect on the primary end point of per patient vein graft failure (436 [45.2 percent] of 965 patients in the edifoligide group vs. 442 [46.3 percent] of 955 patients in the placebo group; or on any secondary angiographic end point, or on the incidence of major adverse cardiac events at 1 year (101 [6.7 percent] of 1,508 patients in the edifoligide group vs. 121 [8.1 percent] of 1,506 patients in the placebo group.

"Failure of at least one vein graft is quite common within 12 to 18 months after CABG surgery. Even though safe and well tolerated, inhibition with edifoligide is no more effective than placebo in preventing these events. (JAMA. 2005; 294:2446-2454)

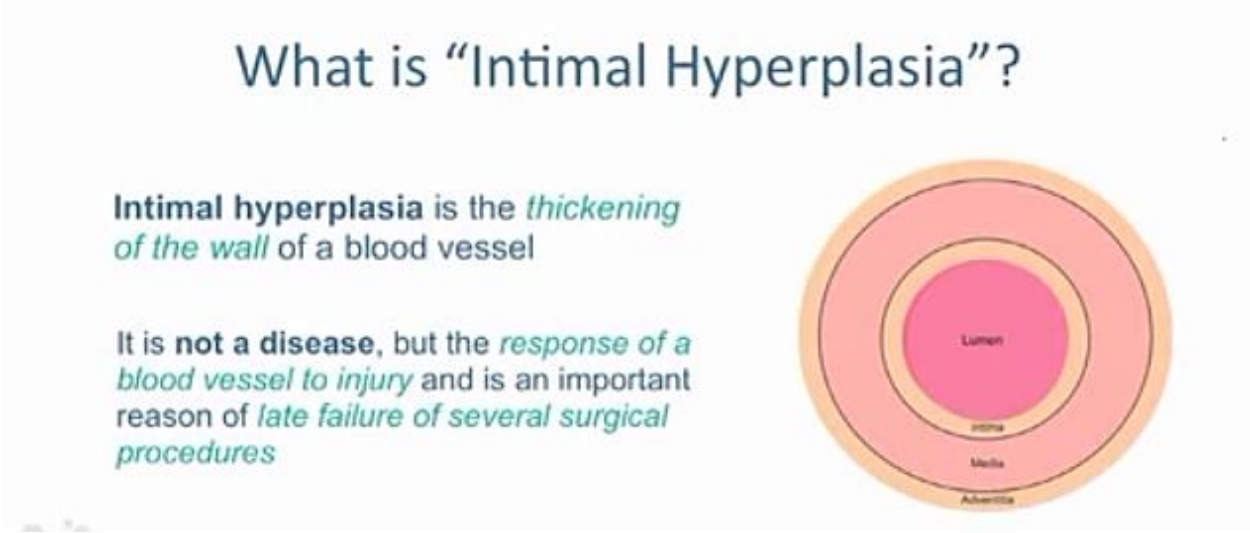
Sometimes 4 or 5 years is what you expect from a stent. We'll discuss the reason they fail. And the same with carotid endarterectomies, a little better result, maybe a 30% failure rate after 10 years.

What causes that failure rate?

What we want to look at is "what causes that failure rate" and it is our old nemesis – Oxidative Stress again. Oxidative stress leads to something that was in the title of that Ohio State paper – intimal hyperplasia.

This is really the culprit that causes those opened vessels, the bypassed vessels, to clog up again after some years. Intimal Hyperplasia is the problem and is what causes intimal hyperplasia is oxidative stress, at least in the context of the Ohio State study. Something Protandim can help with.

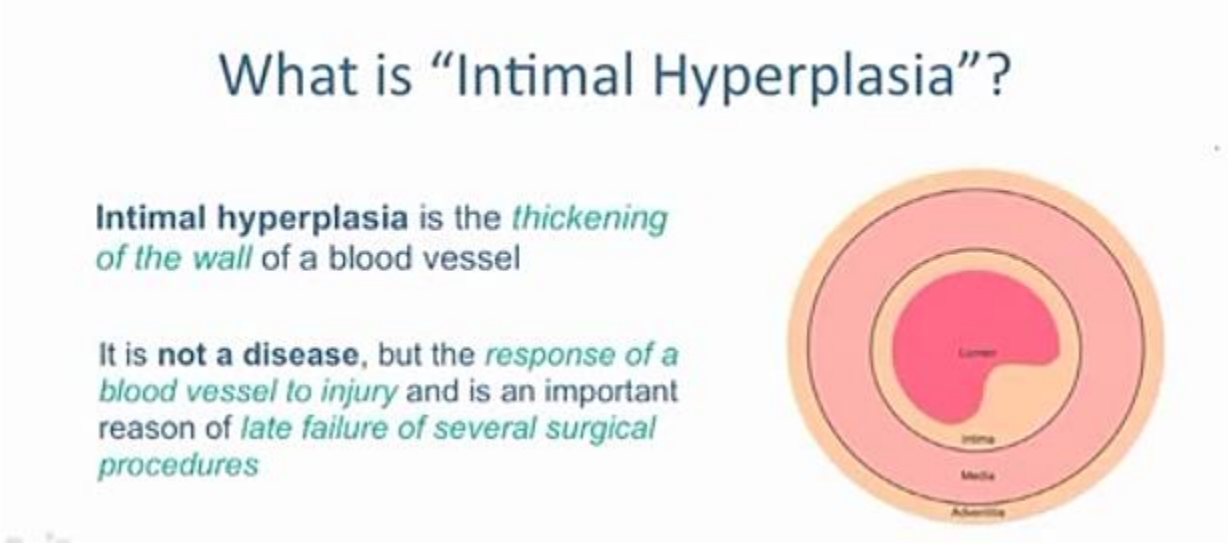
Alright, what do those words "Intimal Hyperplasia" mean?



It is simply a thickening of the wall of the blood vessel. You may wonder why they just don't say that in the first place. If you look at the cross section of a blood vessel what you see is that there are several layers. If you cut a copper pipe open, it's just one layer. If you cut an artery open you will see that there are three distinct layers. The darker pink circle in the middle is the lumen. The lumen is representative of the hole in the pipe that the blood flows through.

The innermost layer is called the intimal – that is what it means – the inner most.

The media is the next layer – and that means middle or the one in the middle. And the outer layer is called adventicia. So those are the three distinct layers. What happens when the intima proliferates (the cells start to divide)?

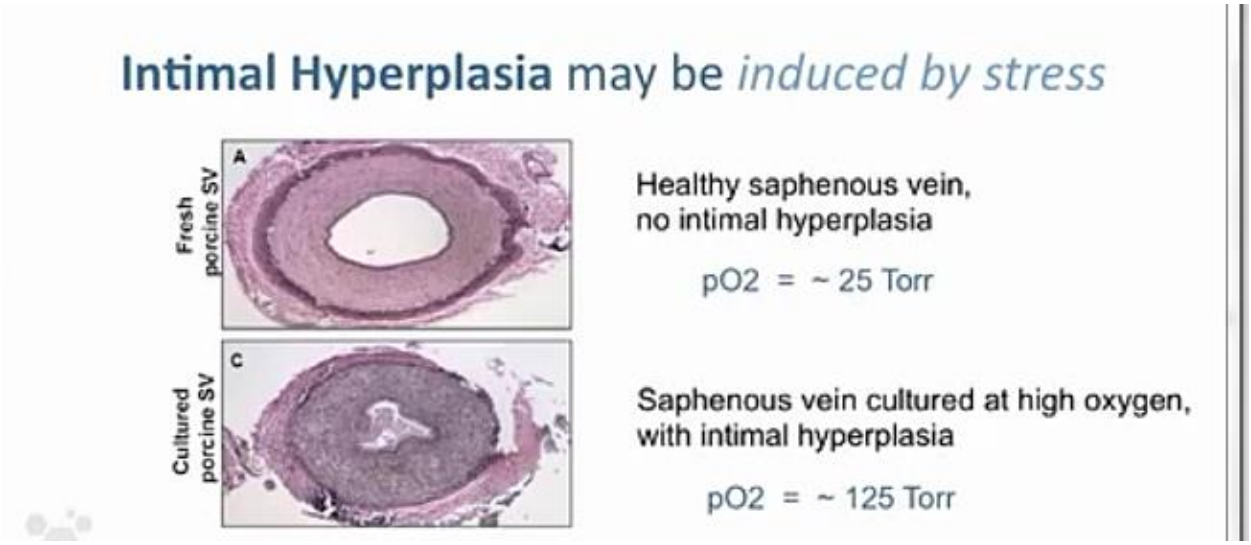


What happens is that inner part of the lining gets thicker and thicker and here you see it protruding into the lumen. If this happened all the way around the vessel, the lumen would get smaller and smaller. The media also gets thicker. Some of those cells in the media, mostly smooth muscle cells, will migrate and protrude into the intima and you get this thickening of the wall that can occlude a vessel.

Intimal Hyperplasia Can Be An Iatrogenic Condition.

What that means is that you may go to your doctor for some procedure and you go back a month later for a follow-up and he may say something like "you have an iatrogenic infection". What that means is that he caused the infection. Not intentionally. It may have just been accidental but iatrogenic means physician induced. This is because a lot of the procedures have consequences and Intimal Hyperplasia is one of those consequences.

It wasn't done on purpose and it doesn't require a malpractice attorney or anything like that. But it is caused by the procedure.



The upper picture is a cross section through a saphenous vein from a pig. You can see the big opening in the middle, which is the lumen. There is a dark intimal layer; a lighter colored media layer with adventitia around it. So that is a healthy vein on top. No intimal hyperplasia. That vein normally lives in an environment where the oxygen concentration is (p02) is about 25 Torr – how oxygen is measured. That vein deals with taking used blood back to the heart. That is why it has a low oxygen concentration. But the vein is built to live in that environment. The vein at the bottom is the same vein, the saphenous vein from the same animal. And this section of the vein was cultured in high oxygen – 125 Torr, five times higher and that's a little higher than arteries see, but it is close. Arteries normally see 100 Torr concentration of oxygen. Here you see marked intimal hyperplasia causing a marked decrease in the size of the lumen.

What's the difference between veins and arteries?

Veins carry low oxygen blood; arteries carry high oxygen blood. And oxygen, believe it or not, is toxic. You may think oxygen is good for you and it is good for you – you die if you don't have oxygen.

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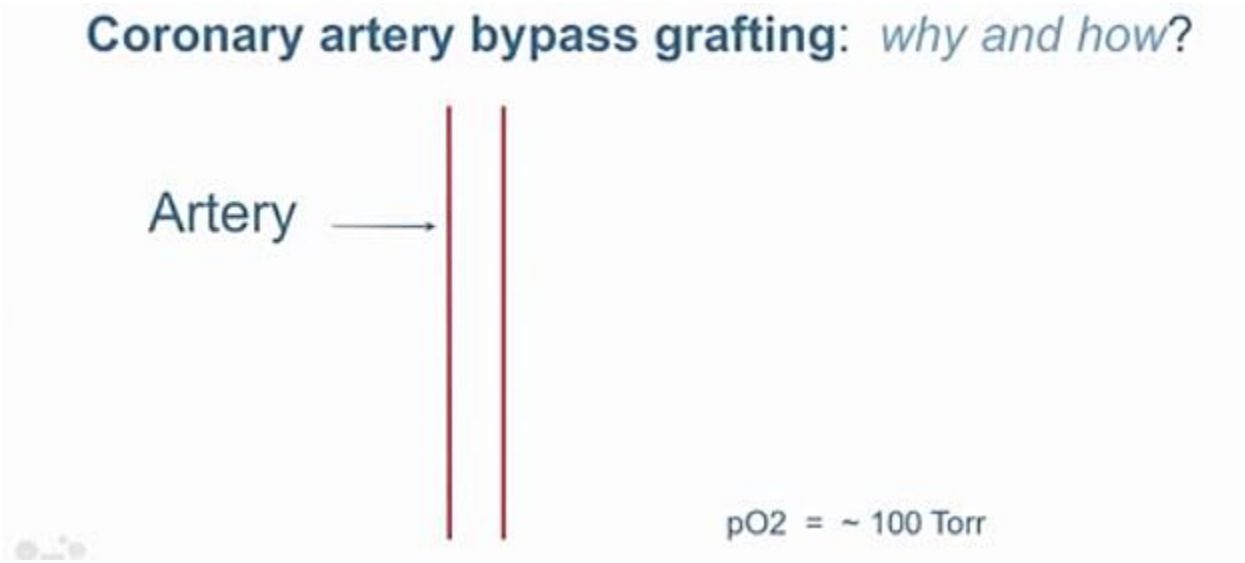
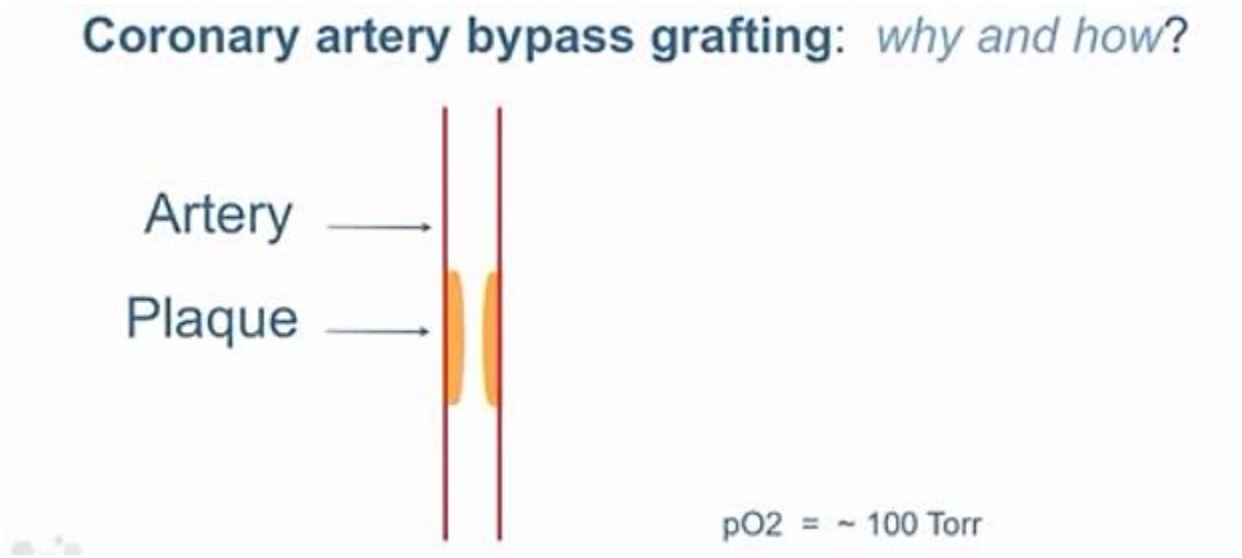
You might be surprised if you took a healthy young adult rat who is breathing at sea level air, an atmosphere that is 20% oxygen – if you put that rat in a plastic box and you gave him 100% oxygen, which is only 5 times more than normal, in 72 hours that healthy animal would be dead. That is because oxygen is that toxic. Five times more oxygen would destroy his lungs, and the animal would die.

When a heart surgeon takes a piece of vein from your leg and uses it as new plumbing to go around a blocked artery in your heart, he is asking a vein to do an artery's job and it is going to see much higher oxygen than it is used to seeing. It does a good job but it pays a price and it suffers.

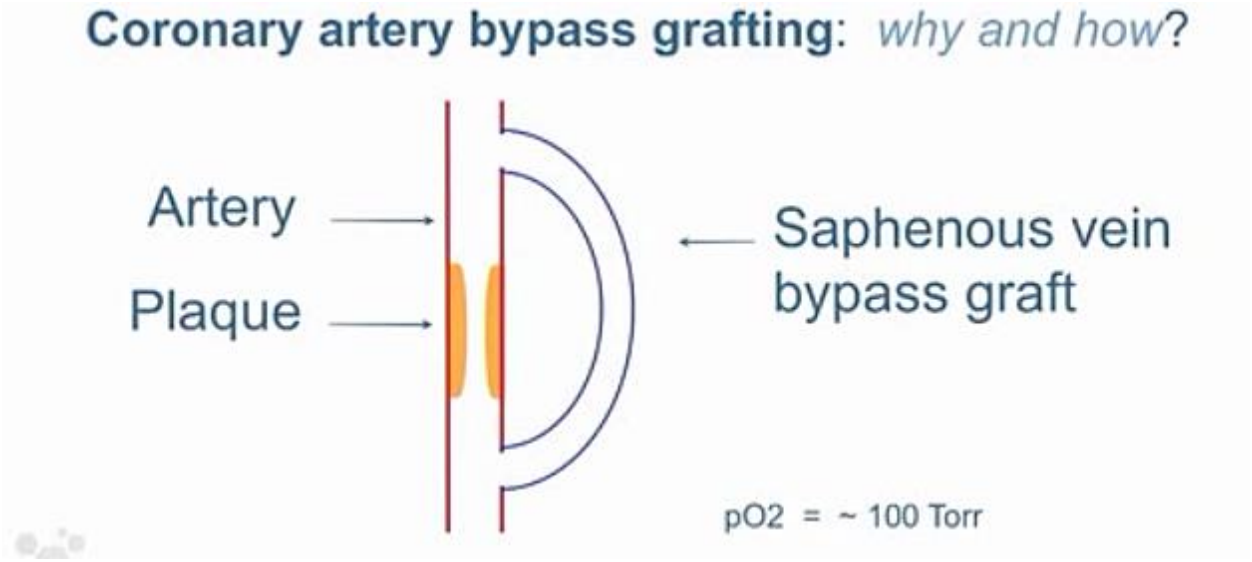
Why is artery bypass surgery done?



If this very simple picture represents an artery in your heart and you develop plaque over the course of 10, 20, or 40 years, again you see the lumen of the artery is closing up.

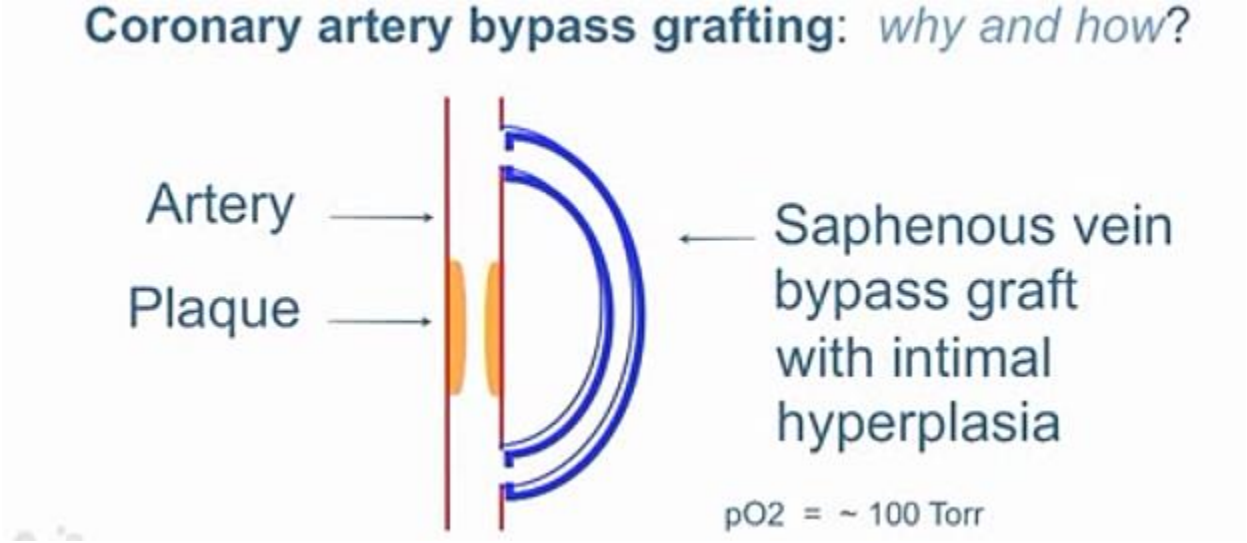


And recall that the artery is at 100 Torr – high oxygen. So the surgeon will take a piece of vein from your leg and he will bypass the obstruction. Similarly, a plumber might put in a new piece of pipe around a clog if you have a drain pipe with tree roots growing into it and obstructing the flow.

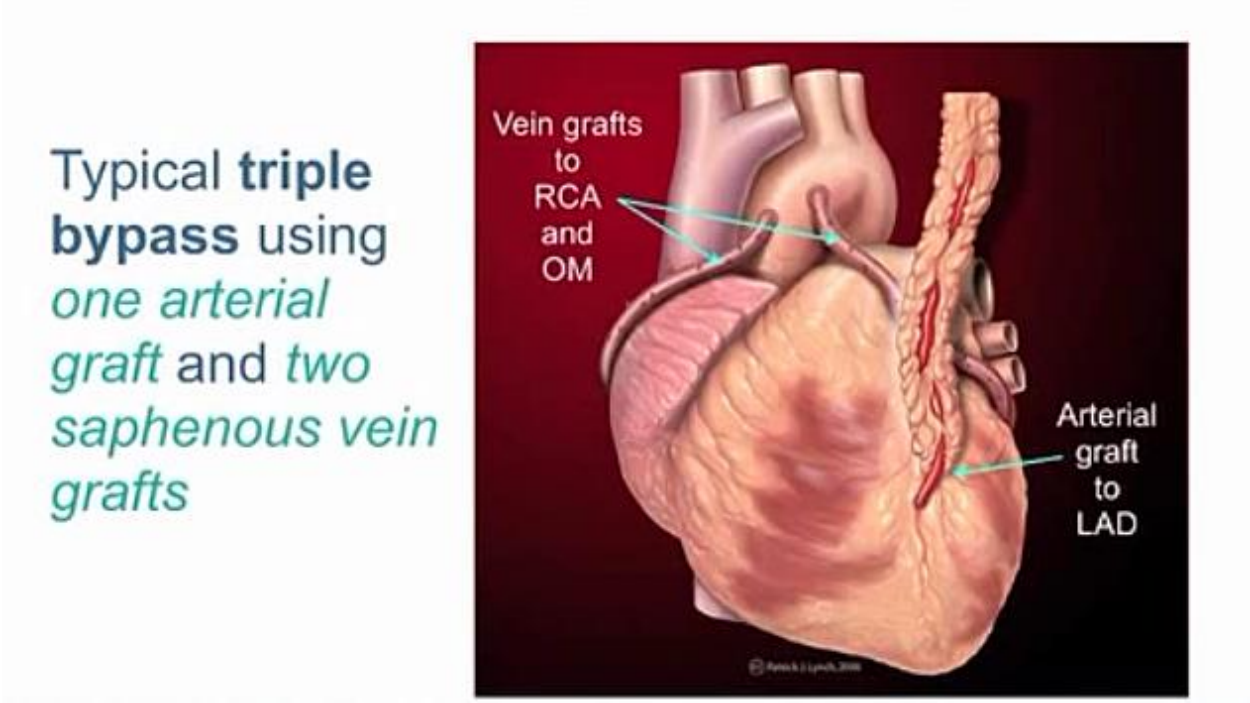


And that is what this vein is used for. So, on the surface of your heart you have a bypass around it.

Now the problem is that the vein, which should be seeing oxygen at a level of 25 Torr, is now seeing oxygen at a level of 100 Torr. It causes oxidative stress uniquely to this vein and the result is the walls of the vein thicken.



This thickening will eventually obstruct the lumen to the point where it may close up and ultimately clog.



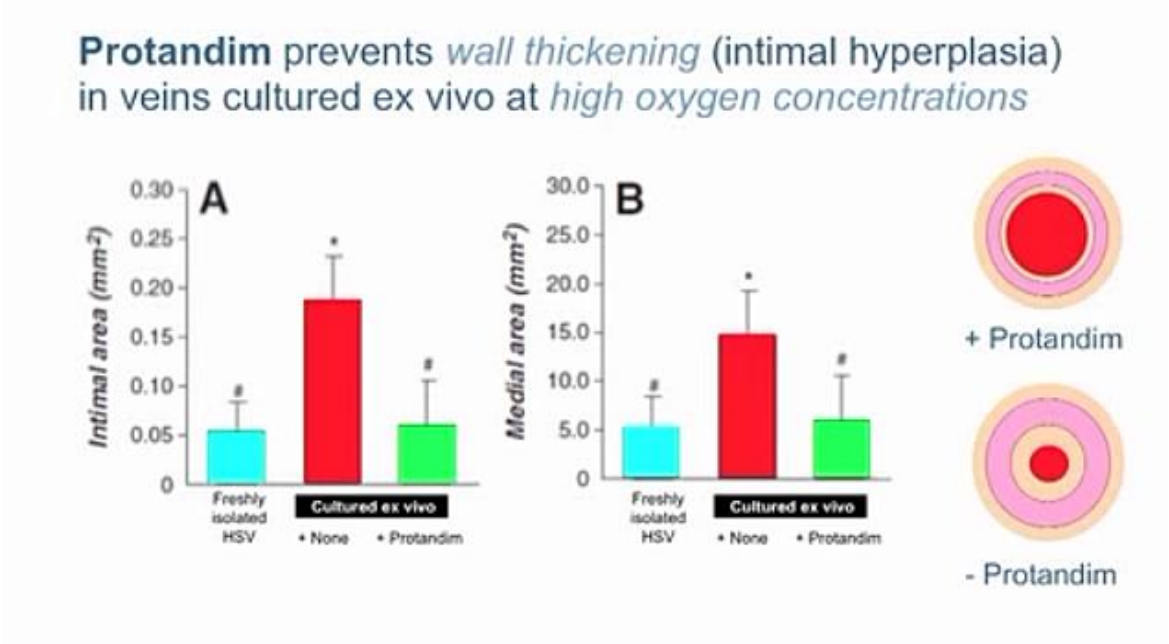
This is a picture of a heart that has just undergone a triple bypass. You hear of double, triple, quadruple bypasses – that means how many clogged arteries had to be bypassed. The most important one is usually that one labeled LAD (Left Anterior Descending Coronary Artery) because that takes blood to that part of your heart that does the heavy lifting – the left ventricle. It has got to supply that part of the heart that contracts to pump blood through your body.

In the last decade or two, surgeons have avoided the use of veins as much as possible and so what you see going to that LAD is an arteriole graft. So that artery has come from your chest wall. It has been dissected out by the surgeon and the reason he is using that interior thoracic artery is because it is a little redundant - your chest wall gets by without it. The surgeon can relocate it and that is an artery supplying a new blood supply spliced into the coronary artery south of the obstruction so that the muscle below the obstruction now gets a new arterial blood supply from an actual artery. This is a good solution because that artery is more stable than the vein because it is used to seeing the high oxygen concentration.

This is a triple bypass, so there were two other blocked arteries on this heart. You only have one thoracic artery so you can only use that artery once. In this case, there are two vein grafts, so vein was harvested from this patient's leg and you see that there are two vein grafts that are spliced in. At the top end you can see that there are two from the aorta so they get new blood supply. And at the other end, which you can't see in this case because they are on the other side of the heart, they are spliced in also to two more blocked arteries. Those veins are going to be more problematic than the artery. The artery has a 10 year failure rate, maybe as low as 10-15%. The veins, 50% or more will fail by 10 years. So that's the problem with this surgery.

The Ohio State Study

This is where the Ohio State Study comes in. I'm going to take you quickly through the results.



It measured the wall thickness in human saphenous veins that were going to be used for surgery. The surgeon removed more than he needed just to be safe. You don't want to run short of pipe if you are a plumber.

So there is left over pipe every time a person undergoes bypass surgery and that was what was used in this study. The veins were incubated either at low oxygen and that is described here as the freshly isolated, they don't change it if they are incubated in low oxygen or at high oxygen. After two weeks of being incubated, where the only variable really is high oxygen, you get intimal hyperplasia. You get wall thickening.

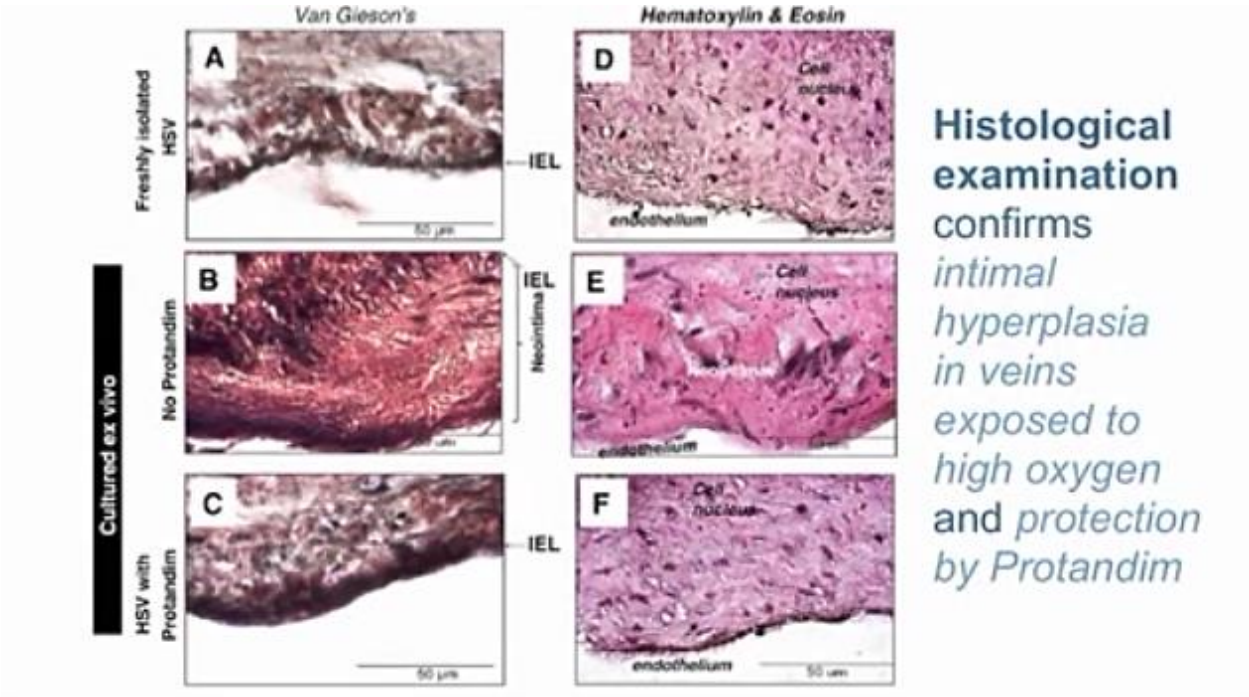
So this was done outside living people in the laboratory model. So the blue bar is where the intimal thickness should be when looking at the A panel. The red bar is after two weeks at high oxygen concentration and the wall has already thickened several fold. And the green bar is the same kind of a culture except Protandim has been added to the culture medium.

And so, even in high oxygen, the Protandim treated veins have avoided intimal hyperplasia. The walls have not thickened. They are staying at the same thickness as in freshly isolated healthy veins.

Here we are measuring the intima Panel A, the media, the next layer in panel B. And what you can see is with Protandim in the diagram on the right, the intima and the media layers are still thin.

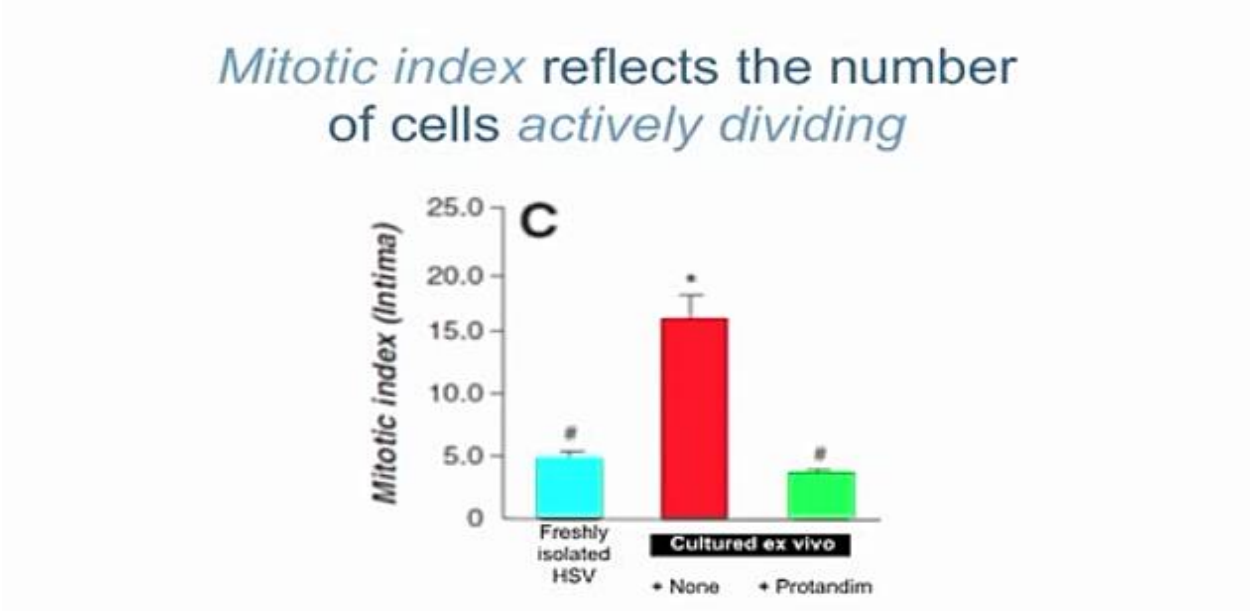
There is a big opening in this pipe and they are conducting lots of blood. The bottom picture is what happens if thickening occurs, the red bars, and you can see that the cross sectional area is reduced by maybe 80% in this diagram. Very little blood is now able to get through.

So, Protandim has blocked this process that is really the bane of cardiac surgeons. They can do their surgery just fine but the procedure has consequences beginning sometimes within weeks or months, but most certainly years following the procedure.

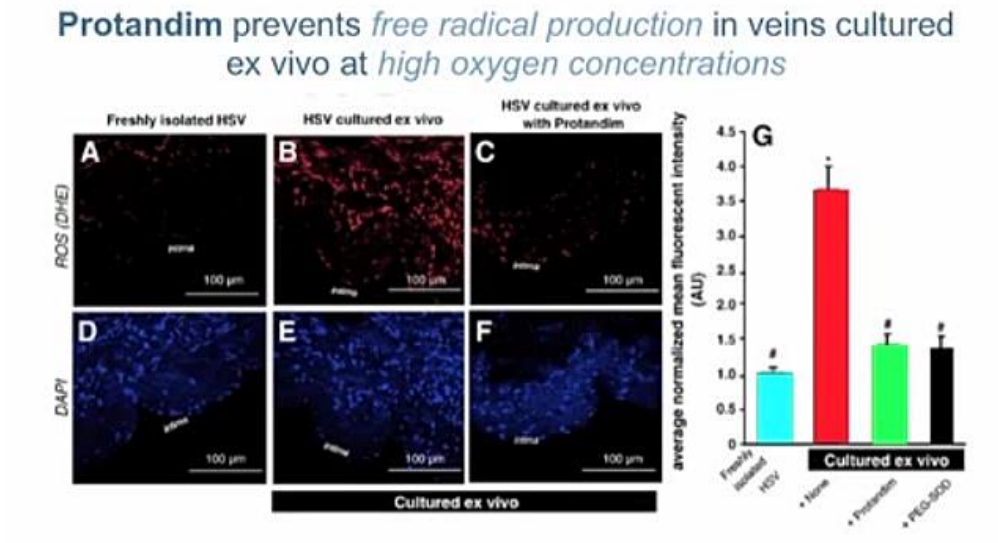


I think I'm not going to dwell on this. I don't want to turn you into histologists and the pictures may be ugly. But if you look just at A, B, C – you can see that one of these is not like the others. You might pick the middle one, so even if you don't know what you are looking at, it certainly looks different. A is a healthy vein freshly isolated. C is a vein that has been incubated at high oxygen in the presence of Protandim which looks a lot like A. The one in the middle looks bad (B) and you can see there a neointimal

layer and it is very thick because there is a lot of vessel thickening happening there prevented in C by Protandim.

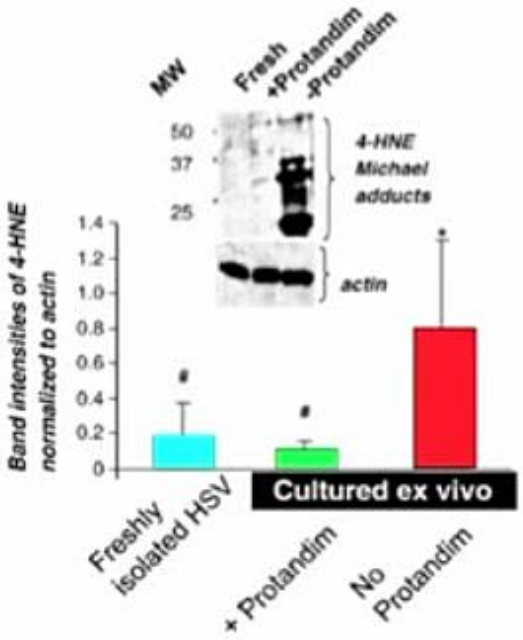


If you look at the number of cells that are actually dividing: the blue bar is a freshly isolated vein, very few dividing cells. The red bar is a vein incubated in high oxygen (the environment where it is going to see higher oxygen concentration as it becomes a replacement for an artery) there are a lot of dividing cells which is required for that wall to thicken. It takes more cells: they are multiplying, getting thicker and thicker.



Protandim, in the right green bar, completely blocks that intimal thickening. If we measure free radical production in these veins, A, B & C are again fresh veins. B is cultured in high oxygen. C is high oxygen with Protandim. What we are looking for is the red fluorescent stain. In the A panel there is very little evidence of free radical production. In B – a lot of it. In C, it is back to the A level when incubated with Protandim for the two week period. So the Protandim is blocking free radical production by scavenging those radicals. They are quantified on the bars to the right. The color code is the same. Blue is healthy: Red is high oxygen; Green is high oxygen with Protandim.

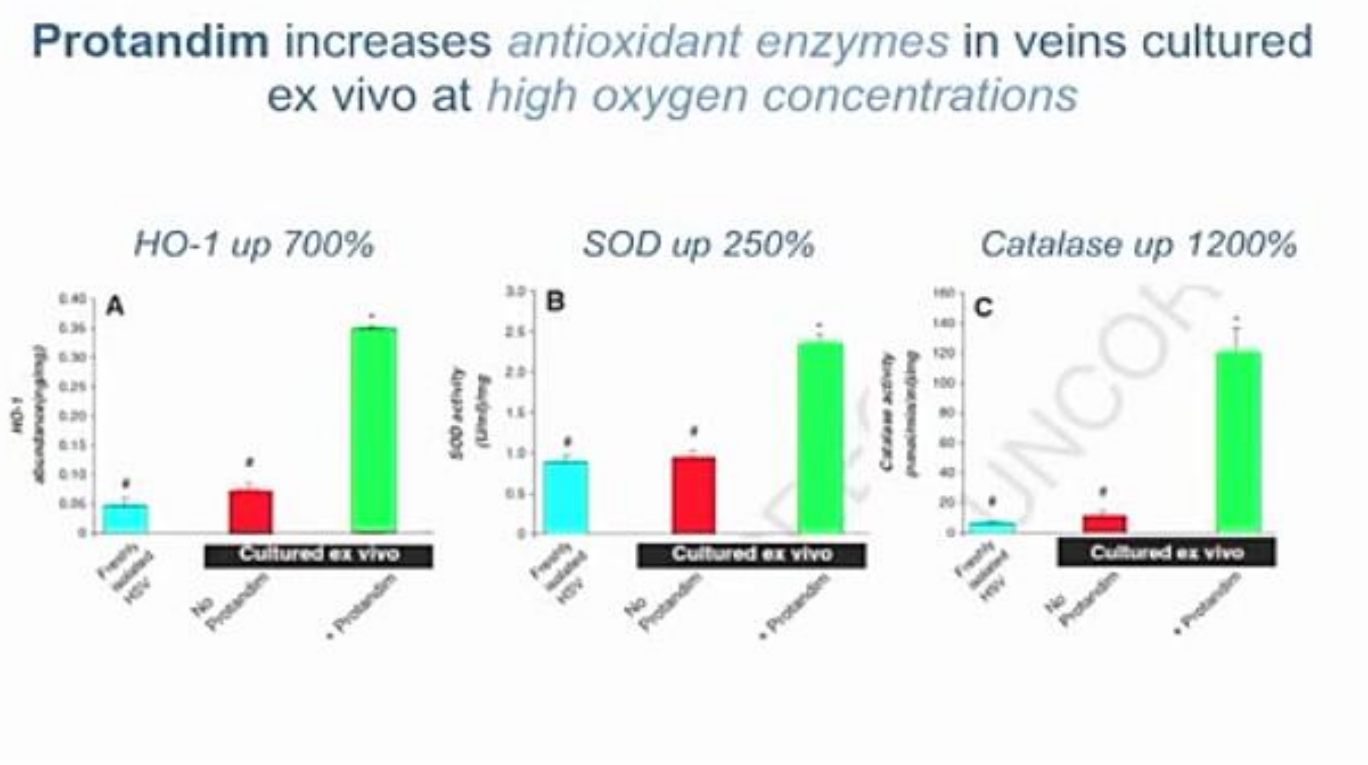
So, again we see the protection with the Protandim.



Protandim prevents *lipid peroxidation (4-HNE)* in veins cultured ex vivo at *high oxygen concentrations*

This is looking at lipid peroxidation markers. This one is very closely related to TBARS which was in the original studies, the specific component of TBARS for HNE. Again, look at the level of 4 HNE in the Blue Bar, that's healthy. The green bar is high oxygen but with Protandim it is even lower this time than the Blue bar. It is better than new. It is better than the freshly isolated veins.

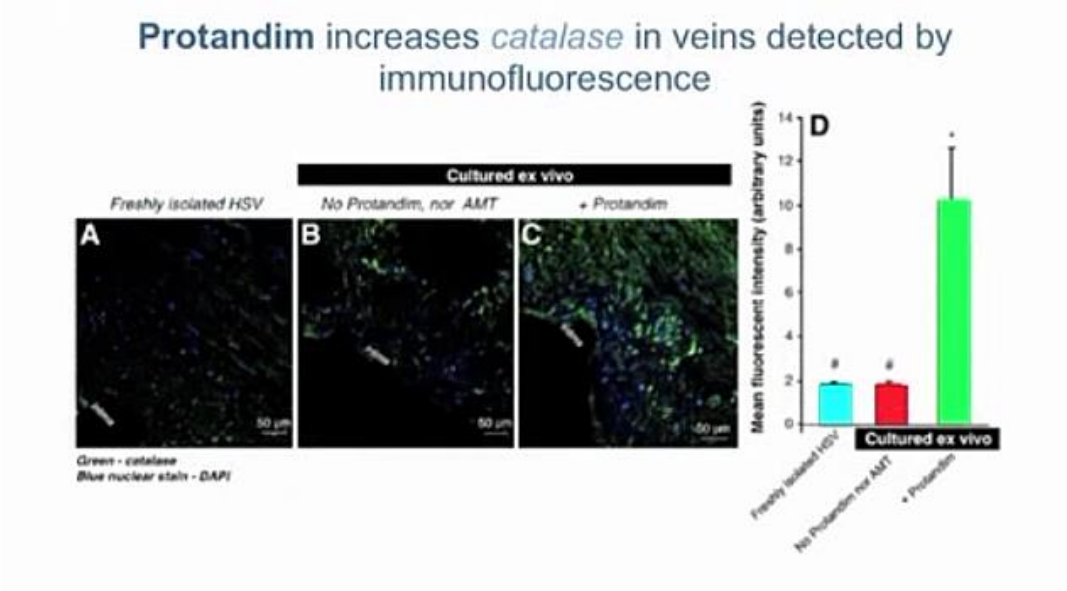
But without Protandim at high oxygen (Red bar) you can see a lot of this lipid peroxidation product, maybe 5 times more.



And why is the vein protected with Protandim?

Again, it's the same old story you have heard about in other studies. Three important antioxidant enzymes have been sharply unregulated (HO-1; SOD; Catalase). Again, the blue bar is a normal healthy vein incubated at high oxygen. The cells haven't induced the enzymes to protect them.

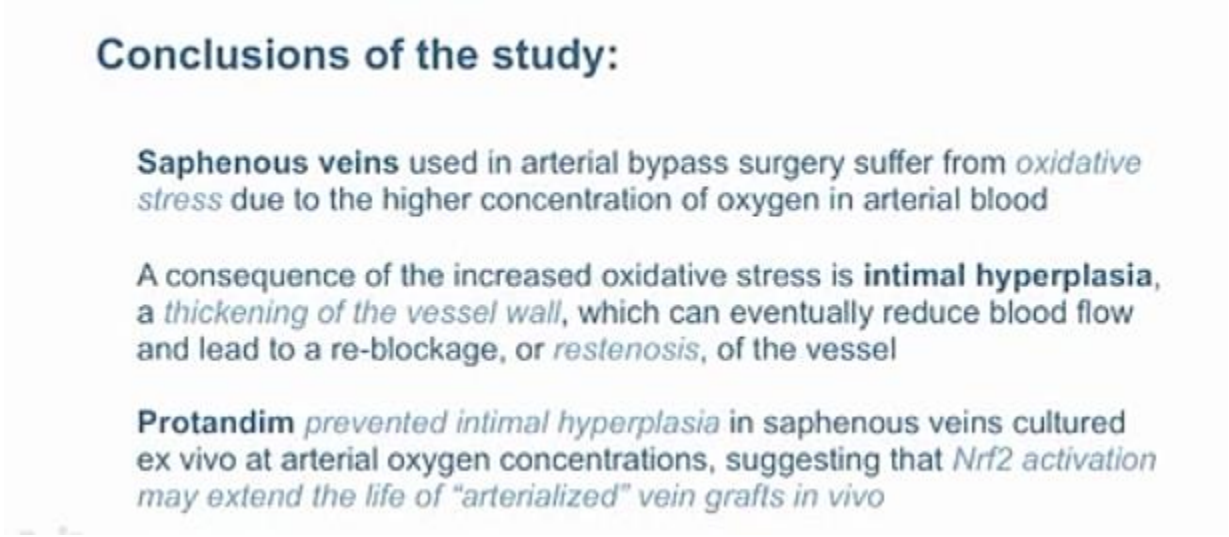
But if we add Protandim, the green bar, all three of these enzymes are dramatically induced to provide the protection you saw in the previous graph.



This is another measuring list. In this particular case catalase was focused on because there was a convenient specific inhibitor of catalase. It turned out that catalase is absolutely necessary but not sufficient necessarily to provide the protection. Catalase is a key enzyme that is one the two we began to study in this research on Protandim. It turns out that it is very important.

Conclusions:

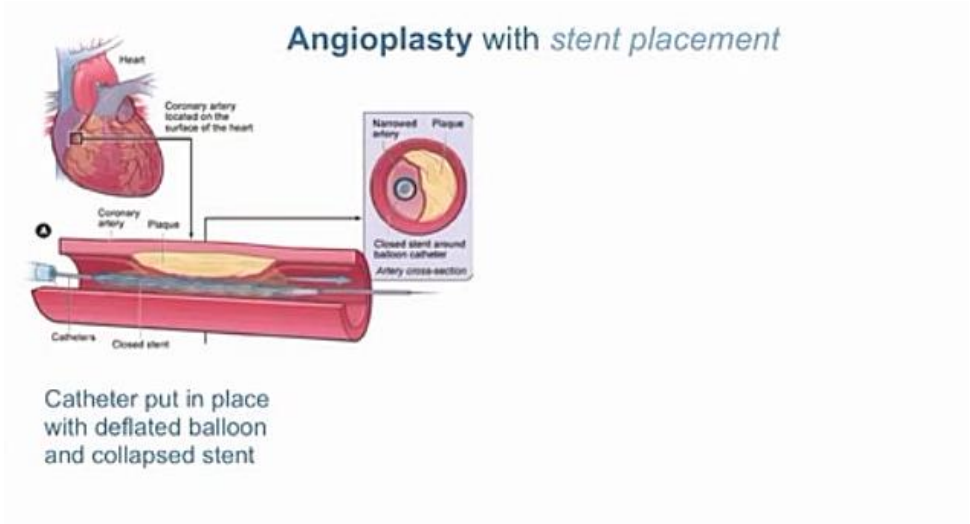
So, the conclusions are that the saphenous veins used in arterial bypass surgery suffer from oxidative stress (that's no big surprise) due to the higher concentration of oxygen in arterial blood that they are now asked to carry.



As a consequence of the increased oxidative stress, intimal hyperplasia or a thickening of the wall of the vessel occurs that can eventually lead to re-blockage or re-stenosis (what was blocked and opened up is now blocked again), of the vessel.

And the important part is Protandim prevented intimal hyperplasia in saphenous veins cultured in high oxygen suggesting that Nrf2 activation may extend the life of arteriolized veins in vivo.

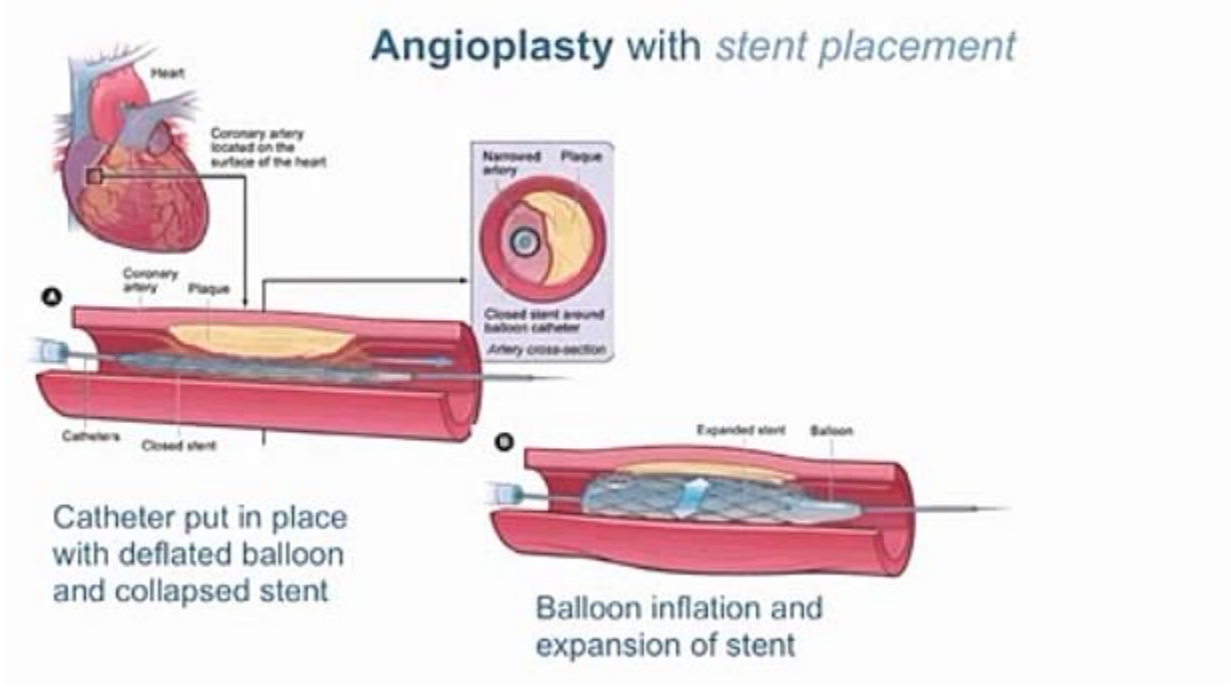
I want to mention angioplasty very briefly.



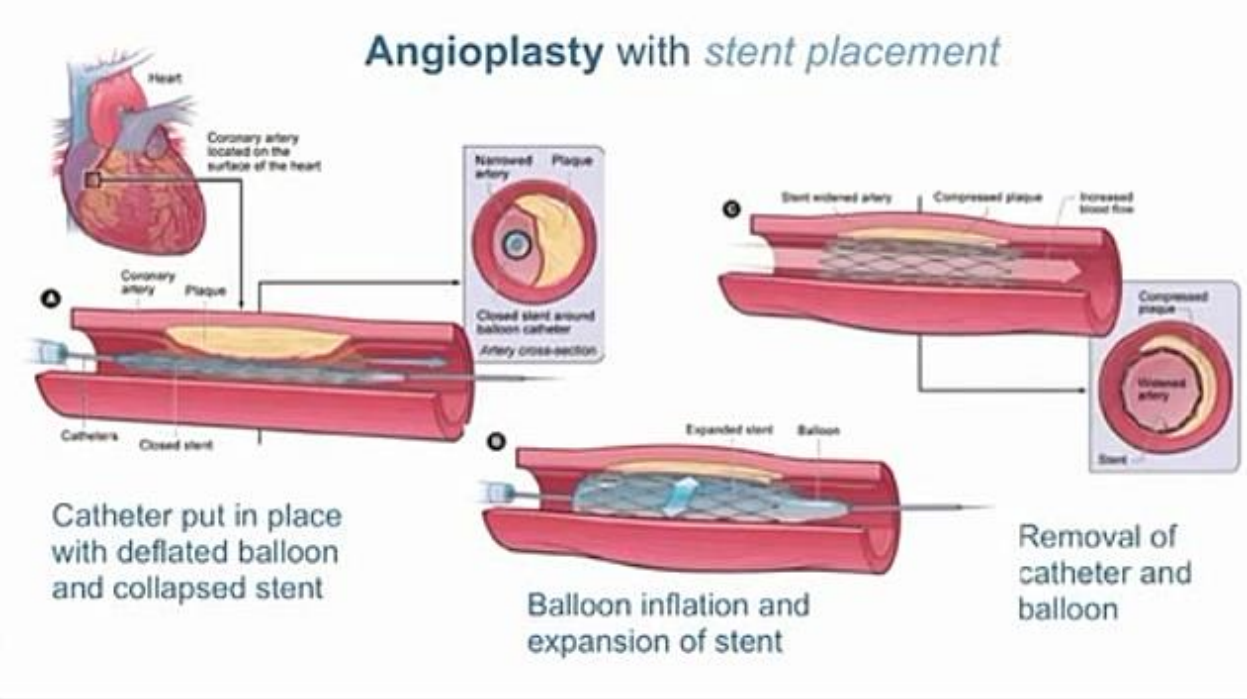
What You Don't Know about Coronary Artery Disease May be Killing You

This is a blocked artery and you see it longitudinally and cross section with a big yellow plaque that is occluding part of the lumen.

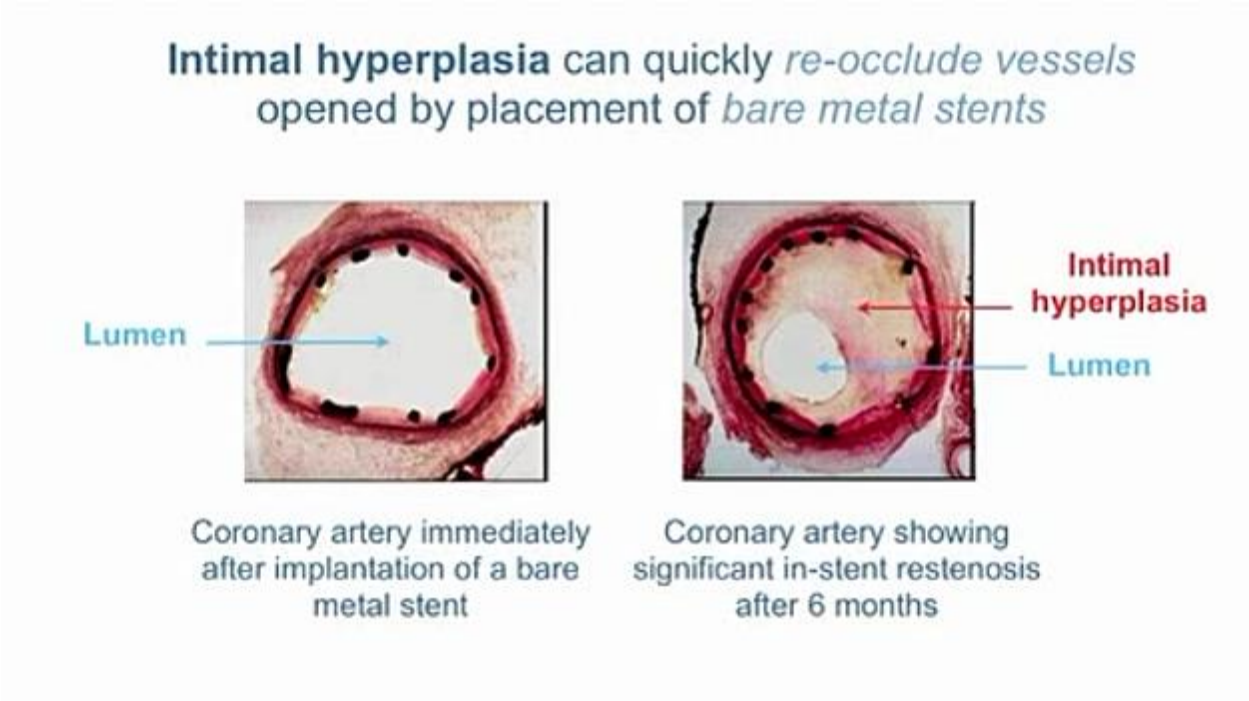
Here a catheter has been threaded up through the aorta into the coronary artery. This is a very thin looking wire but it has an inflatable balloon on the end. And outside the balloon is a little collapsed wire cylinder. Sort of like if you took a piece of chicken wire and made a cylinder you could compress it down into a very thin rod.



And if you inflate the balloon that is inside you can expand that cylinder. So that is what the surgeon does. He locates the area where the plaque is, inflates the balloon and you can see that wire mesh cylinder now being expanded. That holds the vessel open. Without that wire mesh stent, the vessel would collapse when you deflated the balloon.

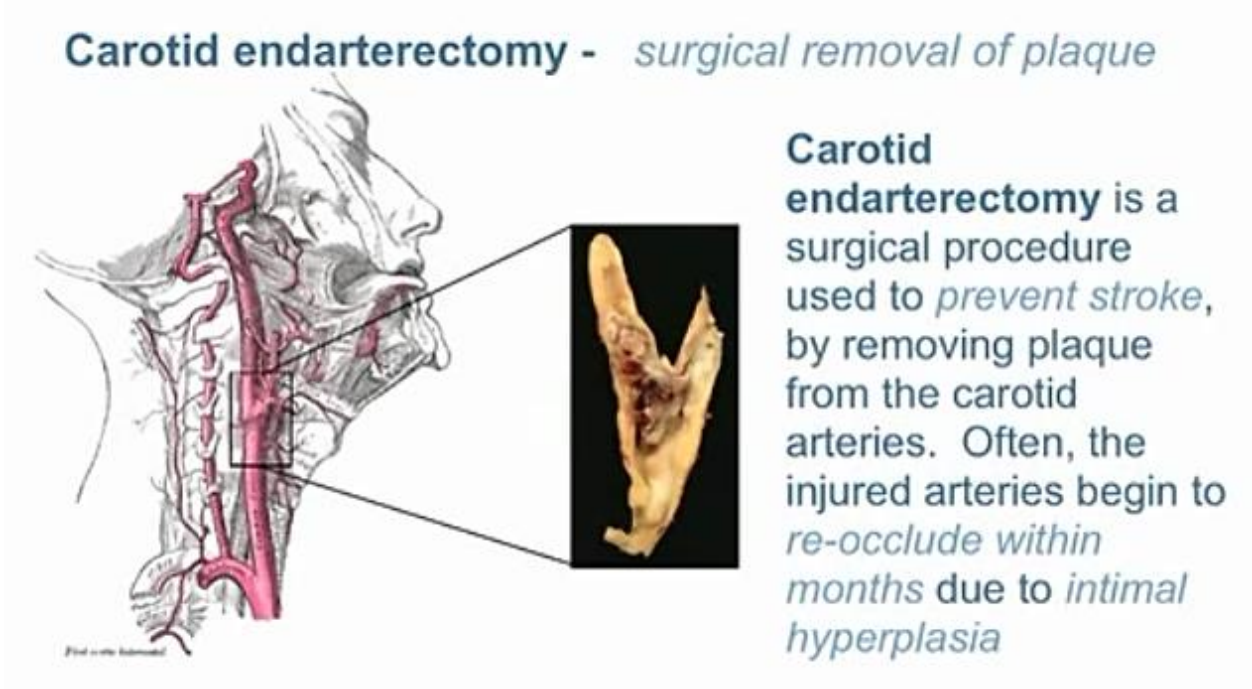


And so here after you expand the wire mesh, you deflate the balloon, pull it out, and now you've got an artery (pictured on the right in cross section) that has a wire cage holding that plaque against the wall, making sure there is a big lumen.



The unfortunate part is that this figure is 6 months later. These are from pigs and on the left you see a lumen that is wide open and those little black dots are actually the wires in cross section of the stent that has been expanded.

You can see it holding that vessel open. If you come back and look at another pig with another stent, after 6 months, look at the difference. You can see that light pink tissue labeled intimal hyperplasia: that is a proliferation of cells that in only 6 months has closed that lumen down probably 80% and that's the iatrogenic problem created by placing the stent. The stent did a great job initially but this is the problem – this is a bare metal stent. One of the ways medical device companies have responded to this is that many stents are now coated. They are called drug illuding stents or drug coated stents and they have time released chemicals that inhibit intimal hyperplasia on the metal frame itself. This lasts for a while and it improves things for maybe a year or two. But not for the really long haul. So, intimal hyperplasia is a real problem.



Finally, this is Carotid Endarterectomy, the other procedure of the big arteries in the neck. And this is an actual picture of where a frequent location of plaque develops: which is a "fork in the road". So the carotid artery has a branch in the side of your neck and that is where plaque often develops. This is what it looks like if the surgeon opens that artery up – it looks like a big chunk of a cheeseburger caught in there. And what they do is they literally scrape that out and sew the artery back together and it works with a high success rate. After about 10 years, 70% of them are still fine. But that is a traumatic event for the artery: it's been opened up – the lining scraped out. When these fail, it is usually due to intimal hyperplasia as well. Finally, the implication is that 1 ½ million people a year undergo this procedure. That is a huge number of people who have processes going on that are almost certainly going to lead to failures of these carotid arteries, the bypass surgeries, the angioplasty, the carotid endarterectomies.

This is a BIG MARKET for something that will prevent intimal hyperplasia.

And so I invite you to get connected with a product called Protandim that might be really useful to do exactly that – prevent intimal hyperplasia.

For more information on how to obtain Protandim for your personal use, please feel free to contact me through www.mylifevantage.com/beyondantioxidants or askdrcox@sbcglobal.net.

Go to: http://www.ncbi.nlm.nih.gov/pubmed?term=protandim and review the 8th Peer Reviewed Published study for more details.

Blessings for Vibrant Health and Prosperity,

David E. Cox, D.C.