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What the Heck Has Been Going on in My World?

By Mark A. Moyad, MD, MPH, University of Michigan

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Note: A total of 71 (YES THAT IS 71…that's a lot…even higher than the number of times my kids said "I am sorry and I will not do that again" and then they did that again!) times in a row (and for 16+ years!) I have written and volunteered for this newsletter. I have yet to receive any personal financial compensation or personalized classic timeless gifts such as PAACT complimentary lifelong mental health therapy for Dr. Moyad after Michigan lost to Michigan State in football on the last play of the game when we were all set to beat those evil guys and their "I am always serious and in a cranky mood" coach (although the guy is really a genius and needs to go coach another team far away, for example some team at the North Pole or Russia, because he is making me crazy) so I can quit seeing him finally semi-smile when he beats Michigan!!! At least it took a miracle to beat Michigan this year and that will be true in the future. Also, by the time you read this newsletter the Mighty Michigan versus the Overrated Ohio State Football game will be over and if we don't beat those dudes, I'm going to need twice as much mental health therapy so PAACT should get ready to pay for my medical needs ASAP! However, if Michigan can beat Ohio State this year, then I'm going to be in a VERY HAPPY PLACE!!! In fact, if Michigan beats/upsets Ohio State this year, please send me beer and money, because I will have deserved it and if they lose please send me beer and money because I will deserve it and need it!

I WANT TO THANK YOU AGAIN FOR CONTINUING TO MAKE "THE SUPPLEMENT HANDBOOK" – my semi-new book a best seller. YEAH!! THANK YOU!!! Second, if you have not picked up a copy please get one on Amazon.com (the very cheapest place to procure a copy) to support my "Just for Men" fund because my hair is

turning even more gray and thin with every issue of PAACT (because I'm getting older, not because I'm experiencing more stress – except when Rick Profit from PAACT sends me an email every 2.5 months stating "your column is due this Friday." Then I experience stress and I place a small picture of him on my office wall and throw darts at it – especially trying

to hit his mid-section, but then after I turn the column in I feel bad that I did this and take his picture down, but I never tell him that I have this nefarious regular habit and I am sure there is no way he will ever find out that I temporarily throw darts at his picture – I mean how could he find out that I do this on a quarterly basis???)! And, for about 19 bucks (the cost of only 10 two dollar candy bars or a few boxes of Girl Scout cookies – I like the mint ones by the way) you get 512 pages of material on over 100 medical conditions and when not using this amazingly big book it also functions as a football or a Discus.

BREAKING NEWS!!!

325) HILLARY CLINTON EMAILS & President Bill Clinton and Monica Lewinsky! (Actually have nothing to do with this article I just wanted to get your attention).

MY TRIP TO ITALY AND WHAT IT MEANS FOR YOU = COFFEE HAS ANTI-CANCER EFFECTS (Maybe) AND POMEGRANATE DOES NOT???! HEY, THIS IS 3 ARTICLES IN ONE! A TRIFECTA! WHAT A DEAL!!!

(Reference: Moyad and Delta Airlines; Guercio BJ, et al. J Clin Oncol 2015, released early on-line; Liu H et al. Nutr Cancer 2015;67:392-400. & Discacciati A, et al. Ann Oncol 2014;25:584-591).

BOTTOM LINE

Italians drink a lot of coffee and now caffeinated, low or no calorie coffee has some preliminary evidence that it could

reduce the risk of colon and prostate cancer returning after treatment OR this positive evidence only exists because some men that drink a lot of coffee harbor a lot of other healthy behaviors. Regardless this is pretty cool stuff! And, pomegranate juice/extract? Let's just say it's not been a good year for pomegranate and prostate cancer evidence, especially when compared to placebo. OUCH!!!

WHAT ELSE DO I NEED TO KNOW?

I just returned from a brief working trip that took me throughout Southern Italy – I know…life is really tough at times, but someone has to be Mark Moyad. Now I am semi- or actually fully addicted to coffee because in Italy it is ubiquitous, you can't escape from it, which is kind of like those lawyer ads on TV that promise you big money if you just take someone to court, and they/lawyers do not get paid unless you get paid (wow!). That's so kind! Expresso, cappuccino, café Americano …yummy for my tummy. I learned about all of them by trying them over and over again! Man, I had more energy than a 16-year old kid getting his driver's license and a new car on the same day! However, wha t was really incredible is that I saw no one – not a single person in Italy use a "to go" cup or simply walk down the street drinking coffee – not a single person in any of the many cities I visited?! What the heck is going on? These well-dressed Italians (Man they look good even in the early morning…I mean who looks that good in the United States so early in the morning…apart from my wife of course – BOOM! Man, I am as smooth as a baby's bottom) stand or sit in a café and drink and talk and then move on with big smiles on their faces.

Now it appears that coffee is healthy for you? Perhaps it's not the coffee but the underlying comprehensive healthy behavior of the coffee drinker in some of these countries. They appear to regularly socialize, relax, remain strong spiritually, walk constantly, and eat very healthy diets, but only in small to moderate portions. For example, I ordered a crab-stuffed ravioli in Rome, a pizza in Naples, Caprese salad in Sorrento, and anchovies in Amalfi that I swear in every case were considered a main course, but were so small that in America they would not even qualify as an appetizer! In other words, the portion sizes were so tiny! I mean even their soda drinks were tiny! This must be the secret of the Mediterranean diet or perhaps it's the fact that I dumped gallons of olive oil on everything because right now the oil is so fresh and yummy with bread and veggies and meat and fish and _____ (insert your favorite food)! You could almost drink the olive oil straight because it was so fresh in Italy! And, olives themselves were so fresh that I ate a plate of them at every meal! Just call me "Mayor of Olive City" because I LOVE to EAT OLIVES (get it…olive is like saying "I love" – in fact it you mouth the words "olive juice" from a distance to a friend or relative they actually think you are saying "I love you." Try it sometime, it's funny!).

Back to my story! Multiple new human (not mouse or rat) studies are also suggesting that coffee (especially the low or no calorie caffeinated type) itself has some anti-cancer/anti-inflammatory properties and could reduce insulin over-exposure, which means not only as a preventive, but also as a way to reduce cancer recurrence. Wow! Is this possible? I mean coffee actually does have some interesting compounds like "chlorogenic acid" that could be healthy! And, in a recent American colon cancer study of patients that had been treated for colon cancer the results were pretty good and got my attention (even though I never drank coffee before except one time in high school before I had to stay up all night for an

exam that I think I ended up failing – thanks a lot coffee). In a recent study a total of 953 patients with stage III colon cancer during and 6 months after adjuvant chemotherapy who were prospectively followed over time and the dietary intake of a variety of foods and beverages were self-reported and recorded. Patients ingesting 4 cups/day or more of caffeinated coffee experienced a significant (p=0.002) 52% reduction of colon cancer recurrence or mortality (HR=0.48) versus never drinkers. Non-herbal tea and decaffeinated coffee were not associated with a clinical benefit. Greater coffee intake could be correlated with a significant reduction in colon cancer recurrence and mortality in patients with stage III colon cancer. I wanted to ignore past data that had been primarily retrospective and observational through the years but the accumulating data in cancer has become difficult to ignore.

Yet, is it really the coffee or the average healthy behavior of the coffee drinker that is the secret? It doesn't even matter because the message of eating a healthy diet but in small portions and moving more and staying skinny is just part of the theme of the coffee drinker. If many Italians would just quit smoking they would live even better and longer, this is what they can learn from us in America (not smoking). Although, many Italians would then start struggling with massive weight gain, which has begun to occur. My trip to Italy was a beautiful educational experience that reinforced some of the similar cultural secrets to a better and/or longer life that I have witnessed from traveling throughout the world from Singapore to South Africa to South America over the past 30 years. However, the smoking part is devastating because although smoking DEFINITELY helps you stay skinnier it also increases the chances of making your life worse while you are living it and ending your life earlier and exposing all those arounds you to this carcinogen. DISGUSTING! In fact, a few times my wife and I walked into a store and were going to

spend an obscene amount of money (aka 20-30 dollars) and the store employee or store itself smelled so much like tobacco we had to turn around and leave the store!

Interestingly, at the time I was writing this column, suffering from massive acid reflux and sleepless in Ann Arbor, moments from drinking coffee, there was another research study from the National Cancer Institute (aka NCI) that was published (Loftfield E, et al. Cancer Epidemiol Biomarkers Prev 2015;24:1052-1060.), which suggested that coffee is potentially associated with lower death rates from colon, endometrium, liver and prostate cancer and that improving insulin sensitivity and decreasing inflammation may be the reasons for this potential benefit. So, NCI researchers decided to measure blood levels of 77 immune system and inflammatory markers in over 1700 individuals. Coffee drinkers appeared to have lower blood levels of several inflammatory blood tests! Man, this is getting weird and awesome (kind of like watching your parents trying to operate an I-phone)! And now the bad news that has to do with another highly touted anti-cancer beverage (please read the next paragraph)!

Despite over 10+ years of excitement in the area of pomegranate extract or juice there were few long-term placebo comparative trials and this is what always worried me. It was also worrisome that when someone ingested pomegranate supplements (juice, pills…) there were no significant beneficial changes in weight/waist size, blood sugar, blood pressure, or LDL or “bad” cholesterol. HEART HEALTHY = PROSTATE HEALTHY = Moyad circa 1999 and beyond. It was for these and other reasons I have for years commented that pomegranate could be getting WAY, WAY too much hype and might not do well overall in more rigorous clinical trials and I predicted in my SUPPLEMENT HANDBOOK (available now on Amazon.com = shameless plug #345) that it would fail to work in bigger and better studies. Many people/experts that will

remain nameless (until I see them and remind them that they were wrong), pushed the pomegranate agenda aggressively and I do not believe this was helpful. Regardless, here are the issues – after 3 high quality trials it seems that pomegranate is not working much better than a placebo for most individuals. One study was for advanced prostate cancer patients (Stenner-Liewen F, et al. Journal of Cancer 2013;4:597-605.), another was for patients having surgery for prostate cancer (Freedland SJ, et al. Cancer Prev Res 2013;6:1120-1127.), and the third and more recent major trial was for men with rising PSA after primary therapy (Pantuck AJ, et al. Prostate Caner and Prostatic Disease 2015;18:242-248). This is not good news for pomegranate juice or other products derived from the pomegranate, but I have always believed that eating a real and NATURAL (can I use that dirty word) POMEGRANATE will always be healthier than drinking the juice or taking the supplements. Now, that's a clinical trial I would like to see….pomegranate juice versus supplements versus a pomegranate itself in a CAGE MATCH for a FIGHT WHERE WINNER TAKES ALL!!! My money is on the ignored low cost pomegranate fruit to win in a knockout in the second round!! Regardless, let me remind you what a "natural" pomegranate gives you and why it's always a healthier choice (in my opinion) versus the pills or juice. It's because there is approximately 3.5 GRAMS OF FIBER in a serving of pomegranate seeds, which is very high compared to many fruits and helps control the amount of sugar absorbed from the juice. And, if you remove the fiber and just keep the juice then what do you have apart from a lot of liquid sugar? I'm not sure what you have, this is why I put a question mark at the end of the last sentence.

Now, let me ask you 5 questions that are more important than any pomegranate or supplement product or almost any product on the market. PLEASE INSERT YOUR NUMBERS BELOW AND THEN BRING THEM TO ME WHEN YOU SEE ME AT A LECTURE, MEETING, BAR, OR A MCDONALD'S NEAR YOU!

1. Do you know exactly your weight/waist size?

2. Do you know exactly your last LDL cholesterol (aka “bad cholesterol”) value?

3. Do you know your blood sugar value?

4. Do you know your blood pressure numbers?

5. Do you know why Coach Jim Harbaugh at Michigan will win the national title in college football in 2017 and 2018 (rhetorical question…of course the answer is “because he is Jim Harbaugh the most brilliant coach in the history of college football” and because he went to grade school with another fabulous person named Mark Moyad…no kidding “St Francis of Assisi” in the 1970s, I think…it was while ago)?

Anyhow, let’s conclude this section on coffee by reminding you that the next time you go to Starbucks just order a tall medium or light coffee with no extras and that’s only 5 CALORIES!! If you don’t like coffee just order their OATMEAL (only 160 calories and 4 grams of fiber and virtually no sugar and 5 grams of protein) with a dash of milk and no extras – you will like it and your colon and prostate and heart and your sexual organs (I was going to use that “p” word for example, but PAACT is a family newsletter so using the word “penis” would have been inappropriate, so whenever you see the letter “p” by itself it means “penis” or it could also mean “PAACT” I guess…you decide) will say thank you very much for consuming such a healthy product!

326) What I ordered at McDonald’s the other day!

(Reference: McDonalds in Ann Arbor, MI or Detroit Airport or

Denver, Colorado or coming to a McDonalds near you)

BOTTOM LINE

Fast food restaurants get a lot of criticism, as they should, because many items are as unhealthy as a swift kick in the groin area that just keeps on hurting, but once in a while they come up with a delicious low calorie option that should be given credit! So, let's give them credit for inventing the EGG WHITE DELIGHT McMUFFIN! Hip, Hip, Hooray, it may actually be good for your waist and hip bones!

WHAT ELSE DO I NEED TO KNOW?

What tastes amazing, costs very little money, and only has 250 calories but also has 18 grams of PROTEIN (that's a lot) and 7 grams of fat, zero trans-fat, only 30 milligrams of cholesterol, 1 gram of dietary fiber, 3 grams of sugar and 230 milligrams of calcium (that's a lot) and again did I mention it tastes VERY YUMMY AND AMAZING AND IT MAKES ME FEEL FULL!!! IT IS THE EGG WHITE DELIGHT McMUFFIN!!! HIP, HIP, HOORAY!!! HIP, HIP, HOORAY!!! HIP, HIP, AND IT'S GOOD FOR YOUR HIP(s)!

Wait, Dr Moyad you are actually pushing fast food and McDonalds, which has arguably kept most cardiologists in business over the past few decades?! So, what's the catch with this newer food or breakfast item besides the fact that McDonalds invented it? There is a catch – it contains 760 mg or 31% of your daily intake of SODIUM – YIKES!!! So, of course there's a catch, but if this is all that you eat for breakfast and you regularly watch your sodium intake or in reality increase your potassium intake then WHO THE HECK CARES!!! I LOVE THIS NEW BREAKFAST ITEM!!! TRY IT AND AFTER YOU LOVE IT SEND ME A GIFT CERTIFICATE TO MCDONALD'S FOR CHRISTMAS or HANUKKAH or whatever you celebrate! Anytime is a good time to buy Mark Moyad a gift!!!

327) Why calcium supplements are not needed anymore for most

people (exceptions include those on osteoporosis prescription drugs and steroids long-term like prednisone and those that rarely consume foods and beverages with calcium, which is hard to do by the way…did you see the amount of calcium in the McDonalds item from the previous news story Moyad discussed?)! (Reference: Moyad MA. The Supplement Handbook- best book in world)

BOTTOM LINE

Calcium supplements (with or without vitamin D) have many risks including: increasing the risk of kidney stones, constipation (Hey, wait slow things down – get the joke…constipation? Really?), inflammation of the throat, swallowing problems, and even heart disease (controversial, but concerning). Additionally, there's so much calcium in food and beverages today that people are being over exposed to it. The goal is to normalize your intake of calcium and vitamin D to prevent falls but there's no reason to get excess amounts of calcium and vitamin D. I have written about this many times but there's new information on the subject so let's discuss it.

WHAT ELSE DO I NEED TO KNOW?

If you want to learn about the highest sources of calcium in foods and beverages go ahead and GOOGLE IT (or in reality I say "MICHIGAN IT" because one of the founders of google went to the University of Michigan and he loved it as much as Tom Brady loved it, because it's the greatest school in the world.

I'm not biased at all….oh and did I mention it's the greatest school in the world and Tom Brady went there and loves it!).

Calcium is so replete in multivitamins (heck I saw one the other day with 500 mg of it per multivitamin pill), food and fortified beverages today it has become easier than ever

before to attain the recommended 1000-1200 mg per day (1000 mg in 19-50 year old males and females, 1000 mg in 51-70 year old males, 1200 mg in females 51 years and older and males 71+ years). The table on this page is a representation of how much easier it is to reach the RDA goal of calcium without having to take separate calcium supplements.

In fact, in the largest dietary supplement trial ever conducted on calcium supplements (WHI) the baseline intake of calcium from foods, beverages and supplements was already approximately 1150 mg/day of calcium before randomization to the calcium or placebo groups! In other words, many of us are already getting too much calcium or enough calcium.

The Women's Health Initiative (WHI) was a double-blind, placebo-controlled clinical trial and the largest U.S. clinical trial to address the issue of calcium and vitamin D supplementation. This trial included 36,282 postmenopausal U.S. women who were to ingest 1000 mg elemental calcium carbonate plus 400 IU of vitamin D3 (OsCal® brand of calcium supplements, GSK Company) or placebo for 7 years. The average BMI was 29 (almost obese) and there were a greater number of obese versus overweight women in the trial, which interestingly appears to reflect the current U.S. population. The primary endpoint was the reduction in hip fractures, and secondarily total fractures and colorectal cancer. Calcium and vitamin D supplementation significantly increased hip and total bone mineral density (BMD) versus placebo ($p<0.01$), but there was no overall evidence to suggest a reduction in hip or total fracture risk. There was an increase in kidney stone risk and there were no impacts on cardiovascular events or colorectal cancer risk. This study, the largest of its kind, continues to suggest that normalization or increased calcium and vitamin D supplementation could improve bone mineral density and may have an impact on hip fracture risk but arguably only in those individuals that are not getting enough

calcium and vitamin D. But, keep reading because you might be surprised as to how calcium and/or vitamin D might be reducing the risk of bone fractures, if they do at all.

A recent extensive analysis of the calcium and vitamin D supplementation data from the U.S. Preventive Services Task Force or USPSTF (the same group that now discourages PSA screening…love them or hate them) found treatment of vitamin D deficiency in some asymptomatic person might prevent falls (not fractures). They concluded their findings the following way: "Treatment with vitamin D, with or without calcium, may be associated with decreased risk for mortality and falls in older or institutionalized adults. Vitamin D treatment did not reduce fracture risk…" This is a critical initial finding from the research, which in my opinion also suggests cancer patients should normalize their calcium and vitamin D intakes to maximize the benefits of bone loss prevention and especially FALLS, which could lead to an increased risk of fractures. And, there is enough evidence from these past reviews of the data that calcium and vitamin D are also important for muscle health and coordination.

Additionally, most major trials of drug interventions to prevent bone loss and fractures in cancer patients, including denosumab (Xgeva®) and zoledronic acid (Zometa®), utilized some form of calcium (1000 mg per day) and vitamin D supplementation (400 or more IU per day) or normalization of intake to ensure adequate responses to these bone medications.

Thus, when these drugs received FDA approval in breast and prostate cancer it was due to phase-3 trial evidence of the drug *with* the use of calcium and vitamin D in combination (not by itself) to normalize daily intakes. So, how much vitamin D is enough? Well, the Institute of Medicine (IOM) has done a good job of simplifying the requirements. Age 18 to 70=600 IU of vitamin D a day and from the age of 71+ then 800 IU per

day! That’s it!!!

Now, without going through all the side effects of taking calcium dietary supplements, which I have covered adequately in past PAACT issues (along with which calcium supplements are better or worse or pose less of a risk of kidney stones…) there is now a new issue “PILL ESOPHAGITIS” (inflammation of your food pipe). Pills come with unique side effects and although life-saving in many cases another reason not to ingest a pill unless needed is due to “pill esophagitis.” This is well-known in the pharmaceutical industry, for example, and often it is due to patients not drinking enough water or standing up when ingesting a pill (for example this is why all osteoporosis pills come with these instructions and warnings). The symptoms of pill esophagitis include difficulty swallowing, pain on swallowing and retrosternal pain. Yet, dietary supplements can also cause pill esophagitis and esophageal ulcers, so the concern or at least recognition over this side effect in the supplement industry should immediately match that of the pharmaceutical industry. Increasing awareness of dietary supplement side effects allows for the identification of pill side effects unique to the industry itself, especially when compounds such as “silicon dioxide” (aka “sand”) are utilized in some products to a large extent. Recently, recognition of an increased risk of 100% silicate based kidney stones can occur in products that contain ample amounts of this compound. And, this is just one of many compounds uniquely utilized in pills, especially supplements that were believed to be inert in humans.

However, back to the famous/infamous calcium supplements for a second because some are as large as the front door of your house (THAT IS A BIG FRONT DOOR Dr. Moyad). Recently there was

a report that suggested over 23,000 emergency room visits occur PER YEAR because of dietary supplements (Geller AJ, et al. N Engl J Med 2015;373:1531-1540)! YIKES!!!! I actually think this number is a lot higher for many reasons that would be boring to you and would just take up a lot more space and I am getting tired typing (I have fingeritis, I wonder if I should call one of those lawyers on TV and hold PAACT responsible for this clear cut disease caused by PAACT)! Anyway what got missed in the publicity around this paper that mostly focused on weight loss supplements or energy products was the finding that **"AMONG ADULTS 65 YEARS OF AGE OR OLDER, CHOKING OR PILL-INDUCED DYSPHAGIA" (problems with swallowing) was responsible for 38% of all those emergency department visits in this age group!!!** And, more than half of the swallowing problems (54%) with pills from this study from emergency room departments around the U.S. were due to "CALCIUM PRODUCTS/SUPPLEMENTS!!!" This is another big problem with calcium supplements today because like multivitamins they are becoming too big or are too big! In the pharmaceutical world the FDA recommends that a pill should not be greater than 22 millimeters, but with supplements there is no recommendation or rule! GEESH!!

328) Fiber Primer and why getting more dietary (not supplemental fiber) is one of the keys to internal anti-aging! So, it's a form of BOTOX®? YES!!! But, wait you have talked about this before in the PAACT newsletter and readers are sick of hearing about it! Nope! There is breaking news and new information on it and it has to do with PSA screening?! And, how about some of my favorite BOTOX jokes you have never heard and why exercise keeps things flowing and lets you sleep at night if your prostate is large and in charge?

(Reference: Moyad MA, 2015)

BOTTOM LINE

Consume more (soluble and insoluble) dietary fiber (20-30 grams/day or 14 grams per 1000 calories consumed), especially from food sources. “Fiber is nature’s internal Botox for the human body” (Moyad Circa 2014) and both soluble and insoluble fiber have unique and synergistic benefits when found together (as in most healthy dietary sources). OH BOY HERE GOES MOYAD AGAIN TALKING ABOUT FIBER!!! That’s correct! I have mentioned much of these benefits before, but let’s review again and add some new information! So, let’s get things moving (get it?) and talk fiber!

WHAT ELSE DO I NEED TO KNOW?

General and numerous health benefits are derived from consuming dietary fiber that have been well documented and include reductions in the following:

• Coronary heart disease (CHD) risk

• Stroke

• High blood pressure

• Diabetes

• Obesity

• All-cause mortality=death from all•causes (which is a good thing)

For example, a pooled analysis of past cohort studies of dietary fiber for the reduction of CHD (coronary heart disease) included research from 10 international studies and included the U.S. Over a period of 6-10 years of follow-up, and after multivariate adjustment it was revealed that each 10 gram/day increase of calorie-adjusted total dietary fiber was correlated with a 14% reduction in the risk of total coronary events and a 27% reduction in risk of coronary death. These findings were similar for both genders, and the inverse

associations occurred for both soluble (also known as “viscous”) and insoluble fiber (both are found in most healthy food sources of fiber compared to commercial pills and powders that normally just or primarily contain “soluble” fiber).

Past studies have not observed a consistent benefit with one class of fiber over the other (soluble or insoluble). Recent large U.S. and other international studies have even found more striking overall potential benefits for consuming more dietary fiber. For example, the NIH-AARP U.S. prospective cohort found not only a lower risk of dying from cardiovascular, respiratory and infectious disease with greater intakes of fiber but a significantly lower risk of dying younger (“total death”) in men and women. This study may represent a major shift into the research behind fiber intake because now the potential health impact may be so much larger than first realized since reductions in the death rates of some of the largest causes of mortality may occur with greater fiber intakes.

Even minor additions of some commercial fiber sources (to your overall large dietary fiber intake) can positively impact medication dosages. A total of 15 grams of psyllium (Metamucil for example) husk supplementation daily with a 10 mg statin (simvastatin) was demonstrated to be as effective as 20 mg of this statin by itself in reducing cholesterol in a preliminary placebo-controlled study of 68 patients over 12-weeks. Although adding soluble fiber from commercial products appears to be safe and synergistic with cholesterol lowering medications, the first choice of increasing fiber intake should be FOOD SOURCES based on cost-effectiveness and simplicity. I’m not a big fan of Metamucil in large amounts, but if you need a little help getting to your daily fiber total, then Metamucil is an option.

More benefits should be emphasized so let’s do this – a meta-

analysis of 24 randomized placebo-controlled trials of fiber supplementation found a consistent impact on blood pressure reduction. Supplementation with a mean dose of only 11.5 g/d of fiber reduced systolic blood pressure by −1.13 mm Hg and diastolic pressure by −1.26 mm Hg. The reductions were actually greater in older and more hypertensive individuals compared to younger and normotensive participants. Recent international studies continue to support the modest reduction or control in blood pressure with greater intakes of **dietary fiber.**

How much fiber should patients be consuming daily? Daily intakes of total fiber in the U.S. and many other Western countries is approximately 10-15 g/d, which is approximately only half or even less than half of the total amount consistently recommended by the American Heart Association (AHA) and American Dietetic Association (20-30 g/d) for adequate overall health. Another perspective on recommended fiber intake for children and adults is that for every 1000 calories of food and beverage consumed there should be at least 14 grams of fiber consumed.

Dietary fiber from food is easily achieved by low cost sources of soluble and insoluble fiber. For example, I often tell patients to consume **a third of a cup of a bran cereal such as All-Bran Buds several times a week,** which is approximately only the size of 1-2 liquor shot glasses, with flaxseed and some fruit, and before they leave the door in the morning approximately 20 grams of fiber will have already been ingested toward the 25-30 gram goal! Low cost fiber sources such as flaxseed can provide potentially numerous heart healthy and overall health benefits. Perhaps the low-cost and non-commercialization of this product on a large-scale has led to the lack of adequate education that I've observed on this product. Flaxseed is one of the highest plant sources of heart healthy omega-3 fatty acids, and chia seed is arguably the largest plant source of fiber and omega-3, and both of these

additions to the overall diet would be ideal. Also, the **original Fiber One® cereal** contains 14 GRAMS of fiber in just a half a cup! WHAMMMO! This definitely keeps the train moving!

Interestingly, the preliminary clinical trial data on ground flaxseed (average of 30 grams or 3 rounded tablespoons per day) in other hormone mediated cancers such as breast cancer has been as or more impressive (reduced proliferation rates or Ki-67, which is a marker of potential cell or abnormal cell growth). Thus, it shouldn't be a surprise that preliminary data of flaxseed in prostate cancer is also impressive and similar to some of the breast cancer observations. Flaxseed oil also has preliminary data against cancer, but this and other oils are a large source of calories (120-130 calories/tablespoon) and contain no fiber so rarely have I recommended them over low cost flaxseed powder (similar to the real whole non-processed fruit versus the fruit juice debate mentioned earlier).

Overall dietary fiber intake (again not pills or powders) continues to garner evidence as a method of cancer prevention. Multiple mechanisms are potentially involved with this fiber benefit including:

• reduction in by-products of male and female hormones that could stimulate cancer growth

• reduction in insulin and growth factors/mitogens,

• reduction in inflammatory compounds potentially via production of short-chain fatty acids when fibers are fermented in the colon by flora and products of fermentation such as butyrate and propionate enter the circulation.

• plethora of heart healthy changes altering cancer risk/recurrence (lower weight/waist, reduced cholesterol and blood sugar…)

Still, fiber itself appears to have become overtly commercialized, and in my experience some patients are turning primarily toward powders and pills to solve their fiber deficit, and this is not only costly, but also provides primarily small amounts of soluble fiber that make it difficult to reach total fiber goals utilizing only these sources. For example, I often ask audiences and students how many fiber capsules/pills are needed to be consumed daily to obtain just 20-30 grams of fiber, and the answer always seems to provide adequate shock value (the answer is 30-50 pills a day or more depending on the commercial source)! A bolus of only soluble fiber without insoluble fiber can also create excessive bloating and other gastrointestinal issues because soluble fiber is utilized by gut bacteria and then subsequently converted to gaseous compounds (aka “passing gas”).

Processed soluble fibers abound today in protein bars and cookies and these items need to be avoided not only for a lack of evidence but again gastrointestinal discomfort with moderate to high intakes. Research continues to support the overall and heart healthy health benefits of fiber, especially when it’s primarily derived from food sources, because these sources also provide a unique and optimal balance of soluble and insoluble fiber. Another comprehensive list of dietary fiber benefits are found in the table on this page (see table) and this is why I often tell patients that “nature’s greatest internal Botox” has to be dietary fiber! The plethora of internal anti-aging effects it provides is noteworthy, from preventing cholesterol and glucose changes to preventing hemorrhoids, and it’s easy to forget that humans don’t just age externally but internally with time. Botox for cosmetic anti-aging is attention grabbing but why isn’t fiber just as notable for preventing internal aging?

I find it interesting that most fruits, veggies, beans, bran, oatmeal and other dietary sources of fiber are primarily an equal mix of soluble and insoluble fiber or insoluble fiber actually predominates over soluble in these products, while again most commercial products are basically almost all soluble fiber. They are both needed to improve overall health (Yin and Yang). **The reason one can consume 2 medium apples (about 10 grams of fiber total) without experiencing significant bloating, gas or discomfort is the majority of the fiber is insoluble (about 30% soluble). Again, the reason one cannot consume a large bolus of processed or commercialized fiber supplements or powders is that the vast majority is soluble fiber.**

Now, you think all of this information would be enough to make you run out and start gobbling (Is that even a word???)

It is on Halloween….bad joke…like most of my jokes) up a ton of fiber! Still, there is another reason to do this and this is the most surprising of all! You may remember the U.S. study called “PLCO” that demonstrated no benefit to general PSA screening and the USPSTF used this information to no longer recommend PSA screening. After that point all heck broke loose and people started arguing back and forth on whether or not PSA screening should be recommended or not. It was kind of like Republicans and Democrats arguing back and forth and not

getting anywhere, which is what happens only 365 days a year (they get things done on the other days of the year). Yet, the USA PSA screening study known as “PLCO” was a well done study not just in terms of asking the screening question, but perhaps more importantly answering other important questions on diet and exercise and this is what gets missed or no one knows about! So, what other findings occurred in this famous study that hardly received any media attention. Here is one conclusion of a finding that was also uncovered in the PLCO study and I quote: “This large, prospective study within a population-based screening trial suggests that individuals consuming the highest intakes of dietary fiber have reduced risks of incident colorectal adenoma and distal colon cancer and this effect of dietary fiber, particularly from cereal and fruit, may begin early in colorectal carcinogenesis.” (Reference is Kunzmann AT, et al. Am J Clin Nutr 2015;102:881-890). THAT IS INCREDIBLE!!! So, while all these folks run around and argue whether or not an otherwise healthy man should be screened for prostate cancer, the same study that helped generate this controversy found that **DIETARY FIBER (not fiber from pills) found a potential large reduction in colon cancer or precursors to colon cancer-premalignant lesions with fiber!** Amazing! Okay, tell me more Dr. Moyad! Tell me more! Okay I will and quit yelling at me with exclamation marks!

In the same PLCO clinical study that generated so much controversy with PSA screening and found a potential great benefit with fiber, also found another potentially incredible benefit with physical activity or exercise that few people know about and again why these researchers did such an incredible job! Here is what they found: “we did find strong and significant associations between physically active lifestyle and nocturia….Combined with other management strategies, physical activity may provide a strategy for the management of BPH-related outcomes, particularly nocturia.”

(Reference is Wolin KY, et al. Med Sci Sports Exerc 2015;47:581-592). SEE IF YOU UNDERSTAND THIS INCREDIBLE FINDING! The same study that generated the PSA controversy and found that dietary fiber could be colon healthy also found that exercise could reduce the risk of getting up at night to urinate (NOCTURIA) when a man has prostate enlargement or BPH! This is amazing!!!

In the meantime, it you are not convinced that you should be more physically active and consume more fiber you could instead pay a ton of money for the real BOTOX. Ahhh, yes the real BOTOX, which is really expensive and comes with many jokes such as:

• "People tell me that Botox is way too expensive but I just met 10 people who paid for the treatment and they didn't look surprised!"

• "There was some major recent controversy over Botox injections but these stories never seem to make the headlines!"

Okay, that's it! I actually don't have any good Botox jokes, but I don't know how to use an iron so I did inject my favorite shirt with Botox before my last talk so that there would be no wrinkles in it – Ouch! That was bad!

329) Over the next 2 years there is a good chance there will be a new Shingles vaccine and it could be one of the best preventive vaccines ever invented! Keep asking your doctor about it!

(Reference: Himal L, et al. N Engl J Med 2015;372;2087-2096)

BOTTOM LINE

The company GSK has a new shingles vaccine and you should ask your doctor about it over the next year or two. Cross your

fingers! If this gets approved it could be incredible because it would be over 97% effective for all age groups from 50 and older! The current shingles vaccine is not that great especially as you get older it gets weaker and weaker. However, this is not the case with the GSK vaccine!

WHAT ELSE DO I NEED TO KNOW?

The current shingle vaccine (Zostavax®) isn't that great as you get older, but it's all we have right now! For example, it's 64% effective for those in their 60s but when you are age 70 and older it's only 38% effective compared to 70% effective for those ages 50-59 years! So, we can do better and better may be right around the corner! A new vaccine that may hit the market in 2017 is currently MORE THAN 97% EFFECTIVE REGARDLESS OF AGE!!! THAT WOULD BE INCREDIBLE! Notice how I like the word "incredible" because it is incredible. GSK completed a study in 2015 with more than 15,000 patients age 50 and older (some 80 years and older). Currently only about 1 out of 4 individuals age 60 and older get the currently available Zostavax vaccine, but if this new one becomes available, I hope we get close to 100% of the people that need it get vaccinated. What's the catch with the new GSK vaccine if it becomes available? Well, the study was over about 3 years, so long-term, researchers are not sure if the results will continue to be this amazing. Also, you will need 2 shots separated by 2 months when or if you get it. Still, if these results stand then I wouldn't hesitate to get this vaccine when it comes out, also because side effects are not greatly different compared to a placebo vaccine.

And, now another new study from Sweden or as I like to say "Svvvvvveeeden" (because it sounds so much cooler) continues to demonstrate an increased risk for stroke and other unpublicized problems when getting Shingles! So, yes I do think the Shingles vaccine will eventually demonstrate that it can prevent cardiovascular disease including shingles! The risk of stroke and sepsis (serious infections) were

significantly higher in the 12 months after getting shingles from this population study of over 13,000 cases of shingles! Yikes! Some researchers theorize that the shingles virus can actually infect arteries in the brain and others suggest that it creates a full body long-term inflammatory response that increases the risk of a number of cardiovascular problems. It's interesting that in this recent study it was found that even younger individuals had a much larger risk of stroke if they had shingles. This is scary stuff and another reason why I am a BIG, BIG FAN of the current and future shingles vaccines. Finally, I think the potential for another benefit could occur with shingles and that is a reduction in the risk of COLD SORES! What? Moyad has lost it (but he never had "it") and thinks the future shingles vaccine could prevent cold sores?! Yes, because cold sores are in the herpes virus family, which is a large family of viruses that also includes shingles. In fact, there are several studies now showing that there is an increased risk of being infected or bothered by one condition if you already have the other and vice versa. HOW MUCH FUN IS THIS STUFF (not shingles or cold sores but just this information is fun right?)!!!

I just love to talk about cold sores and shingles especially at the family dinner right after the family begins to take their first bite! It's really great watching everyone get sick or look horrified at the table (reminds me of the holidays). You should try this some time, it will definitely get the attention of everyone and it's also educational!

THAT'S ALL FOLKS…. See you in the SPRING, when I will write about many other serious issues and give timeless advice in the next newsletter, such as: why it's never good to carry a heavy, hard to manage chainsaw in a crowded male nudist camp, it's never good to talk about shingles and cold sores at the dinner table, it's never a good thing to hear a surgeon say "I can't find my glasses" right before you receive anesthesia as

a patient, it's never a good thing to take a laxative, a sleeping pill and a Viagra at the same time, and why it's never good to tell someone you love them and then burp loudly.

Fall 2015, Article 70

What the Heck Has Been Going on in My World?

By Mark A. Moyad, MD, MPH, University of Michigan

article #70 – Fall 2015

Note: A total of 70 (YES THAT IS 70 – I get tired just saying the word "Seventy") times in a row (and for 15+ years!) I have written and volunteered for this newsletter. I have yet to receive any personal financial compensation or personalized classic timeless gifts such as; a PAACT complimentary hightechnology toilet with dual flush handles and/or dual back-toback toilets, which means you can flush the toilet comfortably whether your left or right-handed or ambidextrous like me and/or you can go to the bathroom with the one you love, who you never want to be separated from even for a single second (twisted but I know some folks that would like this) or a PAACT bad manners alert alarm that makes a really, really loud noise when someone does something obnoxious and stupid like uses their cell phone in an elevator or presses the elevator retrieval button in the lobby more than once or someone tries to back their car into a parking spot to make it easier to exit at a later time while countless cars have to wait for this Bozo the Clown (aka derogatory term in this sense but otherwise a happy term when used to refer to my childhood) to pull this silly selfish parking move or when someone parks in a Handicap Spot that is not handicapped, but since they will "only take a minute" then somehow it is okay or someone decides that their big dog is so special he/she

DOES NOT need to have their droppings cleaned up by their owner with a bag! Remember this Moyad saying “Big Dog=Big Droppings & Small Dog=Small Droppings!” This is why I own a small dog people! Yes, I am still waiting for all of these free PAACT gifts (oh and a box of macadamia nut cookies – love those things, along with a couple hundred dollars that has a note on it that says “we love you so much just keep the money and use it for whatever you want because you are so dedicated”).

I WANT TO THANK YOU AGAIN FOR CONTINUING TO MAKE “THE SUPPLEMENT HANDBOOK” – my semi-new book a best seller. YEAH!! THANK YOU!!! Second, if you have not picked up a copy please get one on Amazon (the cheapest place to procure a copy) to support my beer and macadamia nut cookie fund! For about 20 bucks (the cost of only 20 one dollar lottery tickets) you get 512 pages of material on over 100 medical conditions and when not using this amazingly big book it also functions as a nightstand or coffee table book topic of discussion or a fly swatter or an awkward but effective Frisbee or Boomerang.

320) DONALD TRUMP!!!! (Actually he has nothing to do with this article but I just wanted to get your attention).

ALCOHOL IS A MASSIVE PROBLEM, is a clear carcinogen and increases the risk of countless diseases and disease recurrence. New research suggests it might even increase the risk of prostate cancer like it does with breast cancer and could make some prostate drugs less effective if you drink in excess. And, more fiber a day may keep the prostate cancer away! (Reference: Chhim A-S, et al. Am J Clin Nutr 2015, epub ahead of print. Moyad MA General Knowledge and The Supplement Handbook….)

BOTTOM LINE

Alcohol is a big problem and could increase the risk of prostate cancer especially in men with a low fiber intake, and

new research suggests more than moderate alcohol intake could reduce the efficacy of some prostate drugs!

WHAT ELSE DO I NEED TO KNOW?

What has 7 calories per gram and is arguably associated with more health problems than almost anything else in the U.S. that is legal? ALCOHOL!!!! I have often joked about my beer fund in the PAACT newsletter (as I did earlier) but somehow as funny as these jokes are I am beginning to feel guilty about them. Why? It's because alcohol has become such a massive problem here in the U.S. and around the world. Let's first talk about this study and prostate cancer and then talk about all the damage that alcohol does today. You may find yourself shocked at how much space I utilized on alcohol in this column, but after reading the whole story you shouldn't be shocked.

Alcohol is now a known risk factor for BREAST CANCER, but its impact on the risk of other hormone dependent cancers such as prostate cancer is unknown. There was a recent well-done prospective observational analysis, which included 3771 women and 2771 men that participated in a randomized multivitamin trial (SUVIMAX) and completed a minimum of 6 valid 24-hour dietary records during the first 2 years of follow-up. After a median follow-up of 12.1 years there were 123 prostate cancers diagnosed. Alcohol was not associated with the risk of prostate cancer overall. In a stratified analysis, alcohol intake was directly significantly associated with prostate cancer (37% increase, p=0.02) risk among men with low dietary fiber (less than 15 grams per day) intake but not among those with higher dietary fiber intake. Thus, the researchers concluded that dietary fiber intake could influence the association between alcohol intake and the risk of prostate cancer. It is for this and 1000 other reasons I have pushed for people to get 20-30 grams of fiber per day! Fiber is the "GREATEST INTERNAL BOTOX EVER INVENTED!" What do I mean by Botox? People use Botox to reduce the appearance of external

aging but how do you reduce the internal feeling of internal (inside the body) anti-aging? As we get older the inside of the body ages just as much as the outside and includes problems such as the following:

• Acid Reflux Increases

• Blood Pressure Increase

• Blood Sugar Increase

• Cancer Increase

• Cholesterol Increase

• Constipation Increases

• Diverticulitis Increases

• Heart Disease Increase

• Inflammation Increase

• Insulin Increase

• Unhealthy Gut Bacteria Increases

• Waist/ Weight Increases

BLAH, BLAH, BLAH! So, what has been known to reduce the risk of all those things mentioned above? Give me an F! Give me an I! Give me a B! Give me an E! Give me an R? WHAT DOES THAT SPELL? FIBER! FIBER! FIBER! I know you wanted to say “Go Blue” but that would have been a shameless plug and I am not known for shameless plugs (DON’T FORGET TO BUY A COPY OF MY LATEST BOOK ON AMAZON “THE SUPPLEMENT HANDBOOK”).

Dietary fiber appears to be able to reduce concentrations of higher circulating testosterone or estrogen by products or metabolites. Dietary fiber might also simply increase the number of healthy bacteria that can go on to reduce the impact

of testosterone on some cells. Dietary fiber through many of the benefits listed above from lowering insulin, blood sugar, cholesterol, weight, etc… appears to have anticancer effects especially when alcohol itself can increase the risk of many cancers. Now let's review the MANY MOYAD A to Z REASONS WHY ALCOHOL IS BAD ESPECIALLY IN EXCESS (buckle up I am about to suck up a lot of space and your time but please read the whole thing to understand why you had to read the whole thing to appreciate it)!

A="ALCOHOL IN MODERATION"???-SIZES INCREASED & SO DOES WEIGHT/WAIST SIZE.

I often semi-joke, but it's really not a joke when I say that if kids and adults cut their consumption of sugary soda and/or alcohol down to nothing, the obesity epidemic would be impacted almost immediately and dramatically. Some of the largest sources of calories in adults are now coming from regular alcohol consumption and many of us do not even realize it! This is because the definition or appearance of moderation has changed. Let me give you an example – I had a beer on tap yesterday and the bartender gave me a glass and DANG it was good! However, I noticed that the glass seemed a bit larger than many bar glasses and I asked the bartender how many ounces in that glass and she said "20-ounces"! This means while I thought I was consuming 150 calories of beer at 12-ounces, I was actually getting 250 calories of beer! Yikes! In one glass! Now, if you look at many of the common beer glasses at a bar they are no longer 12 ounces and in fact 12-ounce beer glasses are becoming obsolete. Most of them today are 16-ounces, which means it is providing 33% more calories per glass of beer compared to just 10 years ago! So, moderation with beer has always been 12-ounces of moderate alcohol beer but today most beer glasses are 16- or 20-OUNCES and ALCOHOL CONTENT OF MOST BEER HAS INCREASED WHICH MEANS THE CALORIE CONTENT OF BAR BEER HAS DOUBLED (combine the increased glass size with greater concentration of alcohol=more calories)!

This is crazy! In the old days (10- 20 years ago) if you had 1 drink at a bar it was anywhere from 100-150 calories per drink. No big deal! Today, it is more like 200-300 calories per beer! Now, imagine you have several beers that night and a few times a week for 52 weeks and you are now drinking massive amounts of calories per year that could easily increase weight 5-10 pounds or more! THEY CALL IT A BEER BELLY FOR A REASON!

Okay, now let's look at wine consumption! The last 5 times I have been out to dinner around the U.S. and someone poured a glass of wine for someone at my table and then I measured it (sounds annoying that I'm measuring a friend's glass at the table but this was for science) guess what?! IT WAS 8 to 10 OUNCES OF WINE. Remember 4-6 ounces of wine in moderation from the old days. Today, it's now 8-10 ounces, which means you are now DOUBLING YOUR CALORIE CONTENT PER 1 GLASS OF WINE!!!

Now, let's talk about a shot of hard liquor like vodka. When I go out with friends (not that I have that many friends because most people think I am a bit crazy because I like to do stuff like measure the fluid content of glasses at restaurants) I notice that a shot has become more like 2 to 2.5 ounces in many drinks in combination with something sweet such as a concentrated juice, which means the CALORIES FROM HARD LIQUOR HAVE ALSO DOUBLED! What the he double toothpicks is going on here! What's going on is that we have allowed a new standard for portion sizes when it comes to alcohol, so many of us are getting twice the number of calories from our drinks than we used to get just 5-10 years ago! Say Hello to WEIGHT and WAIST GAIN. So, what can you do about it? Just be aware of it and use the MOYAD METHOD! What is that? Is that where you let other people buy your drinks after you give them some relevant medical advice (that is one method)? It's where you go out and buy Italian size (as I like to call it) small glasses of wine that are only 4-5 ounces per glass! If you have been to Florence or anywhere in Italy and many places in Europe these small glasses are very common at restaurants and in homes. A

quick look on Amazon and other locations allows you to find the kind that you like and they will help control your intake and the intake of your guests. Also, you can purchase 12 ounce beer glasses and get used to that again as well as 1.5 ounce shot glasses. Again, when you have these in your home you REBOOT or become sensitive to glass and portion sizes when it comes to alcohol!!!

B=BLOOD PRESSURE INCREASES WORSE THAN SODIUM

Alcohol in moderation or small amounts can actually help to increase blood flow in the body by acting as a vasodilator (something that increases the size of the blood vessel to allow more blood flow), but in excess it acts as a VASOCONSTRICTOR – actually reducing blood vessel size and increasing blood pressure. It is for this reason that every 10 grams of alcohol (less than a serving size) increases blood pressure 1 point!!! So, several drinks and blood pressure increases can be quite staggering. Interestingly, this blood pressure increase is the SAME REGARDLESS OF THE TYPE OF ALCOHOL CONSUMED! This is why drinking above moderation especially if you have blood pressure problems is “DIPUTS” spelled backward!!!

C=CANCER/CARCINOGEN

Alcohol is a known carcinogen. Long-term exposure increases the risk of numerous cancers! It is well known that breast cancer increases with alcohol consumption and the latest evidence also suggests that prostate cancer or drugs that could prevent high-grade prostate cancer might be reduced by alcohol consumption. In the famous REDUCE trial using the drug dutasteride (aka Avodart) to prevent cancer in high-risk men, alcohol consumption (more than 7 drinks per week) actually appeared to eliminate the drug’s ability to prevent prostate cancer!!! This is somewhat similar to what was observed in the PCPT trial with the drug finasteride! Yikes! So this is what we now know that alcohol might or probably increases the risk

of the following cancers:

• Breast Cancer

• Colon Cancer

• Esophageal

• Laryngeal cancer

• Liver Cancer

• Melanoma

• Oral Cavity Cancer

• Pancreatic

• Prostate Cancer or at least reducing the efficacy of some anti-prostate cancer drugs

BLAH, BLAH, BLAH…this is enough of a reason to drink alcohol in moderation or not at all!

D=DEMENTIA or DESTRUCTION OF BRAIN CELLS

Dementia can occur from a variety of disorders including Alzheimer disease, vascular (such as a stroke) and from trauma such as a head injury. It is also well known now that excessive alcohol intake can cause permanent damage to the structure and function of the brain. This can be caused by reducing levels of thiamine or altering vitamin brain cells! Light to moderate drinking might reduce the risk of dementia, that’s the good news, but in excess look out because the risk of dementia or at least memory problems increases dramatically.

E=EXERCISE PERFORMANCE DROPS including worsening EF (erectile function)

Alcohol delays the ability to recover from workouts and

skeletal muscle injury or in other words for those work out fanatics out there or for those that exercise regularly (that should be all of you reading this column right now) it blocks the full benefits of exercise and delays recovery from injury! This is a bad combination! So, if you want to get the most from your exercise investment then don't drink in excess (or at all for some of you).

F=FERTILITY PROBLEMS

A number of studies already point to excessive alcohol consumption reducing sperm concentration and other potential fertility parameters, so if you want to have a baby then be careful with the adult bottle, baby!

G=GUT MICROBIOME GOES WACKY! Also don't forget GOUT!

New evidence is emerging that alcohol in excess can wipe out some good bacteria just like what is observed with long-term antibiotic usage! Yikes! So, with all this talk about improving your gut health through probiotics it's possible that one of the best ways to improve gut health is not to drink in excess! And, if you have ever suffered from an attack of gout you probably know that alcohol can increase your risk of a first and subsequent attacks of this inflammatory arthritis!

H=HISTAMINE/IgE INCREASE/ALLERGIES

Many alcohols today either contain compounds similar to histamine or activate histamine receptors or increase IgE levels (antibody that binds to the mast cell that helps trigger the allergic reaction)! In other words, it is summer time, spring time or any time of year and you are sneezing, your nose is running and your eyes are watering more than a Barbara Walters interview and you think it's due to an allergen like pollen from the outside! Well, it could be due to the alcohol that you are drinking!

I_3=INSULIN SURGES! IMMUNE SUPPRESSION! INFECTIONS! (The 3 biggies!)

Okay, diabetes increases the risk of many cancers and heart disease and increasing insulin may be the factor that feeds some tumors. So, it's interesting that alcohol, when it hits the pancreas, can increase blood flow to the beta cells that produce insulin so that more insulin is actually made and released! This is part of the reason that alcohol is associated with HYPOGLYCEMIA or lower levels of glucose temporarily! It's also this insulin release that increases the risk of weight gain and other health problems. And, if that was not enough of a reason to control your intake, it's also well known that alcohol can suppress immune function (why alcoholics have higher risk of pneumonia for example) and thus infections! Nasty infections too! Many folks are always looking for added ways to boost their immune system against cancer and one very good way is not to drink in excess.

J=J-SHAPED CURVE!

What does this mean? Well, a J-shaped curve or relationship suggests that in moderation there could be a slight reduction in some diseases (think about writing a capital letter "J") and after a certain minimum amount, increasing exposure leads to more and more health risks or diseases! It's for this reason that alcohol is known as the best example of a J-shaped disease risk curve or another way of saying that something has a J-shaped risk curve is the old saying "everything in moderation." However, instead health care professionals use words like "J-shaped curve" to make us or at least me sound more intelligent than I actually am.

K=KILLS TOO MANY

Alcohol is involved in about half of all traffic fatalities and it's otherwise estimated to be responsible or associated with 100,000+ deaths in the U.S.

L=LIVER DAMAGE/CIRRHOSIS

Enough said on this one!

M & N=MALNUTRITION/NUTRITION

Magnesium, thiamine, folic acid, potassium, vitamin C….is a list of nutrients that are reduced or that are metabolically impacted by alcohol consumption so they are not as effective, continues to grow! In other words, one of the best ways to reduce the effectiveness of a healthy disease preventing diet is to drink alcohol in excess. So, think of this another way, which is – alcohol in excess reduces the efficacy of your exercise and healthy diet!

O=OSTEPOROSIS & ORGANS DAMAGED FROM HEADTO-TOE

Alcohol is unique because it gets into cells by simple diffusion, which is why it's absorbed so rapidly from the stomach and intestine and can reach maximum blood concentrations in one hour or less! This is also why it's so toxic to almost every cell in the body and organ from the brain to bone cells and it's also why any freaking pamphlet you read today on osteoporosis will say that alcohol in excess increases the risk of bone loss and bone fractures. The cells that help produce bone are known as the osteoblasts and they get inhibited with excess alcohol exposure!

P=PREGNANCY?

Alcohol is the number 1 known preventable cause of developmental and physical birth defects in the U.S.!

Q=QUE or LINE OF SIDE EFFECTS FROM CANCER TREATMENT

You name the side effect of cancer treatment and it can get worse with excess alcohol. Bone loss? Yup! Weight gain? Yup! Anxiety, Stress and Depression? Yup! Yup! Yup! Hypertension? Yup! Cholesterol and blood sugar problems? Yup and Yup! Hot flashes or night sweats? Not well-studied but in my

experience? Yup! Fatigue? Yup! Insomnia? Yup! Do I really need to continue? Nope!

R=RUNNING TO THE RESTROOM?

Alcohol is a diuretic and inhibits a hormone that helps you retain and absorb water. Whether it's an overactive bladder (OAB) or stress incontinence, you name it…you might find yourself running to the bathroom more at night with alcohol. This has become very common because alcohol makes it hard for the bladder and urine to stay put so to speak in the middle of the night.

S=SLEEP CYCLE DISTURBANCES

It's well known now that alcohol is a sleep inducer, so it helps you to fall asleep, but once you are asleep it disrupts your sleep cycle and doesn't let you spend as much time in the deeper phases of sleep. This is the reason many drinkers use alcohol to fall asleep and get plenty of sleep, but they don't feel well rested the next day! Imagine if there was a commercial on TV about a drug and the advertisers claimed that it helped you fall asleep faster, but did not allow you to sleep better overall and actually made you drowsier the next day, would you buy that drug? If you would, I have swampland in Michigan with gold in it that I want to sell you! And, if that was not enough, alcohol can also increase nasal and pharyngeal resistance, which can make breathing more difficult and is why sleep apnea can also get worse in those that drink alcohol.

T=THIRD LEADING CAUSE OF PREVENTABLE DEATH & THIRTEEN!

Alcohol and alcohol abuse are now the third (smoking and overweight/obesity are number 1 and 2 but obesity is arguably number 1 now) leading cause of preventable death in the U.S. and one out of every 13 Americans abuse alcohol or are addicted to alcohol. Yet, alcohol is associated with tobacco use and weight gain, so this is a bad problem.

U=UNDERAGE DRINKING INFLUENCES

Research in the past suggested that parents that give their kids alcohol underage might be reducing the glamour of drinking so that when the kid becomes an adult they are less likely to abuse alcohol. However, more extensive and recent research suggests otherwise. Parents that permit underage drinking appear to increase the chances that kids will abuse alcohol. I agree with this because so many parents and grandparents are now abusing alcohol and appear to be SELF-MEDICATING with alcohol and, in time, the kids could be doing the same thing because it becomes so permissive in the household. So when parents drink in excess, the kids have a greater chance of drinking in excess.

V=VIOLENT INCIDENCES

Over half of the violent incidents involving adults are alcohol-related!

W=WITHDRAWAL

Alcohol is a central nervous system depressant and just like drugs that have the same action (like Xanax…) they cause the release of a compound in the brain known as GABA (relaxing compound – reduces excitability and calms things down in the brain). However, with repeated hits or exposure to alcohol the brain begins to adapt to this alcohol intake, which results in HIGHER DOSES OF ALCOHOL needed to get the same result. It’s for this same reason that when individuals begin to drink more and more over time, it takes or intoxicated. And, when alcohol is slowly or quickly removed, it then causes symptoms that are the opposite of GABA or relaxation effects. It’s for this reason that alcohol withdrawal can lead to anxiety, insomnia, increased pulse, respiration, blood pressure, body temperature and even a hand tremor. Withdrawal symptoms usually begin 8 hours after blood alcohol levels decrease, peak after 3 days and are reduced from days 5 to 7 of quitting. In a small

percentage of people (3-5%) grand mal seizures and severe delirium can also develop. So, if you don't think that alcohol abuse is classic drug abuse, then please reread this paragraph.

X=X-RAYS?

We worry all the time about radiation from x-rays and other devices causing harm (and they can) or increasing our risk of cancer or cancer returning, but this doesn't come close to the number of people injured or killed daily from alcohol or from the number of people that increase their risk of cancer daily from alcohol ingestion.

Y=YOUNG (& OLD)

One of the greatest gifts you can give to young people is to set an example and show responsible alcohol intake or no intake. Alcohol and UV light are the 2 carcinogens that young people have a tough time appreciating and being thoroughly educated on, which is why melanoma rates are at an all-time high in the younger population and so is binge drinking. Binge drinking is a pattern of drinking that brings a person's blood alcohol level to that of being legally drunk (4-5 drinks in less than 2 hours). And, although it's more common in younger age groups, it's arguably getting to be as bad in those age 65 and older. So, the age group with the most binge drinkers in 2015 is 18-34 years but the age group that binge drinks most often is 65+ years! Yikes!

Z=Zorro Zero Alcohol Moyad Challenge!

What the heck is this?! If you have read this entire article congratulations. Now I want to challenge you for a second. Try stopping all alcohol intake for just 1 month and see what happens! Many people can't do it, but many that have taken this challenge have told me they lost weight, sleep better, have better memory, better sex and more erections, enjoy life more…. I will never quit my moderate alcohol intake, but when

I stopped for a month I quickly realized that my energy levels especially in the morning skyrocketed! Conversations were more pleasurable and sleep was an absolute pleasure. I thought well since I challenge people and patients to quit all alcohol for one month then why shouldn't I try it! You should too! Let me know what happens! YOU MAY BE ASKING YOURSELF BY NOW WHY MOYAD SPENT SO MUCH SPACE OF HIS PRECIOUS FABULOUS AND FANTASTIC COLUMN WRITING ABOUT THE BAD IMPACTS OF ALCOHOL ON HUMANS. IT'S BECAUSE WITH ALL OF THE EMPHASIS ON MEDICAL MINUTIAE TODAY AND LESS COVERAGE OF HEALTH ITEMS THAT REALLY CAN MAKE OR BREAK THE LIFE OF AN ADOLESCENT OR ADULT IN A SHORT PERIOD OF TIME, I SIMPLY DECIDED AFTER 30 YEARS SOMEONE NEEDS TO ADDRESS THIS EPIDEMIC OF ALCOHOL ABUSE IN THE U.S. AND, IT'S A PROBLEM IN SOME CANCER PATIENTS, SO IF AFTER READING MY A-TO-Z LIST OF ALCOHOL-RELATED PROBLEMS IT HELPED YOU OR SOMEONE YOU LOVE OR SOMEONE YOU DON'T LOVE AT ALL, THEN IT WAS WORTH IT (actually I already know it was worth writing about alcohol, so I was just being somewhat rhetorical folks). **Take the Moyad Challenge! Try to eliminate all alcohol for 1 month of your life and see what you learn from this experience because mentally and/or physically it may change your life forever!** Thank you and now back to my regularly scheduled and twisted column (actually the next story is also somewhat related to the alcohol story we just covered)!

321) There are now more obese Americans compared to overweight Americans for the first time in American History! (Reference: Yang L & Colditz GA. JAMA Internal Medicine 2015)

BOTTOM LINE

We did it! There are now more obese Americans compared to overweight Americans for the first time in American History! New U.S. statistics shows nearly 70% of adults are at an unhealthy weight.

WHAT ELSE DO I NEED TO KNOW?

This was data derived from the National Health and Nutrition Examination Survey or NHANES (conducted by CDC – basically you the tax payer paid for this study so read on in order to get your money's worth), which are cross-sectional estimates which included only adults who were 25 years or older. A total of 67.6 million Americans were obese (BMI of 30 or greater) and 65.2 million were overweight (BMI of 25-29.9) as of 2012. Approximately 40% of men and 30% of women were overweight, and 35% of men and 37% of women were obese.

This report documents for the first time in American history that Americans who are obese currently outnumber those who are overweight. Approximately 75% of men and 67% of women ages 25 and older are currently overweight or obese versus 20 years ago when it was 63% of men and 55% of women. This situation is becoming chaotic in a sense, because a quick review of some of the greatest epidemics in the U.S. that utilize most of the health care dollars and arguably medication spending/utilization is riding on the heels of this epidemic. Whether it's fatty liver, low testosterone, high cholesterol, hypertension, gout, stones, sexual dysfunction, and most other prevalent conditions, are all dramatically impacted by weight gain. IN FACT, RESEARCHERS ARE BEGINNNING TO AGREE THAT OBESITY INCREASES THE RISK OF AGGRESSIVE PROSTATE CANCER AND OF PROSTATE CANCER RETURNING AFTER TREATMENT! Perhaps it's time to increase the education and options delivered to patients and bring back mandatory physical education classes for K to 12th grade in all 50 states. The bottom line is that we are at the bottom line and need help.

PS. There are now medical conditions in 2015 that we never thought would be associated with obesity and now appear to be even more of a problem with weight gain. What are those issues? I'm glad I asked myself that question! An increased risk of IOP or intraocular pressure, which could then lead to eye damage! Even recent studies of "blehparoptosis"=droopy upper eyelids and sagging eyelids. What's next? Oh yeah, by

the way it also reduces life expectancy (did I mention that important point?). It’s funny that prostate cancer researchers argue the impact of obesity on cancer risk and have disagreements on whether it greatly increases the risk of cancer recurrence or moderately increases blah, blah, blah. However, this is like arguing whether or not a bee in your car is more likely to sting you while you are driving 100 MPH toward a cliff?! What?! The point is that you are in a car driving 100 MPH toward a cliff! It’s like arguing whether or not you jump out of an airplane with no parachute, with a storm nearby, will increase your chances of getting hit by lightning?! What?! The point is that you just jumped out of an airplane with no parachute! Okay, these are crude and sick examples but since I am crude and sick, I love these analogies.

322) BeetRoot Juice – the new legal exercise enhancing drink?! Maybe, so why not try it! It might have mini- Viagra-like effects – YEAAAHHHHH!!!! Party time! AND, using lots of dietary supplements can actually reduce the beneficial effects of exercise! 2 FREE STORIES FOR THE PRICE OF 1 (wait does that make cents?). (Reference: Lee J-S, et al. Am J Physiol Regul Integr Comp Physiol 2015)

BOTTOM LINE

15 days of drinking 70 ml of beetroot juice per day increased blood levels of nitrates and nitrites, appeared to reduce systolic and diastolic blood pressure and could delay the onset of fatigue in those that exercise! If this helps anyone reading this column then I’m one happy dude! Oh and by the way, if you are taking lots of supplements to enhance your exercise workout you may be hurting yourself!

WHAT ELSE DO I NEED TO KNOW?

Move over pomegranate juice!? There is a new juice in town that in very small amounts could improve exercise performance.

As you know I am not a fan of many juices, especially fruit juices, because they are just LIQUID SUGAR, loaded with calories and are not generally associated with improved heart health. However, small amounts (even 2-3 ounces) of beetroot juice could be an exception to the Moyad rule (kind of like the exception to the rule I have of dogs sleeping on my bed unless it's my dog Chauncey because he's not only tiny but cute and cuddly. My wife loves him very much so I have no choice in the matter anyway)! You may remember from a previous column that beetroot juice was utilized by the Auburn football team to legally enhance their athletic performance. Some people thought they were a bit wacky, but it seems they might not have been so wacky overall!

As a quick review beetroot juice is one of the largest sources of dietary nitrate found in food, which means it can be converted in the body by bacteria to nitric oxide (NO), which can widen blood vessels and increase blood flow to various parts of the body including the sexual organs (aka penis and vagina for those that cannot pick up on ridiculous politically correct language) and skeletal muscles…and increase oxygen delivery to these areas. This was a small study of young men, but it's essentially similar to what has been observed in older men (aka "seasoned men" for those that are offended by the term "older")! Men were randomly assigned to 70 ml a day of beetroot juice or a placebo juice (nitrate reduced) for 15 days and then they crossed-over to the other group and drank the other juice for 15 days. A variety of measures showed improved potential oxygen delivery, which is what several past studies have found. Remember that the ability to exercise effectively is reduced with a variety of diseases such as heart disease and hypertension or anything that impairs adequate blood flow and nitric oxide to the muscles. Perhaps beetroot juice will be one of only several legal options to really enhance exercise! My favorite options right now are caffeine, protein powder and small amounts of sugar from tootsie rolls or jellybeans when working out! Now I may add

an occasional sip of beetroot juice! Remember when working out for 30, 45 or more minutes the body needs some glucose (jellybeans), improved blood flow (beetroot juice), enhanced attention and performance and reduced muscle fatigue (caffeine from a few sips of diet cola or coffee), and also improved protein synthesis for muscle development (protein powder after the workout). Otherwise LESS IS MORE! Why? Keep reading my friends, family and enemies and lovers (actually I just have one lover and that is my wife and she only has one lover also, and that's our dog because I am now convinced she loves that dog more than me – I mean she scratches his belly and calls him cute names constantly and that's what she used to do for me – sorry I digress, but darn that dog! That dog is my nemesis and I must find a way to defeat him to win back the love of my wife!).

There is new research to suggest that contrary to previous thoughts that supplements could improve exercise performance. There is now a growing amount of evidence to show that most individual dietary supplements (C and E…) in large amounts on a regular basis could actually block or disrupt cell signals in muscle tissues, which could also block adaptations to training or essentially reduce the beneficial effects of exercise! I actually subscribe to this theory (not all supplements but many supplements). There are some studies now also suggesting that supplements not only shut down some important cell signaling pathways but they also decrease the production of new muscle mitochondria (the powerhouse energy producers of each cell) and blunt internal or body production of its own antioxidants! In the past, one way to get folks excited about taking supplements in many situations was to mention that exercise and many diseases create free radicals which can potentially damage cells of the body, but it appears that temporary free radical production from exercise is a good thing and is one of the triggers of the human body to begin to increase its own production of endurance and fitness molecules and cellular changes that are ultimately healthy. In other

words, free radical generation from exercise is a key signal to tell the body that you are actually exercising and that intrinsic body mechanisms are activated in this manner to improve future muscle performance! So, a supplement that can "block free radicals" basically could also be telling your body that you are not exercising when you actually are exercising by soaking up all those free radicals needed to activate the intrinsic body mechanisms! YIKES!!!!! It's for this reason I take few supplements for working out and instead take my jellybeans, caffeine from a beverage, protein powder and occasional beetroot juice when I exercise and leave the rest up to God (so to speak).

323) MEDICARE & MEDICAID turns the Dr. Moyad age of 50! Feel free to send gifts of money and praise to me and not MEDICARE for example. Why are we still happy but confused about MEDICARE and why are some cancer drug prices so ridiculously high? (Reference: Moyad MA, 2015)

BOTTOM LINE

People are still confused about Medicare. Reviewing the basic information now and in the future can make your life a lot easier and save you a lot of money that you can eventually just send to me! Oh, and the people will change drug prices and not the politicians in my not so humble opinion.

WHAT ELSE DO I NEED TO KNOW?

The Social Security Amendments of 1965 (the year I was born and my parents and brothers became the luckiest people on planet earth – no worries I remind them of this fact weekly and they also remind me weekly that I am delusional) helped to create Medicare and Medicaid in the U.S. Medicare is a federal program that provides health insurance to folks aged 65 years and older and younger people with permanent disabilities. So, let's focus on Medicare a bit. Medicare turned 50 in July and over 90% of the over 55 million enrolled in the program

(according to a recent Kaiser Family Foundation poll) say that their experiences with this program have been positive. However, the biggest issue it that folks are still confused as to what it does and does not provide. Remember the following when it comes to 4 parts of Medicare (A, B, C and D):

–**Medicare Part A** covers hospital stays, short-term stays in skilled nursing facilities, some home health care and hospice care. Most do not have to pay a premium for Part A.

–**Medicare Part B** covers doctors' visits and other outpatient services such as medical equipment, laboratory tests and some preventive care including vaccinations and some cancer screenings. It usually requires you to pay a monthly premium.

-Both Part A and B (also called "original or traditional Medicare") could have co-payments or deductibles, so if you are still working and receiving insurance coverage from your employer, you should think about delaying your enrollment in Part B because your current income could essentially lead to higher premiums. So, essentially you pay for Part B and you pay if you want to add supplemental insurance, for example to help cover the cost of prescription drugs or dental or vision services. And, keep in mind that Medicare does not cover long-term care (despite the fact that the majority of folks my age will eventually need it and are not looking into their options on this now)!

–**Medicare Part C** is also known as "Medicare Advantage" and it allows folks to enroll in private health plans, such as HMO to receive Medicare covered benefits. These Medicare approved private plans provide all benefits covered under Parts A and B, and many plans offer other benefits like vision and dental services. The majority of these private plans also provide prescription drug coverage (Part D). Also, Medicare Part C plans are required to place a ceiling or limit on beneficiaries' (for example out-of-pocket expenses for A and B covered services of 6700 dollars in 2015). However, there is

no out-of-pocket limit in traditional Medicare (A and B). Some of the disadvantages of Medicare Part C are the potential for restrictions to doctors that are only in the network, requirements for a primary care doctor referral before being able to see a specialist, and the potential for a higher monthly premium versus traditional Medicare.

–**Medicare Part D** covers outpatient prescription drugs for those who enroll in Medicare-approved private drug plans (either stand alone for those in traditional Medicare or Part C-Medicare Advantage drug plans).

-Medicare only pays for medically necessary nursing home care such as help with IV medications and wound care. In order to qualify for skilled nursing home care patients need to have had a recent inpatient stay of 3 or more days, be in need of skilled care for a medical condition associated with their hospitalization, and then obtain the skilled care from a facility that is Medicare certified.

-Again, Medicare does NOT pay for LONG-TERM nursing home care for assistance with daily activities, such as using the bathroom or eating. Patients needing these services could qualify for financial help from Medicaid. A good source on paying for long-term nursing home care is found at longtermcare.gov (THIS IS A REALLY GOOD SITE).

Talk to a financial advisor or look into the many apps that insurers now have where consumers can put in their medications and compare coverage costs! Also Medicare.gov is a decent web-site folks!

Hopefully this has helped a little bit with Medicare. Here is an interesting fact – many doctors and most medical students from surveys were opposed to Medicare when it came out but this was based on bad education. In fact, only a small percentage of students even read the act and understood what it did and did not do, and were responding to outside

informational sources. I hope the Affordable Health Care Act ends up with the same fate despite all the initial negativity (who knows? Now, does this mean I was for or against Obama Care? Good question…OOPS – sorry folks we have run out of time on this issue so perhaps next time we can address it).

So, why do some cancer drugs cost so much and cannot be reduced in price like in some other countries? Please read the next story and find out why you are the only major hope of bringing drug prices down to an affordable level!

324) Melanoma rates have doubled over the past 10 years! What does this mean for prostate cancer? A lot, because immune therapy drugs are getting approved in metastatic melanoma that are now being tested for prostate cancer in clinical trials. (Reference: Melanoma review articles. Kwon ED, et al for CA184-043 Investigators. Lancet Oncol 2014;15:700-712.; http://www.usatoday.com/story/opinion/2014/04/20/medicare-part-d-prescription-drug-pricesnegotiate-editorials-debates/7943745/ ;
and http://www.medscape.com/viewarticle/845707)

BOTTOM LINE

Right now, melanoma immune therapy drugs are being tested in prostate cancer and show a lot of promise, so talk to your doctor about the ongoing research and clinical trials. However, the catch – the prices of these drugs, are not borderline insane but COMPLETELY INSANE! And, do you pay less if you are not obese?

WHAT ELSE DO I NEED TO KNOW?

Prostate tumors are often observed by pathologists to be surrounded by human inflammatory cells, which suggest the body did mount some kind of personal immune response to this tumor. And, this is also observed with some standard treatments that are not considered immune drugs. For example, LHRH or hormone suppressive drugs also seem to create some kind of moderate

immune response by the body! Amazing! So, if researchers can amplify that response or help the body fight cancer even more, perhaps this could be a big breakthrough. Let's look at some of the melanoma drugs in clinical trials and the ones you should talk about with your docs, because clinical trials keep opening up and new research on some of these drugs will appear this year. Ipilimumab (also known as "Yervoy®" from the company Bristol-Myers-Squibb. By the way "Yervoy" sounds like the name of a Pirate Ship or something that a Pirate says that is going into the ocean to collect or seize "booty" from innocent people) is FDA approved for metastatic melanoma. Ipilimumab is a fully human monoclonal antibody that binds to something known as "CTLA-4," which then allows greater anti-cancer activity by your immune system. However, there was a phase 3 trial of this drug compared to placebo of men with CRPC that had failed docetaxel treatment and it did not appear to work better than placebo. Still, to say it failed is really not fair because it did find improved survival but the statistics were not significant, but about as close as I have seen in a trial of being significant (it was p=0.053 and if it was less than p=0.05 it would have been significant or looked at in another way there needs to be a more than 95% chance the results were accurate and showed a benefit with the drug and in reality there was a 95% chance but not a 96% chance, etc…SO, SO CLOSE!!!).

Yet, another look at this study showed something quite interesting. When researchers took a further look at the research there appeared to be a survival benefit for the patients that did not have prostate cancer in their body organs. Amazingly, there is another phase 3 trial (called "CA184-095; ClinicalTrials.gov NCT01057810) going on that is looking at the effect of this drug before chemotherapy and prostate cancer patients are asymptomatic or minimally symptomatic without visceral/organ disease. What all of this suggests is that the potential for a benefit with this immune drug appears to be greater in men with a better prognosis or

cancer that has not spread as far around the body. In the ongoing prostate cancer trial with Yervoy, patients will receive an IV dosage (10 mg/kg) every 3 weeks for up to 4 doses (induction phase) and then every 12 weeks (maintenance phase). Results are expected any time! Currently for melanoma Yervoy (3 mg/kg) is given as an IV drug (over 90 minutes) about every 3 weeks. Still, the side effects of this drug are more serious compared to other drugs and these basically all evolve around the possibility (although fairly rare in terms of serious toxicity) that the body also attacks itself and not just the tumor. It's for this reason past studies have shown that some patients experienced inflammation of the colon, liver, skin, nerve issues and other problems. However, it's possible that developing a certain side effect with these drugs (we do not yet know about this one) could be a predictor of a better clinical response to the drug! There are other FDA approved drugs for melanoma and one is called "Keytruda®" (also known as "pembrolizumab" from Merck) and the other is known as "Opdivo®" (also known as "nivolumab" approved by FDA in December, 2014 for melanoma from Bristol-Myers Squibb) and these drugs are known as "PD-1 INHIBITORS" because they target the PD-1 receptor, which really means they also help improve the immune response to tumors and allow the body a better chance of fighting cancer. They may also have more or similar efficacy and less side effects compared to Yervoy, but this needs more research. Keytruda is also given as an IV drug (over about 30 minutes) and right now is usually given every 3 weeks for melanoma patients. And, Opdivo is also an IV drug (over about 60 minutes) that is given usually every 2 weeks. Interestingly, a recent publication found that for patients that had a cutaneous or skin side effect (itching, redness…) from the drug Keytruda for example there appeared to be a better response to the drug. The excitement and the great news is that the combination of 2 drugs for melanoma is far greater than either drug alone, so for example the combination of Yervoy with Opdivo! Amazing! And, I know some more desperate prostate cancer patients that are being treated with these

drugs right now off-label and are willing to pay for it! Wow!

Now for the real catch! The cost! The cost of some of these drugs are insane, so it's critical to have an open discussion in the future of how to control these costs so that the average American whose name does not end in Trump or Rockefeller or Gates, etc. can also afford them. Additionally, we need more patients and health care professionals to not be afraid to take some kind of stand on rising drug prices. This happened recently with a number of oncologists signing a document that basically said some (not all) of these drug prices are getting out of control. I am asked all the time why Medicare cannot negotiate drug prices like most countries around the world. This is due to a ruling put in place with Medicare Part D a while ago (Medicaid and VA can negotiate). However, this ruling now looks silly and needs to be reevaluated. I have found that many good pharmaceutical companies are open to this discussion and new ideas, but we have to get the conversation started and it will not help if we whisper but SPEAK LOUDLY AND WITH COMPASSION AND SENSITIVITY. So, I will help in leading a future effort with some of my friends and colleagues on requesting a reevaluation of some of the prices of cancer drugs! Stay tuned!

PS. Are you ready for another crazy Moyad observation (besides the fact that my nose is too big and I should leave my job and become an international male model or sex symbol)? Many drugs are given in milligrams per kilogram of body weight (mg/kg body weight), which makes sense, but insurance and/or you are charged for the amount of drug given in cents based on this weight. So, if you are given a melanoma drug in milligrams of drug per kilogram of body weight and you weigh 90 kilograms versus 70 kilograms then you could theoretically and realistically pay a heck of a lot more for your drug!!! I can't make this S_____ UP! (Note the "S"____ used previously represents the word "Stuff"). For example, it costs roughly 28.78 per single milligram (mg) for Opdivo, 157.46 for Yervoy

and costs 51.79 per milligram for Keytruda. And, say you are getting a 10 mg per kg infusion of Yervoy (standard used in prostate cancer clinical trials) then you cost 31,492 dollars more per infusion compared to a 70- kg person, but this is just the difference and not the total cost. For example, a 90 kilogram person would cost 141,714 dollars versus a 70-kilogram person at 110,222=total difference of 31,492 dollars! That seems crazy! All of this stuff seems crazy! I need a Dairy Queen Banana Split at 520 calories to relax and feel better and understand all of this stuff, because you have to be bananas to understand this stuff!

THAT'S ALL FOLKS…. See you in WINTER, when I will write about many other serious issues and give timeless advice in the next newsletter, such as; why it's never good to be the man that jumps in Lake Michigan in January right before doing a nude photo shoot, unless you feel really comfortable with your manhood or why it's not smart to eat a pound of asparagus before submitting a urine sample to your favorite health care professional that you never ever want to offend!

Article #69, Summer 2015

What the Heck Has Been Going on in My World?

By Mark A. Moyad, MD, MPH, University of Michigan

article #69 – Summer 2015

A total of 69 times in a row (and for 15+ years!) I have written and volunteered for this newsletter, and I have yet to receive any personal financial compensation or personalized

classic timeless gift s such as: a PAACT complimentary concert tickets to see a Justin Bieber concert or a back stage pass to meet Miley Cyrus (wait I don't even want those things), a package of Double-Stuff Oreo Cookies (amazing), McDonalds French Fries (doubly amazing), Five-Guys Junior Hamburger (triply amazing) or a Del Taco baby Burrito with extra green sauce (quadrupley amazing) and finally a free PAACT state-of-the-art elliptical or treadmill machine and church pew because after I eat all that stuff (aka junk food that tastes incredible) I will need a few hours to run it off and pray real hard that it does not stick to my belly, coronary or penile arteries forever!" YIKES!!!

FIRST AND FOREMOST I WANT TO THANK ALL OF YOU FOR MAKING "THE SUPPLEMENT HANDBOOK" – my new book a best seller in the winter and spring of 2015! AN AMAZON BEST SELLER!!! YEAH!! THANK YOU!!! Second, if you have not picked up a copy please get one on Amazon (the cheapest place to procure a copy) to support my beer fund! For less than 20 bucks you get 512 pages of material on over 100 medical conditions and when not using this amazingly big book it also functions as a beer coaster or a potato chip or pizza plate holder when you're watching the big game on TV (or for those in my kids generation – watching the big game on your computer or phone (because 20 years from now someone is going to read this column and ask "What is a TV"?). NOT BAD!

314) If you cannot tolerate your statin/cholesterol lowering drug or need to go to a lower dosage of a statin drug because of side effects then Zetia (ezetimibe) is NOW an option and it's also being studied as an anti-prostate cancer drug! How groovy/awesome is that!

BREAKING NEWS!

(Reference: IMPROVE-IT Investigators. New England Journal of Medicine, published on June 3, 2015.)

BOTTOM LINE

LOWER IS BETTER! The combination of a statin drug with ezetimibe (also known as “Zetia”10 mg per day) resulted in a greater reduction of LDL (aka “bad cholesterol”) and reduced cardiovascular events greater than a statin alone. Side effects including muscle, gallbladder, and liver side effects and rates of cancer, over the course of the clinical trial, were the same in both groups (a good thing). It’s also being studied right now against prostate cancer but this is very preliminary.

WHAT ELSE DO I NEED TO KNOW?

Ezetimibe (Zetia) blocks the absorption of cholesterol from food/intestines and it’s a prescription drug. Someone can expect to get a 15-25% reduction in LDL with one pill of ezetimibe (not bad). However, here is the most recent, fabulous news! JUST PUBLISHED clinical trial data (called “IMPROVE-IT”) with statins have actually found a moderate positive impact on clinical endpoints and not just cholesterol values with ezetimibe. This should increase the use of ezetimibe immediately in those patients with problems taking statins or higher dosages of statins and reignite the discussion of a “lower is better” philosophy, because in high-risk patients ezetimibe and simvastatin lowered LDL to almost 53 mg/dl compared to approximately 70 mg/dl in simvastatin only participants. TELL ME MORE!!! (Okay, when you see all CAPS in texting it means you are YELLING – so I WILL STOP YELLING AND TELL YOU MORE!). The IMPROVE-IT trial was more specifically a double-blind, randomized trial of 18,144 patients from 1147 medical centers in 39 countries who had been hospitalized for an acute coronary syndrome (acute heart attack or high-risk unstable chest pain) within the previous 10 days. Th e combination of simvastatin (used to be known as Zocor-a statin drug) at 40 mg and ezetimibe (again Zetia) at 10 mg was compared to simvastatin (40 mg) by itself. The primary endpoint of this trial was the combined end point of

cardiovascular death, nonfatal heart attack, unstable chest pain needing re-hospitalization, coronary revascularization (procedure like bypass or stent placed 30 or more days after randomized in the trial) or nonfatal stroke. The average age of the participants was 63-64 years of age (50 years or older to be eligible), 76% were male, 84% were Caucasian, 61% had hypertension, 27% had diabetes and 33% were current smokers! Additionally the mean BMI was 28, which is overweight, and the mean LDL was 84 mg/dl before they the trial started. YIKES!!! Apart from the fact that they already had a low LDL, these were not the healthiest group of boys and girls. In fact, I was really disappointed that the researchers and the editorial in this New England Journal of Medicine article point out that this group as a whole was very unhealthy. And, apart from the higher smoking rate this group is actually reflective of the U.S. population! DOUBLE YIKES!!! Okay, back to our story boys and girls and dog (my dog Chauncey is watching me while I'm typing this article probably, wondering why PAACT has never given him a free official PAACT bone, squeeze toy or squirrel look alike)!

The median follow-up in this clinical trial was 6 years and the LDL cholesterol average at the end of the trial was 54 mg/dl in the combination statin-ezetimibe group and 69.5 mg/d in the statin only group. The rate of the primary endpoint at 7 years was 32.7% in the combination group and 34.7% in the statin only group, which is only an absolute difference of 2 percentage points but this was still significant (p=0.02). Muscle, gallbladder, and liver side effects and cancer were similar between the two groups. Discontinuation of the medication in either group because of side effects was approximately 10-11% (again no difference). However, in reality compliance was a big issue throughout the trial because 42% of the participants in IMPROVE-IT (combination or statin alone group) stopped their study medication prematurely (for any reason), which is about 7% per year, which actually closely resembles what has been observed in other trials! In

other words, it’s not the side effects that are causing patients to stop these drugs but the lack of compliance (boredom, forget, don’t like it, would rather be watching Tiger baseball or Michigan football, travels a lot… blah, blah, blah). I make fun of this but with lifesaving drugs or even supplements that help it is hard to find folks that will take pills almost all the time. So, this is why I always say that I love it when someone does not qualify for taking any pills because they are so healthy because pill taking is a PAIN IN THE GLUTEUS MAXIMUS (aka “buttocks” as Forest Gump used to say…and “Life is Like a box of chocolates – you never know what you are going to get unless of course you see the one in the box with nuts in it before you bite it then you know it is going to taste great!” Sorry I digressed!

BACK TO THE STORY….Adding ezetimibe lowered LDL by 24%. Keep in mind that no differences between the groups were found for death from cardiovascular disease or death from any cause (cancer…), but significant reductions were found in the combination group for the rates of heart attack and ischemic stroke [113]. This is a credible finding since the differences began to emerge after 1-year into the trial and it was only conducted for about 6 years (not a long time actually). Thus, overall it represents a moment where a non-statin therapy to reduce LDL can also reduce cardiovascular outcomes (something missing with niacin, and others). It appears that lower is better, and had these patients started with higher LDL levels arguably even better results would have been observed. It is also interesting that in the combination group the reduction in the inflammatory blood marker hs-CRP was also significantly reduced compared to the statin only group. This is part of the reason that I believe ezetimibe should continue to be studied against breast and prostate cancer marker.

Still, the IMPROVE-IT trial offers important new evidence for the “LDL Hypothesis” that lowering of this blood marker is the primary driver of what changes cardiovascular risk (after the

first year of the study the LDL was 53 mg/dl in the combination group and 70 mg/dl in the statin only group. I know that there are many nice folk out there that want you to believe that cholesterol has nothing to do with heart disease and I think you know how I feel about that, which is similar to how I feel when Michigan State or Ohio State beats Michigan in any sport (it is just plain wrong). Despite just a 2% difference in the primary endpoint in favor of the combination group, this is almost identical to what would have been predicted from past trials based on the LDL difference!

Again, offering more evidence for the LDL hypothesis. Ezetimibe was being studied by Harvard researchers in their laboratory, and they found preliminary evidence years ago that it may have some anti-prostate cancer effects. Regardless, this drug represents new options or hope for those that cannot achieve their target LDL with diet, exercise and statins. This also offers hope for new medications in the pipeline such as "PCSK9 inhibitors" that reduce LDL via reducing/blocking LDL receptor removal to allow for more LDL to be cleared from the circulation, and these agents have the ability to lower LDL (bad cholesterol) as much as 60%. ZOWIE BATMAN! However, the problem with these drugs is that they are supposed to be given by subcutaneous injection once every 2-4 weeks, and with overall compliance in the IMPROVE-IT trial not being very good, this is not a good sign of future drug compliance if PCSK9 blockers work. Personally, I don't get excited about sticking myself with a needle every few weeks unless of course it helps me with my…you know what down there…. in my pelvic region! I mean my wallet or helps to make me more money! What were you thinking I was thinking???????!

315) Statins don't work in women? Hmm really? BREAKING NEWS!(Reference: Wang A, Aragaki AK, Tang JY, Kurian AW, Manson JE, Chlebowski RT, et al. Statin use and all-cancer mortality: prospective results from the Women's Health

Initiative. J Clin Oncol 2015;33 (suppl; abstr 1506). & THE SUPPLEMENT HANDBOOK by Dr. MOYAD (Hey I know that dude he is the one that I love to love…okay I made that part up…but my new bestselling book is real.)

BOTTOM LINE

Interestingly, at the time of this chapter's submission, data from the noteworthy Women's Health Initiative (WHI) clinical trial was released at the annual American Society of Clinical Oncology (ASCO) meeting (again the largest cancer meeting and it is held in Chicago – the place with the big tower and beautiful winters). **The study enrolled women aged 50-79** from 1993-1998 at 40 U.S. clinical centers. There were a total of 146,326 participants with a median follow-up of 14.6 years. A total of 23,067 incident cancers and 3,152 cancer deaths were observed. Numerous confounding variables were adjusted for, and compared with those that never used statins, those that did use statins had a significant 22% reduction in cancer mortality. The reduction in cancer death was not associated with statin potency, duration or type of statin itself. **Current statin use was associated with significantly reduced mortality of numerous cancer types, including breast, colorectal, ovarian, digestive, and bone/connective tissue cancer deaths.** Interestingly, statin use was not associated with a decrease in cancer incidence despite its impact on mortality (THIS IS WHAT HAS ALSO BEEN OBSERVED IN PROSTATE CANCER BY THE WAY OR AS I LIKE TO TEXT "FYI"). The conclusion of the study was as follows: "In a cohort of postmenopausal women, regular use of statins or other lipid-lowering medications may decrease cancer mortality, regardless of the type, duration, or potency of statin medications used." Thus, in the worst case scenario if cholesterol lowering does not alter the course of breast cancer and continues to only lower the risk of morbidity and mortality in women that is still a worst case scenario with ample merit don't you agree? So, why wasn't this headline news? Beats me! It doesn't prove cause

and effect but it’s one of the largest indirect looks ever conducted in women. Maybe the media was too obsessed with important stuff that day like whether or not Kim Kardashian was going to

– **STATIN PRIMARY PREVENTION TRIALS ONLY AND IMPACT ON WOMEN (insert table here)**

wear the blue or the black dress at a Hollywood party! COME ON PEOPLE WAKE UP! FYI – I think she should go with the black dress because like my wife she looks stunning in black and then for shoes I am thinking Jimmy Choo or Manolo Blahnik shoes which are actually on sale this week at Neiman Marcus…. sorry I digress again! Darn it!

STATIN PRIMARY PREVENTION TRIALS ONLY AND IMPACT ON WOMEN TRIAL

WHAT ELSE DO I NEED TO KNOW?

The leading cause of death in the U.S. for women and men is cardiovascular disease (CVD), and this has been the case for 116 of the last 117 years. CVD causes more deaths than cancer and chronic lower respiratory diseases (CLRD) combined. CVD causes 1 death per minute among females in the U.S. or over 400,000 deaths, which is approximately the same number of female lives lost by cancer, CLRD, and Alzheimer disease combined. The most recent U.S. statistics have recorded the following: approximately 41,000 deaths were from breast cancer, 70,500 female deaths from lung cancer, one in 30 deaths are from breast cancer whereas 1 in 7 was from coronary heart disease (CHD), and 1 in 4.5 females died of cancer and 1 in 3.1 died of CVD. CVD is also still a disease of the young and old. Approximately 150,000 Americans died of CVD last year who were less than 65 years of age and over one third of CVD deaths occurred before the age of 75 years (life expectancy is 78.7 years). The number 1 cause of death in women and men from age 65 and older is CVD (number 2 is cancer). Thus, it could

be argued that the overall impact of lipid lowering with statins or lifestyle changes should be of paramount importance in women treated for breast cancer, concerned about prevention and a reduction in all-cause mortality.

BUT, DOC MOYAD I HEAR ALL THE TIME THAT STATINS HAVE NO EVIDENCE OF WORKING IN WOMEN! Well, that statement makes me as mad as at long-tailed cat stuck in a room full of rocking chairs or a mouse stuck in a room full of mouse traps or a hamster stuck in a room with a defective spinning wheel or….you get the idea! This is not accurate. Statins like any drug or supplement comes with benefits and catches and ideally I don't want anyone taking any pills, but for the women (and men) that really need them it has changed lives so let's review the trials with women that were healthy but at an increased risk of a cardiovascular events. Here we go…..Interestingly, in the AFCAPS/TexCAPS study, the effect of lovastatin on the risk of first major coronary event was greater in woman versus men (-46% vs -37%), but the number of women having such an event was small (20 out of 997), so there was no treatment difference between genders. In the MEGA study, which used pravastatin, there was a 37% reduction in men versus 29% for women. Almost 70% of the participants in MEGA were women, but interestingly the average BMI was 23-24, which is far below what is observed in U.S. trials (BMI of 27-28) for men and women. In the JUPITER trial, which was stopped in 1.9 years because of its significant impact on reducing CVD events the average LDL reductions were 50% and high-sensitivity C-reactive protein (hs-CRP) was reduced by 37%. Positive impacts were observed in all subgroups evaluated and risk reduction in the rosuvastatin group was -46% for women and -42% for men. Women in JUPITER experienced a significant reduction in revascularization/unstable angina (-76%), and there was a non-significant reduction in nonfatal heart attacks (-44%) or heart disease death (-27%). However, it needs to be reiterated that this trial was stopped in 1.9 years for already meeting its primary endpoint and other

primary prevention trials also had short follow-up and smaller numbers of events. Thus, I find it striking in primary prevention that some "experts" make claims that the impact of statins in women is not known. A -76% in revascularization procedures means that these women were NOT getting BYPASS SURGERY or STENTS placed in their arteries and this is one thing that ALWAYS gets missed when talking about cholesterol lowering. These medications have dramatically reduced the need for getting your chest cracked up and needing bypass surgery! (SEE CHART ABOVE)

Statins, Safety and Type 2 Diabetes…THIS STUFF IS REAL!

In the appropriate individuals statins reduce all-cause mortality, cardiovascular events (especially costly cardiovascular procedures) and are of low cost (5 are now generic) and well tolerated overall. Regardless, the primary issue that still needs to be resolved is whether or not statins significantly increase the risk of diabetes, and if so is that risk negligible or relevant? For example, it may be dose-related or primarily in those with diabetes risk factors. In the notable JUPITER trial there were 2.5 cardiovascular events or deaths avoided for each potential case of diabetes with rosuvastatin (Crestor). Thus, for most qualifying individuals the benefit appears to outweigh the risk, but more answers and clarity on this topic are desperately needed. The association of statins and type-2 diabetes is indeed a real finding from meta-analyses but causality has not been proven, but it appears women, the elderly and those on higher dosages may be at higher risk. Recent laboratory evidence suggests a potential mechanism of action whereby statins increase the risk of diabetes. Investigators from McMaster University in Ontario, Canada have found that these drugs may activate an immune response pathway that hinders insulin signaling. Multiple statins activate NLRP3/caspase-1 inflammasome, a multiprotein complex (SAY WHAT?), which is known to encourage inflammation and insulin resistance. Interestingly, combining

a statin with the drug glyburide (an inhibitor of NLRP3/caspase-1) suppressed these harmful effects in fat tissue of obese mice. These negative effects of statins were also not found in mice genetically engineered to lack expression of NLRP3/caspase-1 inflammasome. WHAT ALL THIS SCIENTIFIC MUMBO JUMBO (Hey that was an elephant! Oops – his name was Dumbo) MEANS IS THAT NO ONE SHOULD TAKE A STATIN WITHOUT REALIZING THAT YOU WANT TO BE ON NO PILL OR THE LOWEST DOSE POSSIBLE BECAUSE HIGHER DOSES PROBABLY DO INCREASE THE RISK OF DIABETES IN SOME FOLKS! Thus, especially in high-risk patients there may be value in monitoring insulin sensitivity during statin use and using anti-diabetes medications may even further reduce risk. Ultimately, if the overall risk of type 2 diabetes becomes consistently clinically significant researchers may find a way to improve this drug class or reduce diabetes risk with another pill, for example CoQ10 supplementation is also being investigated for this purpose. Still, one mantra of this drug class (and others) NEEDS TO BE REPEATED… It appears more relevant than ever that DOCTORS need to encourage patients to be on the lowest dosage of a statin, along with moderate to aggressive lifestyle changes to maintain small dosage needs (or no drug). PATIENTS NEED TO TRY TO BE ON THE LOWEST DOSE OR NO DRUG…In fact, there is also recent data to suggest that consistent lifestyle changes such as exercise may provide similar benefits to these and other preventive medications at least in a secondary prevention setting. For example, a total of 4 exercises and 12 drug meta-analyses and the addition of 3 recent exercise trials were utilized in a recent investigation for a total of 305 randomized control trials with over 339,000 participants. A total of over 14,700 participants were randomized to exercise in 57 trials (Naci H, et al. BMJ 2013;347, published October 1, 2013). Four conditions with evidence on the impact of exercise on mortality outcomes were the focus: secondary prevention of coronary heart disease, rehabilitation of stroke, treatment of heart failure and the prevention of diabetes. No statistical differences were found between

exercise and drug interventions in the secondary prevention of heart disease and pre-diabetes. Exercise was more effective compared to drug treatment among patients with stroke, and diuretics were more effective than exercise in heart failure. More studies are needed but current randomized data suggest the mortality benefits of exercise and prescription medications are similar in the secondary prevention of heart disease, rehabilitation after stroke, prevention of diabetes and even provide unique benefits in heart failure. It will be of enormous interest in the future to determine the impact of exercise on a variety of other diverse and similar medical conditions.

316) Statins and prostate cancer treatment. And the beat goes on….BREAKING NEWS AGAIN…JUST KEEP ON BREAKING…

(Reference: Harshman LC, J Clin Oncol 2015;33: Abstract 148 & Hamilton RJ, et al. J Clin Oncol 2015;33: Abstract 145.)

BOTTOM LINE

Recently, at ASCO (largest cancer meeting in the world, a large study from Harvard and Canada concluded with the following statement below (note: this does not prove cause and eff ect but

makes the lower cholesterol and statin theory against prostate cancer more interesting don't you think? -"…statin use at the time of ADT initiation was associated with a significant increase in TTP on ADT even after adjusting for established prognostic factors." (n=926 folks) Moyad comment – Patients appeared to have a better response to hormone therapy if they were also

taking a statin drug. -For ADT following primary or salvage radiation-"statin use was associated with improved overall and prostate cancer-specific survival and improved quality of life." In terms of intermittent androgen deprivation (IAD)- "more off treatment intervals and longer off treatment."

(n=1364 folks studied) Moyad comment – Patients had a better response to IAD if they were on a statin drug.

WHAT ELSE DO I NEED TO KNOW?

I have nothing else to say except if men and women reduce their cholesterol while being treated for breast or prostate cancer and it doesn't work in fighting cancer, then I apologize that all it might do is reduce the number 1 cause of death in men and women for 114 of the last 115 years. HEART HEALTHY = PROSTATE HEALTHY!!! (Moyad Trademark Circa 2003 in the medical literature and if you do not believe me look it up. So, if you use these terms at any point in your life you need to donate some money to PAACT and then donate some Money to the Moyad Beer fund, which is also known as MBF. T-shirts will be available soon!).

317) Metformin, breast cancer and a phase 3 trial! Why do I have to know about this? Please read on…AND TEACH ME ABOUT THIS DRUG and REMEMBER THAT EXERCISE AND DIET WORKED BETTER THAN THIS DRUG TO PREVENT TYPE 2 DIABETES (but you never get to hear about this!).

(Reference: Goodwin PJ, et al. Eff ect of metformin vs placebo on weight and metabolic factors in NCIC CTG MA.32. J Natl Cancer Inst 2015;107: epub ahead of print. & Diabetes Prevention Program or DPP in New England Journal of Medicine 2002.)

BOTTOM LINE

Metformin (generic "natural" drug derived from the French Lilac") given to non-diabetic women in the hope of preventing breast cancer from returning at least appeared to make participants more heart healthy! So, should patients ask their doctors about it in order to lose a little weight, drop their blood sugar and prevent type II diabetes if they are at higher risk? Yes, but remember that exercise and weight loss via diet arguably worked better in preventing type 2 diabetes.

WHAT ELSE DO I NEED TO KNOW?

(THIS IS A LONG ARTICLE SO BUCKLE UP…IT'S INTERESING, BUT IT'S ABOUT AS LONG-WINDED AS My grandfather when he talks about the positives and negatives of his colon health and latest bowel movements just as I am about to take the first bite of my pizza…sorry Grandpa I suddenly lost my appetite!) Metformin has actually been available in Europe since the 1950s but was not approved by the U.S. FDA until December 30, 1994. An extended release (XR metformin) version was approved in October 2000. Metformin was actually first synthesized and found to lower blood sugar in rabbits in the 1920s and then put aside for decades because of an increase in insulin synthesizing/utilization research. A 1957 published clinical trial of diabetes (by French physician Jean Sterne – who coined the name of metformin as the glucose eater or "Glucophage"…REMEMBER THIS DRUG NAME) was then completed and the U.K introduced it in 1958 and Canada in 1972. Metformin is now considered a first-line drug treatment along with diet and exercise for adult and pediatric patients with type 2 mellitus because of its favorable overall profile (glucose control, weight loss and low risk of hypoglycemia). It is arguably the only drug proven to prevent pre-diabetes (high-risk diabetes patients) from becoming diabetes and is a primary treatment in patients with metabolic syndrome. Overall, few drugs in medicine cost less with such a long-term safety profile and even added potential heart health benefits. WOW and WOW SPELLED BACKWARDS!! Metformin works by reducing liver glucose production ("inhibiting gluconeogenesis") and increasing skeletal muscle tissue uptake of glucose. Metformin essentially leads to a maximum 75% reduction in liver glucose production. It also reduces blood insulin levels (not directly), increases insulin sensitivity, suppresses synthesis of proteins, fatty acids and cholesterol, and increases the utilization of free fatty acids. Metformin has also demonstrated some evidence of reduced intestinal glucose absorption. Metformin increases insulin sensitivity by

activating hepatic and muscle AMP-activated protein kinase (AMPK – “metabolic master switch”), which results in reduction of fatty acid synthesis and stimulation of fatty acid oxidation in the liver and increase in muscle glucose absorption. BLAH! BLAH! BLAH! Metformin is generally available in 500, 850, and 1000 mg tablets. The starting dose is 500 mg twice a day or 850 once a day, given with meals. The most common dosage utilized in the Diabetes Prevention Program (DPP) was 850 mg twice a day. In general, clinical experience suggests 500 mg once a day with a meal and increasing dose in 500 mg increments every 2-4 weeks until maximum dosage is achieved. Metformin XR can be prohibitively expensive and available in 500- and 750-mg tablets utilized with the evening meal. The half-life of metformin is on average 5-6-hours in plasma (longer retention in red blood cells or blood-up to 18 hours), which suggests 94% of the drug is removed by the body in 24 hours. This short half-life emphasizes the need for daily compliance whether it is for patients or when measuring glucose and other parameters in clinical trials. Metformin is limited by gastrointestinal complications (soft stool, diarrhea, gas, abdominal pain and more rarely nausea and vomiting) in up to 50% of patients, but these adverse effects are usually transient and resolve within days to weeks of initiating treatment. Additionally, gastrointestinal side effects are reduced greatly by again, titrating increasing dosages of the drug every 2-4 weeks (for example 500 or 850 once a day for 2 weeks and then 500 mg additional) and when it is consumed with food. Although food has been reported to reduce the rate and extent of metformin absorption by increasing the time to peak plasma concentration by approximately 40 minutes, but this appears to be a small issue especially compared to the overall importance of long-term compliance. Less than 5% of patients in clinical trials are not able to tolerate the drug due to side effects. Extended release (XR) metformin appears to improve gastrointestinal tolerability and can be given once a day, but is more expensive (no thanks!). Metformin can reduce vitamin B12

and/or potentially magnesium levels, so these values should be monitored by the doctor that you adore or love the most in your life (not a romantic love but a “hey let me buy you a cold beer” kind of love). It has been known that this drug interferes with B12 absorption in the last part of the small intestine and can lower B12 in 10-30% of patients. The reduction of B12 by metformin appears to be dose-dependent. Rarely, patients complain of a “metallic taste” with the drug, which has been more commonly found with similar medications. Regardless, “metallic taste” has been reported in clinical trials in approximately 3 to 11% of patients. It also appears to be self-limiting with only 0.5% of patients complaining of metallic taste after 3 months of treatment. Regardless, a reduction in dose or the passing of time appears to resolve this issue almost immediately in patients distressed by this issue. The most serious concerning adverse event with metformin is lactic acidosis, where a low pH in body tissues and blood (acidosis) along with increases in lactate is problematic. The overall incidence of lactic acidosis on metformin has been estimated to be less than 1 case per 1000 total patient years on the drug. In other words, it has become as rare as almost any other drug especially when working closer with your doctor. Still, metformin is contraindicated in some individuals because of impaired kidney function and the potential concerns of lactic acidosis (many doctors think this is overrated and metformin should be available over the counter, but that’s not going to happen. You should talk to your doc about these things and not a newsletter with a guy that likes to make funny jokes a lot for personal therapy who also happens to be a doctor). Iodinated contrast media administration given for some imaging tests could result in lactic acidosis in a patient utilizing metformin. However, this rare adverse effect occurs if the contrast causes renal failure. Metformin is excreted primarily by the kidneys so continued utilization of metformin after the initiation of kidney failure causes toxic concentrations of the drug and subsequent lactic acidosis. In order to avoid this

complication metformin should be withheld after the administration of contrast agent for 48 hours, and if renal function is normal after 48 hours from receiving contrast then metformin can be reinitiated. However, despite what the package insert recommends, which is also to withhold metformin 48 hours before contrast medium is given, others have argued there is no justification for this before and then after procedure (for 48 hours). Still, it seems prudent to stop metformin two days before and after contrast in any person with a hint of kidney issues simply because the benefit exceeds the risk in my opinion THE TRIAL THAT SHOCKED THE WORLD (DPP = Diabetes Prevention Program)!!!

This landmark trial was published on February 7, 2002 in the New England Journal of Medicine. This trial consisted of 3234 non-diabetic individuals with elevated fasting blood glucose (mean of 106 mg/dl and hemoglobin A1c of 5.9% and 67% with a fasting glucose of 95-109 mg/dl and 33% with 110-125 mg/dl) were assigned to placebo, 850 mg metformin twice daily (850 mg for first month then 850 mg twice a day thereafter) or lifestyle changes with a goal of at least 7% weight loss (via low-fat low caloric diet) with 150 minutes of physical activity per week. Mean age and BMI was 51 years and 34, respectively, with 68% women, 45% members of a minority group and 20% 60 years of age or older. However, almost 33% of the participants had a baseline BMI of 22 to 29! Approximately 70% of the participants had a family history of diabetes and 16% of the women had a history of gestational diabetes. The average follow-up was only 2.8 years and compared to placebo the group utilizing metformin reduced the risk of diabetes by 31% (95% CI 17- 43) and the lifestyle intervention reduced the incidence by 58%. (LIFESTYLE CHANGES BEAT ONE OF THE BEST SELLING DRUGS OF ALL TIME…EXTRA, EXTRA, READ ALL ABOUT IT IN THE PAACT NEWSLETTER). In addition, one of the key findings of this landmark publication was the “lifestyle intervention was significantly more effective than metformin.” In fact, the number needed to treat (NNT) or to prevent one-case of

diabetes over 3-years for metformin was 13.9 persons for metformin and 6.9 for lifestyle-intervention. Regardless of BMI group (22-<30, 30-35 or >35) metformin or lifestyle was beneficial in reducing the incidence of diabetes regardless of gender and race or ethnic group, but metformin appeared to have a greater impact in those with a BMI of 35 or more. Overall, treatment effects did not significantly differ by gender or race or ethnic group. Daily caloric intake was reduced by 249 kcal in the placebo group, 296 in the metformin group, and 450 kcal in the lifestyle group (p<0.001). The average weight loss was 0.1, 2.1 (4.6 pounds), and 5.6 kg (OVER 12.3 POUNDS) in the placebo, metformin, and lifestyle groups (p<0.001). Interestingly, side effects with metformin were significantly (p<0.02) greater than placebo in terms of gastrointestinal symptoms (diarrhea, flatulence, nausea, and vomiting), but were significantly (p<0.02) lower with lifestyle changes compared to placebo!!!!!! YEAH BABY!!! LIFESTYLE RULES!!! Anti-Cancer!? Now, perhaps, the most observed and truly landmark event is a phase 3 trial being conducted in North America, the United Kingdom, and Switzerland and it has already completed enrollment of 3649 non-diabetic women receiving conventional treatment for T1-3, N0-3, M0 breast cancer diagnosed during the previous 12 months. Interestingly, patients needed to have a fasting glucose of less than or equal to 126 mg/dl (7.0 mmol/L), which is the threshold for diabetes diagnosis, but essentially enrolls only pre diabetics or those with normal blood sugar. Women with a history of lactic acidosis, current use of diabetes drugs, previous or recurrent breast cancer, greater than moderate intake of alcohol or “marked” liver, kidney, or cardiac abnormalities were excluded. Subjects were randomized to metformin 850 mg oral caplet twice a day for 5 years, which included a 4-week initial metformin acclimatization period of 850 mg a day for 4 weeks and then the addition of another 850 mg per day. Interestingly, this study also included a metabolic substudy that has been completed!!! AND YOU ARE ABOUT TO GET THE BREAKING NEWS RESULTS!!! Th e first 492

individuals with fasting blood samples at baseline and after 6-months were included. Mean age, BMI, and glucose of participants in the substudy was 52 years, 27-28, and 95 mg/d or 5.3 mmol/L (range 88-101 mg/dl or 4.9-5.6 mmol/L), respectively. The results from this substudy were impressivem because the results below "did not vary by baseline BMI or fasting insulin" including the following:

• Weight reduced 1.7 kg (3.7 pounds) or -2.3% with metformin and increased 0.5 kg or +0.7% with placebo ($p<0.001$). BMI change vs placebo also was significant ($p<0.001$).

• Glucose reduced 1.9% with metformin and increased 1.9% with placebo ($p=0.002$).

• Insulin reduced 11.1% with metformin and did not change with placebo ($p=0.002$)

• hs-CRP was unchanged with metformin and increased 6.7% with placebo ($p=0.002$).

• Leptin (hormone that when it goes down is a symbol that the drug has positive/beneficial metabolic changes…

GOOD NEWS!!!) reduced 9.5% with metformin and increased 10.7% with placebo ($p<0.001$). Interestingly, members of this research group had found previously that higher insulin levels in breast cancer were associated with two times the risk of distant recurrence and three times the risk of death.

318) Adult vaccines may reduce your risk of a heart attack and have anti-cancer eff ects? Has Moyad lost it? (well yes, I never had "it" but I do believe this preliminary research!). VACCINES = HEART HEALTHY!!! (References: 1. Corrales-Medina VF, et al. JAMA 2015;313:264-274. 2. Mitchell DA, et al. Nature March 19 2015.).

BOTTOM LINE

If you qualify for any adult vaccine right now, please go get

it because it may not only reduce your risk of cardiovascular disease (CVD) but it might also enhance the effects of your cancer treatment. This is preliminary research but who caresthis is a SIDE BENEFIT (get it….not a side effect) of some of these adult vaccines.

WHAT ELSE DO I NEED TO KNOW?

Vaccines are no longer helpful just for kids, they are incredibly helpful for adults! Adult men and women need to be more vigilant about getting them. People will not hesitate to take an unproven supplement to boost or support the immune system but they are probably not aware that there are vaccines that do a much better job of doing this than any other over the counter pill.

I have explained in the past how many adult vaccines like the fl u vaccine are heart-healthy and you need to get these vaccines for all the side benefits! And now comes the latest research that preventing pneumonia might fight heart disease and other vaccines could enhance the effects of cancer treatment! Okay, this is preliminary stuff but it’s quite groovy, cool, and hip! A recent study of over 5800 adults found that pneumonia might be an independent risk factor for cardiovascular disease (CVD)! Hospitalization for pneumonia was associated with an increased short- and long-term risk of CVD! Why? Infections can cause proinflammatory changes in the composition of heart disease plaques and make them more vulnerable to causing sudden cardiac events (heart attack, stroke…). And, in other research it seems when someone suff ers from a serious infection like pneumonia and recovers, the inflammation in the body continues for arguably months and months after the time the person has recovered. So, you feel better but the body is still dealing with all the effects of the infection. Not nice! Additionally, in a somewhat stunning recent small randomized human study with brain tumors researchers gave a small number of individuals a tetanus/Td shot (actually tetanus/ diphtheria toxoid) to enhance their

immune response to an experimental dendritic cell immune therapy and for some of the patients it did appear to provide a "boost" or enhanced treatment effect! In fact, it appeared to significantly enhance survival in patients with glioblastoma. Among the 6 patients that received the Td shot, three lived between 20 and 24 months from diagnosis, and three lived longer than 3 years – including one patient that is still alive after 9 years. And, this data compares with a median survival of 18.5 months in the control group of this study. Researchers thought the Td shot would work by causing an immune response locally at the vaccine site but were surprised that it actually appeared to cause a systemic (body wide effect) immune response. This is only a small human study of brain cancer. However, I do think it is time to get excited about getting both pneumonia vaccines if you qualify. PCV13=Prevnar and PPSV23=Pneumovax since September 2014 are now both recommended just not at the same time, so talk to your doctor because if you are 65 years or older or in many other special circumstances you may qualify ASAP. Also, for all those adults that have let too much time go by since they had their tetanus shot or never had one – it is time to go in there and get it ASAP if you qualify!

319) Ginseng looks good again to battle cancer-related fatigue (CRF)!! This is really getting interesting! And, it should be an option now because many of the new drugs work very well, but fatigue is a big problem in some patients (for example with Xtandi, chemotherapy, hormone suppression or listening to your kid tell you the many reasons why they could not clean up there room over the past month – that is also exhausting after a while). BREAKING NEWS! YEAH!!!

(Reference: Yennurajalingam S, et al. Integrative Cancer Therapies 2015; and Barton DL, J Natl Cancer Inst 2013;105:1230-1238 and Moyad MA. Th e Supplement Handbook, 2014.)

BOTTOM LINE

If you are experiencing fatigue from cancer treatment or just trying to prevent it then 1000-2000 mg American ginseng (3- 5% ginsenosides) is a good option and/or 800 mg per day of Panax ginseng (Asian ginseng at 7% or more ginsenosides) may also soon be a good option. This research was done at two places you may never have heard of – Mayo Clinic and MD Anderson Cancer Center (sarcasm alert #546). Look at Ginseng Board of Wisconsin web site for the low cost brand that was tested in the Mayo clinic trial (www.ginsengboard.com). Also, several clinical trials of weight lift ing or resistance exercise just 2-3 times a week also reduces CRF.

WHAT ELSE DO I NEED TO KNOW?

It was already time to make ginseng an option for cancer related fatigue in 2013 when the Mayo clinic and 40 other medical centers completed the results of an 8-week study of American ginseng 2000 mg per day versus placebo to reduce fatigue and it worked! They used a ginseng from the Ginseng Board of Wisconsin (www.ginsengboard.com) so this is the one I recommend! The one from the big clinical trial is the one you can trust. The reason this needs to be an option soon is simply due to the LACK OF OPTIONS FOR CANCERRELATED FATIGUE (CRF) THAT ARE SAFE. How bad is CRF?! In clinical studies it can range as high as 60-90% and it's also a limiting factor of one of the best prostate cancer drugs ever invented known as "Xtandi." In this new MD Anderson Cancer Center study 30 patients with CRF (rated as 4 or more out of 10 on a scale) ingested 800 mg a day of Panax ginseng (Asian ginseng prepared from the root with 7% or more ginsenosides – the active ingredient) for 29 days. Median age of patients was 58 years and capsules were provided by Indena S.p.A. (Milan, Italy). It's also interesting that 10 of the patients were being treated for genitourinary cancers. Feelings of well-being and score for appetite significantly improved as well as fatigue on ginseng. The median improvement was a nice 5 points on a scale! This is outstanding, but keep in mind that this is

preliminary but past research really supports that this is a real impact! Th e results of this small study not only show efficacy that the product was safe and no side effects were associated with the supplement. It also suggests that again not just fatigue but appetite, quality of life and pain improved over 4 weeks. A total of 63% of the patients noted moderate to vast improvement in their CRF with ginseng treatment. Ginseng appears to be impacting or reducing the effects of pro-inflammatory compounds via some mechanism that is being studied now at Mayo Clinic and many other centers. Ultimately the study concluded in the following way “We conclude that high-dose Panax Ginseng is safe and tolerable and rapidly improves CRF. Our findings also suggest that PG can improve symptoms such as pain, appetite, sleep disturbances, and overall Quality of Life. Randomized, placebo-controlled trials of Panax Ginseng are justified.” BEAUTIFUL SENTENCE DON’T YOU THINK?! (of course it is!). THAT’S ALL FOLKS…. See you in FALL, when I will write about many other serious issues and give timeless advice in the next newsletter, such as why it is never good to wait more than 1.214 seconds to say “ABSOLUTELY NOT” if your spouse asks you if he or she “looks fat in this new summer outfit?” And why it is never smart to drink 5 glasses of water before renewing your driver’s license at the DMV with the no on-site bathroom (you are number 103 and they just called number 12 and now it is decision time folks).