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THE SQUIRREL'S NEST 2017

Terrence McGarty

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Friday, December 22, 2017

[Bad Data, Been There Done That](#)

I read a piece in [The Harvard Gazette](#) which tries to explain the use of the Harvard herbarium, or plant collection, to try to validate global warming. They note:

With their records of flowering times and details on how plants have adapted to climate over more than a century, herbarium collections play a key role in understanding how climate change impacts the natural world and how those effects might be felt by humans.

Now I have been doing this for over a quarter of a Century and have a massive data base on flowering times and variances for a multiplicity of species. The problem is micro climate. Namely if there is a tree in front of the plants after twenty five years the tree can change the micro environment and thus alter bloom time. They continue:

“Plants are at the beginning of the food chain,” “So if there is a disruption in flowering time, it effects everything that depends on that. It may be that 100 years ago bees came to pollinate plants in May, but now that flowering time has shifted to earlier, into April, then there is potentially a mismatch in terms of timing ... and everything is affected downstream.”

A truism in part but it is a very complex issue. First is local variation. Second is seasonal impacts such as prior year water shortages, changes in soil texture, and so forth. Note that all herbaria are for single location and time samples. You really must sample over at least a quarter century and at multiple locations and record any micro environmental changes. Frankly the study above is fatally flawed just for this reason. Just because a plant flowered on June 10th in 1875 but then on May 21st in 2017 means nothing! There are so many variables that it is truly meaningless. I have done this and still I wonder with almost 30 years of data what variables must be accounted for.

Junk in is junk out! Perhaps Harvard needs someone doing real field work.

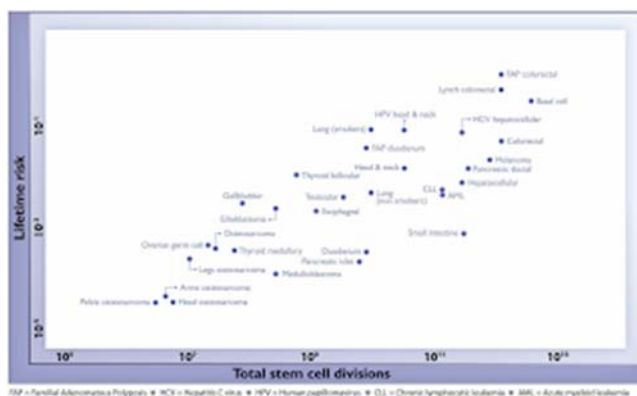


Labels: [Global Warming](#)

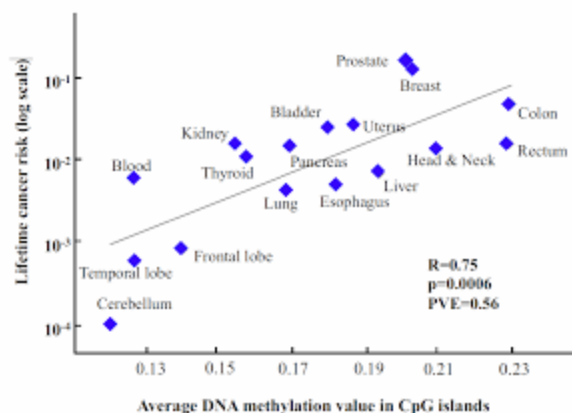
[Some Interesting Cancer Metrics](#)

There has been developed a set of slides depicting cancers categorized by a variety of metrics. We present a few here just for interest.

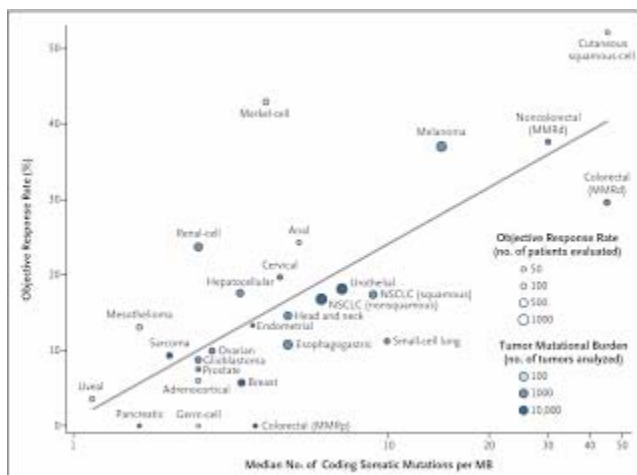
From Tomasetti and Vogelstein we have the chart showing the risk of cancer by type based on the number of stem cell divisions. Namely certain types of cancer arise from cells where there are many stem cell divisions thus allowing for genetic errors.



In contrast we have a similar chart from which depicts incidence versus methylation for various cancers. Methylation is a common element of epigenetic cancers. It is interesting to compare these two charts.



Finally we have the chart depicting incidence versus the number of somatic mutations in base pairs over a large stretch of DNA as obtained from Yarchoan et al. This is a compelling chart as we look at cancer from the perspective of mutations.



Thus we have three factors; number of stem cell generations, methylations, and mutations of somatic cell locations in DNA. Thus we ask; what is the most important?

Good question!

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1. Tomasetti and Vogelstein, Variation in cancer risk among tissues can be explained by the number of stem cell divisions, Science, 2 January 2015 • Vol 347 Issue 6217
2. Yarchoan et al, Tumor Mutational Burden and Response Rate to PD-1 Inhibition , NEJM 377;25, Dec 21, 2017
3. Klutstein et al, Contribution of epigenetic mechanisms to variation in cancer risk among tissues, PNAS | February 28, 2017 | vol. 114 | no. 9
4. Vogelstein et al, Cancer Genome Landscapes, 29 March 2013 Vol 339 Science



Labels: [Cancer](#)

Wednesday, December 20, 2017

[Happy 9th Birthday](#)

Well this Blog is now 9 years old. There have been almost 300,000 visitors over that period from hundreds of countries. Hopefully those who came received something of interest.

A while back I read that people found this a very idiosyncratic site. It made me pause and think just what that meant. It was a word I knew from my SAT tests but had never incorporated into my expression. Now I think I understand it if I have become one.

What makes this idiosyncratic:

1. A diversity of topics. We had examined economics, healthcare, international politics, nuclear weapons, taxes, philosophy, religion and the like. Generally the approach was to focus on some recent news article and then make an assessment.
2. We have been fortunate to have seen certain advances before others. Take CRISPRs. I actually taught my grandchildren's 6th grade class about them some five years ago. Instead of "plastics" I told them about CRISPRs. Not that any will ever remember. My second focus was on CAR-T cells. That exploded even faster than CRISPRs. I now wonder about Gene Drives.
3. Politically I am an Ockhamist, which is an individualist somewhat reminiscent of de Tocqueville's observation. There is a great deal which flows from that view. History is critical to understanding the human beast. Great ideas are not all recent, they come from a long process of give and take and one must examine their progression. Individualism came from an understanding that each individual was responsible for their own actions and that each individual had the same rights. For Ockham that meant Natural Rights, and what flowed from that.

4. Cancer had become a focal point. Not that I am a hypochondriac, I guess I leave that to Woody Allen et al, but because I saw that understanding it and controlling it had become a "systems" problem. I was fortunate to live long enough to see the beginning of treatments of this set of diseases. Namely they must be understood as a system not as a cell only problem. I expect that even more advances will occur in the next none years.

5. I have really become annoyed with the plethora of opinionated folks who are telling us how to deal with our health. Take the collection of women writers telling men not to treat their prostate cancers. In the [NY Times](#), the most trusted source of truth (I am really kidding), we have some woman telling men that they should just forget about their prostate cancers. The author writes:

With prostate cancer, doctors today try to reduce the harm by offering men with early-stage disease "active surveillance" instead of immediate treatment. A study published last year in the New England Journal of Medicine found that men are just as likely to survive 10 years whether they choose to be treated or monitored. was found to have a low-risk prostate cancer last year. Since then, his doctor has monitored him with additional tests. He'll be treated only if tests suggest his cancer has become more aggressive, an approach that aims to spare him from long-term side effects. Among men who have had prostate cancer surgery, 14 percent lose control of their bladders and 14 percent develop erectile dysfunction.

Words mean something. You must note they changed "Watchful waiting" to "active surveillance" which tells you something. Every time they "power that be" change the in word they are losing the battle. The NEJM analysis mentioned above is flawed since as we have discussed herein we have about 5-8% of PCa patients with an aggressive form, which we unfortunately cannot identify. Thus the result is dominated by the massive amount of benign types. The statistical analysis was flawed due to a small sample size. Welcome to statistics 101 folks.

6. Politics. Here we have a plague on all houses. It seems that every time Congress does something it gets messed up. Take the ACA. Is healthcare any better? Not really. The costs have exploded due to the increased administrative overhead, massive. Now to taxes. This recent bill was almost a disaster. Fortunately we save the medical expense deduction as well as the Graduate Student exemption for tuition assistance. These two we discussed in this Blog. So we are 2 for 2. The SALT taxes frankly may be good. If you do not like New Jersey taxes then move! Go to Florida, Texas, or New Hampshire. Definitely not California!

Well some thoughts on being 9!



Labels: [Commentary](#)

Tuesday, December 19, 2017

[Some Thoughts on Today's Students](#)

The recent discussion on the House version of the Tax Bill, where graduate students would have to pay tax on tuition, led to its collapse, but the reason was logic not the whining of students like those in [Science](#) who wrote:

As engaged members of the scientific community, we must urge our academic institutions to take action. Universities should lobby elected officials, make public statements, and amplify graduate student organization efforts. If the repeal of 117(d) passes into law, our top priority will then be reworking tuition schemes to protect graduate student research and teaching. However, while the tax bill is still in committee, we have a more pressing goal: to unequivocally oppose the repeal of 117(d). We can call our elected representatives [some of whom seem open to the change] to voice opposition, sign petitions, and advocate for safeguarding graduate studies. This legislation will devastate productivity and innovation in higher education. As a scientific community, it is our duty to embolden young people to think and create. We can never recuperate the costs of lost potential.

There is no description of the strategic risk to the country, to the impact of foreign students who will be supported by tax dollars etc. These are just a bunch of millennials whose argument is that as "engaged members" to have the University urge Congress. No reasons why other than they "feel" it should be so.

Where did logic go, rhetoric, or even basic grammar. We need a return of the Trivium, not the self serving sniffles of children whose view of the world is as an entity that owes them something. By the way, Congress did get to recognize that Yamamoto did go to Harvard and did send his forces to Pearl Harbor! That my young millennials is why we need to have more citizens partake productively of our tax payer funded Universities, despite their abusive overhead, due to prior Government mandates.



Labels: [Academy](#)

[One of the Most Incompetent Companies in the Universe](#)

AMTRAK, yes that Government owned and managed train company, the one where trains speed along sharp turns killing passengers, the one which closed New York City for three months, the one where there are two CEOs each getting a bundle for doing nothing. Today, as usual the message is:

Train service in and out of PSNY remains subject up to 90 min. delays due to earlier single tracking following an Amtrak overhead wire problem.

Yep, a wire problem indeed. You see the bridge across which this wire goes one must cross to get to New York. It is on the verge of collapse. Any progress? Nope, it will take a deadly event and then the folks in charge will get more money for more loss of life!

And where is our Secretary of Transportation? Good question folks.



Labels: [Government](#)

Thursday, December 14, 2017

[A Conversation with Ockham](#)

The following is a recollection penned by a Franciscan Friar, one Brendan of Dublin, a physician trained at Oxford, Montpellier, and Bologna, and serving the Court in England. It recounts a trip to visit William of Ockham in the Spring of 1347, just prior to the massive outbreak of the plague. This is a translation from the original Latin, although it has been converted into a twenty-first century American-English dialect. Certain phrases were difficult to translate and certain English words are employed to best reflect the mid-Fourteenth Century intent.

It was the Spring of 1347, and I went to see Ockham on my way to Prague. He was still being protected by Ludwig and resided in his castle grounds in Munich. I had left London in early February, and had a rough crossing of the Channel and then a circuitous route down the Rhine, then cross to Munich. It was a six week journey when I arrived in mid-March, and Spring had yet to arrive. Ludwig was at war with some and aligned with others. He was close with Edward, King of England, and this allowed him some leverage, since he had positioned himself against the French King John, the rather stumbling egoist who was attempting to rule France. Although I was off to see King Charles in Prague, a putative adversary of Ludwig, as a Friar I could hopefully navigate amongst these competing players. The Battle of Crecy had been a bloody mess with so many killed and yet there was no peace between England and France. It encompassed almost all the Principalities and Kingdoms in Christendom.

Added to this was the continual turmoil in Avignon with the Popes in residence. John XXII was dead several years now and despite attempts to come back to a sense of normality after his extremely arrogant dicta, some thought his rulings even heretical, and having the Bishop of Rome appointed by French Cardinals rather than the people of Rome, had always been a stumbling block. Worse yet, this Bishop of Rome refused to go to Rome. Instead this Bishop built a massive castle in Avignon, surrounded by riches and staffed with enough people to populate a small country.

It was Ockham, my old teacher and friend, who had spent the last twenty years under the protection of Ludwig, with his writings had introduced concepts in political governance, secular as well as religious, which I saw as the basis for dramatic changes, whose time would eventually come.

Ockham had examined several areas whose influence was slowly penetrating the minds and thoughts of those would in turn were to spread it across our domains. First was his understanding of nominalism. Namely that there are only individuals, and there is no ultimate single essence, man is nothing more than a collection of people, men and women, and there is no abstract whose existence we refer all to. Namely individuals are the elements of the world, and individuals who are born free, no matter what their ultimate state may be, individuals who are equal as humans.

Second, the derivation from the poverty debate with the Pope. Namely, poverty if it were to be observed needed to have a clear definition of property, and property meant the understanding of rights. Rights in turn linked to individuals, since ownership inured to a person not some class.

Third, was the concept of how our leaders should be chosen, namely by the people. For it was for centuries that the Pope was the Bishop of Rome selected by the people of Rome. The people selected a Pope, a leader. Now we had a "Pope" selected by a class of incentivized "Cardinals" who were also selected by Kings and Princes in most cases.

Fourth, and furthermore, the Pope had managed to interject himself into secular matters in contradistinction to the Gospel.

Fifth and finally Ockham had stressed Faith and the Bible as the two elements of our religious belief. It was not to be left to the complexities of reason as attempted by Aquinas and the Bible is and must always be the cornerstone of what we believe in.

These elements had been mulling in my mind over the past decades, even though my focus as a Friar was to be a physician to the body, rich and poor alike, but Ockham was always in the back of my mind. He had a sense of clarity and a sense of correctness that was overwhelming. All one had to do was to see to what irrational ends John XXII went to try to silence him, and then to see that Ockham's assertion of the heresy of such actions of John, for all this was enlightening. The Pope was not infallible, he was a man and as a man prone to error. As our Saint Francis has said to his followers more than a century ago, we must follow our vows of poverty and chastity, and we must be obedient only to the extent that it does not conflict with our Faith. Obedience for Francis was the delimited vow, poverty and chastity had bright lines.

Francis also was a believer of the individual. Charity was an individual to another individual. It was not the "Church" as a group, nor the "King" as a ruler to dispense to the poor. My practice of medicine was a "giving" to the individual whose body I served as a healer.

I thus looked forward to seeing Ockham again. I suspected that like many of us he was aging, and although a somewhat healthy man he was always somewhat on the frail side. Ockham resided in a residence aside the main castle. Munich was an interesting city, it has its strong Germanic ties, and the people were themselves Germanic but lively. They lived in relative peace and there were many craftsman resident in the city. What amazed me each time I came here was that beer was consumed like water. There were open halls where men would congregate and consume what appeared to be volumes. Even in winter one saw this phenomenon.

I came to Ockham's residence and asked the young man who greeted me for Ockham and told him who I was. In a matter of mere seconds Ockham came forth with a great smile on his face. I was a bit set aback because the gaunt man I knew well had put upon himself a great girth. I gathered it may have been the beer. Yet it may also have been the proximity to good food and the lack of the arduous travel I have set myself upon over the years. He was cheerful, a ruddy face with a grey beard, and he retained his tonsured and wore his Franciscan attire. We embraced and he ushered me to the rear, which was a small room with a fire looking out onto a small garden area, still barren from the winter.

We sat down in front of a large fireplace in a heavily beamed room. It was warm, pleasant, and a far cry from the rather Spartan quarters we had in London at Greyfriars. Ockham asked how I was doing and what news I had. I recounted the past few years and he was a bit surprised as to my proximity to King Edward. I reminded him that I had spent time as his tutor and knew his mother, the Dowager Queen. Ockham expressed his concern as to Isabella and her reputation as a rebel who had worked to overthrow her husband with her lover, Mortimer. I muted my reply saying that royalty seems always to be at each other's throats. Ockham smiled and said it reminded him of theologians as well. I smiled and said it did, the difference is that royalty hacks each other to death, theologians burn each other to death! To that he let out a hearty laugh. I let it sink in a bit and then continued:

"Yet William, although Royalty use the ax, sword, and arrow as means to death, they fight equally, no side claiming Divine correctness. In contrast, and perhaps this is from my associations with Gui and the Inquisition, the battle between believers, over differences in interpretation, is a bit one sided, with the Church having the ultimate say, and any new voice silenced by fire."

His smile disappeared and he looked at me and replied:

"I know that all too well. Yet I have continued to write, excommunication and all. Now tell me, I gather you were at the Battle of Crecy, a bit of a hero on the battle field, a physician at war, so they say. Tell me some details."

I now began to understand the phrase, "War stories". Those not there want to hear what they want to hear, perhaps glory, perhaps fine deeds. I replied:

"William, I was there as a physician to the King and his son the Prince of Wales. Yet the brutal battles, the blood shedding, the dismemberment, left me more as a priest administering Last Rights to dying men than a physician healing wounds. William, there is no glory in war, no dignity in a battle. The Knights take glory of a conflict, in the killing of an adversary. In reality it is an argument between two men, the King of England and King of France, over who is to claim what under what conditions. All that will change with the next succession, yet men go to kill each other. The reality as I saw it was that the battle enriched those who survived, taking whatever they could, and often choosing who they would slay based upon what they could get in ransom if they kept their captive alive. On one hand it was a battle of Kings, on the other, and this I believe is the true reality, it was a barbarian assault of one group upon another. The men at arms as they went to battle, and then upon their return, took freely from those whose lands were in their path. They committed acts that they confessed as they died in my arms, and as a priest I gave them absolution, knowing full well that these men if allowed to live by God, would continue their barbaric acts on a successful return. William, war brings out the evils of the human soul, and I can do more as a physician than as a priest, that at times is truly terrifying. The beasts of the forest are often more gentle than a good Christian soldier."

I gathered that Ockham was a bit taken aback by my response. It had been but a year from Crecy but I, at times, still has the scent of the spilled human blood in my nostrils, the sight of hacked limbs in my eyes, and the screams of dying men in my ears.

We sat quietly for a while, Ockham drinking a large stein of beer, and I a cup of a white wine, for I never truly had a taste for beer, the drink that was everywhere. I then told him of my travel to Prague and my meeting of King Charles. He said he had never been to Prague and that he heard it was a beautiful place. He knew little of the Czechs, the Slavic people, yet he did indicate they were unlike the Germans, more quiet and thoughtful. We had dinner and rested.

Over the next few days we had long conversations regarding the development of his thought. My objective was to distill what he had developed in a manner in which I may be able to convey to other people, those not trained in the Scholastic manner. Ockham's work was elegant but ponderous, enlightening, but demanding too great a preparation to absorb. The following recounts my discussions. I have left it in a dialog manner to demonstrate my own need for clarity. Although trained under Ockham, my reach was as a Bachelor of Arts, a mere tyro in a land of giants. Yet perhaps to spread his insight, such a simplification was demanded. Besides, as I was to spend time in Prague with Charles and the many who would come and go there, this would be an opportunity to develop a precis, as accurately as I could, regarding Ockham and his work.

We started our discussion on his now somewhat accepted understanding of nominalism. I began by phrasing what I saw as his proposition:

"William, as I recall, your acceptance of nominalism, namely that there are no universals and that the terms we general use as a universal is nothing more than a name, thus nominal. There is no ideal "red rose", there is only this red rose and that red rose. That the accident of redness is merely an attribute of a specific red rose and not a manifestation of some ideal, some abstract essence of redness. Is that a reasonable approach to your thought?"

Ockham replied:

"Yes. One can also say that "The red rose is a plant" and yet this does not imply the existence of some universal essence called a plant. It is a plant because it has a root, it grew from a seed, in a soil, and it needs the sun to exist. Now even more deeply, it needs this specific soil, or perhaps that soil over there. It needs a specific embodiment of soil, not a universal called soil. Indeed the universal does not exist. It is not the argument between Plato and Aristotle, that the universal flow from the individuals or the individuals are manifestations of the universals. There are just individuals. The rest are just names we throw about to try to get the listener to stay attuned to what we are arguing or explaining. Redness is an abstraction, the reality is the specific red we observe. Remember that when we say red, we can hold in front of our eyes say a dozen roses, and each we call red, but each may be slightly different from each other."

"Then is it fair to say that the redness of the rose is the result of what specific rose plant I have, and what soil I have grown it in, and how much I may have watered it, and how much sun it is

exposed to?" I continued, "Thus indicating that the redness is an accident at best but one based upon some specific set of processes in the growth of the flower over time."

"Interesting" he replied, "Indeed we can always take this accident related to color and explain it more so in terms of things, individual things, that impact and result in that color. Yes indeed, this is a good simple example."

"Now on to the issue of Individualism." I replied, "You have essentially used the term regarding individuals as individualism. The meaning here is that each human is an individual, and individual person. You then investigate this in terms of individual rights, or Natural Rights coming from Natural Law. You also argue if I am correct that the Bible focuses on individual salvation, individual good deeds, individual redemption. Christ did not demand that Rome and the Emperor follow the Gospel teachings, only those who were individual Christians. In fact the Gospel teaching separates the Church and the State, more so, the individual's commitment to God from the individual's commitment to Rome or the State. It was even Saint Francis who in his rule of obedience gave a caution that the individual member of the order would have to make the individual decision. Finally, in the argument regarding poverty, it was driven by the individual possession and use of property, use such as consumption of food, and ownership of that food. It was the individual member of the Order, be they a Friar, a Third Order, a Poor Sister, we were equally and individually so obliged. From this amalgam of insights, we then can understand that the individual person, be they man or woman, free or slave, have a duty but moreover we have individual rights, Natural Rights, given equally by God to all people. Is that a reasonable articulation of what you have said William?"

He sat back and smiled. He then said:

"Brendan, you have simplified my many words, you sound like a preacher. Yes that is the non-academic answer."

I then replied:

"The advantage that one has with many hours riding a horse, a boat, waiting in a battle field, is that one thinks. I have tried from time to time to explain your thinking, but I learned that most men have to be fed simple yet compelling ideas. They do not sit for long periods of contemplation. I have an opportunity with King Charles to perhaps convey some of these ideas, yet simply. I have tried in the Court of Edward, not the best place to convey my thoughts, I have even tried with good Queen Isabella, the strongest supporter of royalty I have seen, but a willing listener."

"Your approach, William, takes a person from a subject to a citizen, from a part of a collection to a separate and independent individual. As Marsilius of Padua had also noted, I believe, the individual has both status and rights."

"Indeed" replied Ockham, "And there is both a civil as well as theological issue here. For being just a subject one has to obey no matter what. As a citizen, one has a duty and in return certain rights. Thus a Knight may have a duty to serve the Lord but he in return has the right to

ownership in land. The same is our relationship with God. It is the individual who has that relationship as, if you will, a citizen in the family of Christ. We are held individually to account for our deeds. We are individually given Grace for redemption."

"Then I would ask, if this is the case, why then do we have such a concern for Original Sin?" I asked, "Why have this communal guilt for which Christ came and died for us? After all we as an individual, with no nexus to our deep dark past, may have had no part in that sin, and thus how does one look back and retain that sin?"

"Your question has merit. But allow me to return to it when we discuss Faith. The day is long, I am getting old. Perhaps a good dinner?" Ockham smiled and went forth to eat.

We spent a bit longer simplifying the idea of individualism. It was not an idea of selfishness, not an idea of separation, but an idea of individual duties and rights. Duties as regards to the understanding of what the individual was obliged under the law of the land and the law of God. The rights were rights rendered by God to the individual. These were Natural Rights. There were other rights, such as those that the King or other ruler may give to their subjects, but those were not Natural Rights, they could be taken away, changed, or even negated without reason. Natural Rights superseded these and were the result of Natural Law.

I began by asking Ockham:

"William, in your work, *Decretum*, you articulate three types of Natural Law. May we discuss them a bit. I understand that a great deal of your motivation was directed at the choosing of and powers relegated to a Pope. But let us leave that to the side for a moment, let us discuss just the definitions of natural Law, and then we can move to Natural Rights."

Ockham replied:

"Excellent, this is always a complex issue but a critical one for the understanding of the Pope and his powers."

"There are three types or understandings of Natural Law. The first understanding is based upon law in conformity with natural reason which never fails. Gratian uses this definition. It means that "thou shall not kill" is understood by all by means of our natural reason as a human. This First Natural Law definition is one concomitant with the existence of humans."

I interjected:

"However, and excuse me if I am inferring incorrectly, but you define Natural Law as something from Natural Reason. This seems to me to have the risk of circular logic, for in both cases the predicate "Natural" infers it is part of our nature as a human, all humans. You then relate it to say, "Do not kill" and unfortunately I have seen much too much slaughter. It thus raises two questions. First if something is "Natural" then it must be inherent in our nature, and our nature must somehow be the same in all humans. Does this not then conflict with individuals? My second point, is that again if in all humans, we see what we understand to be

humans slaughtering incessantly then are then they not humans or are they then just sinning all the time?"

Ockham smiled and replied:

"Brendan, you have spent too much time in the real world. Let me continue with my other two definitions. You raise valid concerns. On the second, yes indeed this is sinful, unless it is dealt with as an unjust aggressor issue. That you know. It is the basis of a valid war. The first question is perhaps at first sight circular, but as we would have started with natural reason as a philosophical construct we would not have found a circular reasoning. Let me continue to the issue of the other definitions."

He continued:

"The Second Natural Law is the one where one uses only natural equity without reference to any human law or custom. For example it is the law that was present in nature when first initiated. It was the law at the time of the Fall of Man, yet this Natural Law definition can be mutable. Again the definition here is as Rufinus and others has agreed to. It may be disturbing as to its mutability. And yes Brendan, it relies on natural equity, fairness, or even justice if you will. My usage here is I believe consistent with the Gratian and the Decretum. But here in the Second Natural Law, that consistent with the Decretum, I also find that one sees that such things as property were thus created after the Fall, were part of the evolving Natural Law."

"Now the Third Natural Law builds upon the above two. In this case Natural Law is defined as that which can be ascertained by evident reason from the law of nations or some other law or even from some divine or human act, unless the evidently contrary can be established by those concerned. This I call the natural law by supposition. This is a conditional natural law, derived from rational responses to contingent situations. I was to understand this from a statement by Isidore of Seville. He noted that "the common possession of all things" and "the return of a thing deposited or money loaned" These he relates to Natural Law. Thus this refers to property, to the individual ownership of property. Moreover the repayment refers thusly to actual private property. Finally, private property as instituted by man. We thus have both common property by understanding the Second Natural Law and private property as understanding the Third Natural Law. Private property is an alienation concept, the taking of what was in common and making it private. Yet it is a Natural Law. A law based upon a temporal evolution of agreed principles with agreed to equity. As I will argue later, this Third Natural Law also is the basis by which we individuals have the right to elect our leaders, civil and spiritual."

I replied:

"I believe we can relate this one. Yet there is a concerning note. You state that it may be changed if "the contrary to those concerned". Thus this Natural Law is not only a contingent law but one which is changeable, and changeable by those concerned, namely I would gather the people?"

"Yes and the point then leads to the understanding of Natural Rights." Ockham replied. "If one can alienate, change, refine, then one has a right. Can you see where I am going? I am working

with those who came before, working within the law as we know it, consistent with the Bible, and from this we can now start to understand the scope of Natural Law and from it the clear presence of Natural Rights. A very basic right is to elect our leaders. That include the Pope, as was the case from the time of Christ. We elect the leader, not some appointment by those of political stance."

I returned to the issue which had led to the fact that Ockham was here in Munich and not back at Oxford. Namely the issue of poverty, and the driving issue of property and use versus ownership. Until John XXII entered the fray, Franciscans and the Pope were satisfied with the vow of poverty as one where Franciscans had use of things but their ownership was held by the Pope. Now I always felt that this was a splitting of hairs but everyone was comfortable. It was when the conservative Franciscans, called the Spirituals, took the position that poverty was the way of Jesus and the Apostles and it was that way that they were following. That put John XXII in a bit of a tight spot. Here he was turning Avignon into a palatial estate, a castle to compete with any King or Emperor, clothes that shamed all of them, jewels, food, wines, while the poor wandered about helpless. The Spirituals walked about barefoot and with rags, often unclean as well. As Franciscans we spent our time not in a monetary hidden from the world but as an integral part of it. As a physician I was intimately so involved. Ockham was an academic and not truly a Spiritual but when he saw the arguments that the Pope was promulgating he began to study it and in no time saw the Pope was in error.

Ockham being Ockham then went and exposed this to the Pope, as well as the Order, and then all Hell broke loose. Popes as it would seem do not like being told they are wrong, after all they are Popes. Academics also enjoy an intellectual battle. Thus off it went. But no sooner than telling the Pope he was wrong, and having is reasonable well accepted the Pope rebelled. But to Ockham, and many others, this made the Pope a heretic. Thus did Ockham state. On to Munich he went. Excommunicated. But many felt Ockham was correct. The Pope is a man, he can err, and he is not infallible. Popes have made errors again and again, and if precedent is any claim, then Popes seems to err more frequently than most. Yet one does not tell the Pope this to his face, especially an English Friar to a French Cardinal, now Pope.

I had gotten to know John, the current Pope, quite well when I worked with Umberto Gui, helping him with those who were ill. John was imperious, arrogant, and prone to dicta which were baseless in fact but subsumed in form. He knew the techniques of a Canon lawyer, the Code of Justinian, the twists and turns of battles at court. None of that related to reality. Frankly many who I knew about this man disliked him, yet the feigned recognition as well as adulation. That was the way at Court, it was the way at Avignon.

I replied:

"William, it would be of interest to consider the following. It is an example from commerce called bailment. Bailment is the process whereby a third party take possession but not ownership of an item. For example, my mother's family had ships, and they carried goods from Bristol to Marseille or Brest or Bordeaux. At no time did they "own" the property, they just held it in the possession to transport. At the other end another party held a contract to receive the property in payment. Then my uncle for example would return with the payment, which may have been

other goods, again having possession but not ownership. Now consider the case of the "locked chest", tried at Court in 1315 under Edward II.

The locked chest case was one where the bailee had a chest which was locked and the goods or property was in the locked chest. The chest was stolen but while locked. If the goods had been stolen with the chest open the bailee was liable but since the chest was closed when stolen then the bailee had kept his duty and was not liable. Thus in the understanding is that if the bailee keeps his duty of care and security then he has no liability if the property is lost or stolen. However it does not release the bailee or carrier from a duty. There have been several other similar cases recently just before my departure under Edward III our current King. Specifically the case was of a pledge which came up, which seems always to have been regarded as a special bailment to keep as one's own goods.

The defense was, that the goods were stolen with the defendant's own. The plaintiff was driven to reply a tender before the theft, which would have put an end to the pledge, and left the defendant a general bailee. The issue was taken which confirms the other cases, by implying that in that event the defendant would be liable. Thus the issue of property and possession is a key to commerce and frankly it supports your position regarding Franciscan poverty! Frankly it may also presage why England may develop an excellent system of commerce, where in France the rules are still too complex and dated."

Ockham replied:

"Yes, I see, and this is an example of the law being reflective of the Third Natural Law definition. It is reflexive and adjustable. As new facts are ascertained it adapts to the facts. This is an intriguing approach, yet so foreign to Roman Law, or worse Canon Law. Gratian would never have considered this. It is a law of cases not of codes. The Civil Law tends to have the ability therefore to adapt. The basic Law from the Bible provides core elements but it too is open to interpretation. One must just think of the tale of the prostitute who sought forgiveness, of the thief who sought the same at the crucifixion."

He continued:

"If you recall, part of my arguments were related to two issues. The right of use, or *ius utendi*, was the legal right of an individual, one not expressly not the owner, to utilize some external entity, which if not warranted by the owner would be illegal. The second is ownership itself, or *dominium*, which is the right of the individual owner who lays claim to an entity and furthermore has the right to deny access or use by any third party. You see that here I have included two elements. First the element of the individual, for the property has been now associated with this person, not the Prince, the Lord, the state, but the very singular person. Second, and this I believe is most critical, is the fact that this is a right, in fact a Natural Right, as we have already discussed. If everything was common in the Garden of Eden as is understood, then after the Fall, mankind began to acquire individual ownership, usually perforce of labor, such as the clearing of a field, the planting of a crop, the raising of a sheep, the building of a house. The result then of man's actions was ownership, by the individual, and then the natural right resulting from that action allowed for an alienation in the use by others."

We would spend time discussing rulers and their powers. I recall my discussing with him my observations of the city states in Italy. I stated:

"William, I understand some of your thoughts on rulers and their powers, and what is the best form of rulers. But allow me to give you some observations which I have made in my travels. As you know, I had spent time in Bologna, and as I went about the northern cities in Italy, I found a new form of rule, let us call it leadership. People chose their rulers, not everyone participated in the process, but it often was enough to make many feel they had a voice. Rulers thusly chosen had then a sense that their duty was to the people whom they governed. Unlike Kings, who often believe that they have a Divine Right of ruling, somehow being chosen by God, and the result is that their acts are beyond reproach."

Ockham replied:

"You are aware that it my contention that monarchy is the best form of governing. My reasons are many, but ultimately it comes down to the inability of the masses to act reasonably. The masses become the mob and mob rule is always the worst kind. Your argument of city states has merit, but it does so because of two reasons. First the populace in those states who select their leaders are educated and enlightened. The selection is not open to all, only those who have an interest in good governing. The second reason is size. These are rulers of city states, small with common interests. Now take England, a King must deal with a massive and disparate set of interests. He cannot reflect the interests necessarily of all, but must seek a common good. Furthermore in England, France, and many other locales, the people have no knowledge of what the needs of a kingdom are, they see at most their local and personal needs, their individual needs if you will."

"Brendan, you recall my fundamental thesis. The people cannot render more power to a ruler than that which they possess themselves. There are thus limits to the power of any ruler. The people fundamentally have conveyed willing the power to a ruler, if that ruler be selected directly by them or via kingship, or even if you will the Pope himself."

I interjected:

"But William, as regards to a Pope, we have the biblical dictum that Peter has the power to bind, namely Christ has given Peter, and perforce of continuity, the Pope a set of powers supra to that of a civil ruler. For in Mathew 18:18 we have:

Verily I say to you, Whatsoever ye shall bind on the earth shall be bound in heaven, and whatsoever ye shall loose on the earth shall be loosed in heaven.

How then can we delimit the powers of a Pope? Does this not give to a Pope almost an unlimited power?"

Ockham replied:

"Your point has been well taken. In my work *Contra Benedictum* and *An princeps* I noted that it is accepted Canon Law, as evidenced in Gratian, that evangelical liberty limited papal power. The very natural and civil rights we possess delimit the powers as presented under Mathew. If this were unlimited power, religious and civil, then the Pope could overthrow a King, and in contrast Christ also said to give to God what is God's and to Caesar what is Caesar's. There is a natural liberty whereby men are free and not slaves. In *Dialogus* I extended this by the argument with my Student, my interlocutor. The Pope cannot regulate or command things, that would be against our liberty, our free will. Each individual gains or loses redemption by their individual acts, by their individual choices. Not by Papal dicta.

After discussing civil rulers we had finally got to the ultimate ruler, the Pope. I had read and re-read Ockham's "Work of Ninety Days", the brutal and brilliant response to John XXII attack on the Franciscans. It left any who read it with the clear understanding of John's heresy and of Ockham's correctness. It was so compelling that the Popes would pretend it did not exist so as not to confront it.

I began by asking:

"William, when discussing the Papacy you said:

We are left with the conclusion that papal principate was instituted for the utility of its subjects and not for its own utility or honour, and. in consequence is worthy to be called not 'of lordship' but 'of service' ·In which ... it is assimilated (more than any worldly principate instituted in practice) to the most noble form of royal principate ... and m which it excels all other principates in dignity.

This clearly is consistent with what Gregory I said of himself, namely he was the "Servant of the Servants of God". Namely he was there for the utility of the Faithful, not to rule them. He eschewed the trappings of a religious ruler, at least in his sayings. He entered into dialogue with those with whom he disagreed. The most famous to us Irish is he dialogue with Columbanus on the argument on the choice of the date of Easter. Columbanus and the Irish state, at the time the only remaining stable and educated state in what was left of the Western world, sided with the Greek Patriarchs, and it was Gregory who stood alone, rejecting their selection of a date. But that debate became a debate on frankly a scientific basis of a new calendar, solar versus lunar, and Columbanus gracefully acceded to Gregory. Thus we have a clear precedent of Papal authority and behavior. Yet we have had Popes since who have taken the "purple" if you will. Whereas Gregory was a Benedictine, eschewing the riches, John XXII was regal, and covering himself and his office with unlimited wealth. How do the Faithful come to deal with the changing disparity?"

His response:

"We have a Pope, and originally that Pope was the Bishop of Rome, and that Bishop was selected as were all Bishops by the people they represented. Like your City State examples Brendan. For Gregory I was himself so selected, despite his please against being so. Yet Gregory was also delimited by the Emperor in Constantinople. So with Gregory we have an example of a

saintly monk, selected by his people, approved by his Emperor. Now we have a Pope selected by Cardinals which in turn he has the authority to appoint. It is circular reasoning, and the Pope now tells the Emperor what to do, and unlike Gregory sees all the Faithful as his servants. The Pope does not see individuals, he sees a mass of people who must comply with his every word, and that often includes the controlling of Kings and Princes. Just look at Ludwig, he was duly appointed but Pope John did not want him. What power does the Pope have to overthrow a leader? Frankly what power does a Pope have over any leader. The leader is an individual and has a moral responsibility as an individual. The King will face God alone, not with his armies."

It was clear that as Ockham spoke he had not only hardened his position but had dramatically strengthened it as well. We began a discussion regarding faith and reason. Ockham commenced:

"Brendan, you have known for quite a while the limits of human reason, do you not?"

I replied:

"William, more now than ever. I am a physician by practice and education. Unlike many, I have taken a Bacon like approach, namely I must observe what is there, not just rely upon what is written, and less upon reason. Medicine is akin to philosophy. It often rested upon the ancients. But for example, when at Bologna, under Mondino, we studied anatomy, and in that context I saw things that Galen had said which were false. Had I relied upon Galen and just reason, rather than facts, I would have made great errors. For example, I have seen men whose hearts are on the right side, very few, but they exist. Reason would have told me otherwise. Actually hearing and feeling and understanding tells me otherwise. There are many things which are well beyond reason. Cancers, the growths that kill, I have seen many, what is their cause, how do I treat them. They are not a result of bad humors, that are unknown but I firmly believe are knowable, yet only with a better understanding of the facts. Moreover, permit me an example. Tools, instruments, which allow me to examine what before one could not see. Each time I get a new tool, such as a lens, I can see more and understand more. It is the reality of what I observe rather than the internal process of just reason which allows me to expand my understanding.

Ockham replied:

"Yes then I have asserted that human reason is not up to many tasks and especially many that relate to our religion. I take the example of the Trinity. It lies beyond any reason. The same holds for the Eucharist. The complexity of the Trinity requires, no demands, faith, not reason. In the case of the Eucharist one believes via Faith that Christ is present. To reason a process which we cannot either understand no less demonstrate makes the result a farce. Thus *sola fide*, by faith alone, do we come to this and many other mysteries of the Faith. We have had many, especially amongst the Dominicans, who try to create what are at best word games to explain these Mysteries. They are Mysteries of Faith and by Faith alone can we accept them."

"In many such cases we see a dilemma." I replied, "A dilemma in that adherence demands belief but that belief is to be buttressed by reason, and yet faith abandons reason and is then the only

door to belief. We must abandon reason, and thus our very humanity if you will, if not also our very individualism. Are you saying then that we must accept all just by faith?"

"No," he replied, "like you and your medicine, reason is a tool, to use the tool you need something tangible to work upon. Your lens is an example. You mention the man sick with what you say are worms. You can examine his droppings without a tool and you see nothing. There are no worms. Yet you use the lens as a tool and you get to see the worms, what was small is now large, what was unseen is now seen. In my view faith is such a tool. What was unseen in the Trinity, faith allows us to see, what was unfathomable in the Eucharist, faith allows us to accept. Moreover as you note, these tools evolve, improve, overtime, and as we the Faithful do likewise, we will be better able, through Faith, to grasp these facts of our belief."

As we got to the end of our discussions I raised a critical issue with Ockham. Namely the issue of words and their meaning, especially as they may change over time. I began by asking Ockham the following:

"William, as we have been discussing these issues, and I believe that now in our later years they become more clear and concise, I have noticed that we often use words, such as *ius*, in a manner which is not necessarily what it may have meant not a millennia ago but even a century ago. As such this raises several issues. First, and this is most critical, when reading the Bible, are we seeking understanding in the words as they are understood now or as they were understood then? Furthermore, if we seek clarity, who has such clarity to give, a Pope, a Council, or is it to be left to each person. All have faults, all are subject to error. Second, when looking to the Bible as God's word, we look at translations. Not only in Latin do words change over time, namely the same word gets a different meaning, but in translating we get a double problem; first the selection of a Latin word for a Hebrew or Greek word, and then the time at which the Latin word was selected may have been of such a past that we no longer accept its meaning now. How do we ever try to reconcile these issues?"

"You raise a very good point. I give you a simple example. Take the word *fundus*, a field, a piece of land. To the Romans a *fundus* was not just the earth, the field, but it entailed all rights we have to a field." he continued, "Yet to day in our current time, depending on where one lives, it is merely a thing, a piece of land, and the rights of use accrue from laws which are enacted apart from the piece of dirt. We have managed to separate rights and even obligations from the thing itself. Thus in this simple example, we are using the simple word *fundus* and over time its meaning has changed dramatically."

I responded:

"Then it is important to understand that time, and in a sense history if you will, is a progression and reflection of human understanding. The more we learn, and even the more we may forget, changes the way we see the world, the meanings we give to words, which are merely a reflection of our combined understanding of this reality."

As we finished our discussions on philosophical issues Ockham proceeded to ask me about the wars. He had heard a great deal but he had never been a part of a battle, had not seen the carnage

that I had. As a philosopher he inquired about the issue of a "just war" which was the theologians way to justify this carnage. This was not an area for which he had any exposure or understanding, and mine was limited to that of a physician trying to heal or as a priest trying to comfort.

I told Ockham:

"William, war is as close to hell as one can consider. One side attacks the other. That I can see, armed men trying to overcome one another. But what I cannot understand is the brutality on poor people, unarmed peasants, where the men at arms ride horses, setting fire to homes, crops, killing the farm animals, poisoning the water, salting fields. This is a tactic to deprive the Lords and Kings from profiting from the taxes on these poor people. Frankly William I can see how there could ultimately be a revolt, a revolt against the privileged Knights and Lords, whose sole interest is self-aggrandizement."

Ockham's response was as one would expect from a theologian and philosopher. He came back with the "just war" theory. He said to me:

"Brendan, I understand your intensity. But often war is justified. Is it not, to defend one's own subjects. From my understanding a war is just if it were to meet the five requirement. Permit me to discuss them. They are persona, res, causa, animus and auctoritas. That is the persona must not be religious. I assume that you were brandishing a sword. The second is res, the fundamental cause of the action would be defence of the country or the seeking return of a purloined possession or person, causa was the necessity of the act of war in that there was no other alternative, animus or the spirit in which the war was executed was to be one of justice and avoiding hatred and unjust acts, and finally auctoritas, namely the war must be waged under the authority of a prince or similar accepted lord. If these are met then is not this a moral and just act?"

I replied:

"William, in a world where all is logic and all men are rational and act according to both reason and God's law, then yes, a just war exists and can be a moral act. But I have seen men act as beasts, nay beasts are more kind and moral. God does not permit the bear or wolf to slaughter for pleasure, leaving decaying men, women and children in barren fields. The chevauchees wherein the men at arms ride their massive steeds through peasant lands slaughtering all violates the very rules you have just presented. Yet the Popes never protest. In fact the Popes often embolden the Lords in such acts as they do in attacks in Crusades. The result is often bilateral butchery. Then again, William, who is to say that the cause of action is correct and not just an excuse to engage in war, is the decision of a cause solely in the eyes of the beholder? As to the causa, the necessity to act if you will, if there be a just cause is there then a true necessity to act, that there is not alternative. I await the day when a Pope leads an army! Indeed, with some of the Bishops and Cardinals in the Italian states, I can see that as a possibility also. That would I believe be a fundamental violation of the persona clause, would it not?"

Ockham burst into laughter and noted:

"A Pope leading an army! Yes, that would perforce of definition be an Unjust War!"

We both laughed but I privately wondered if the Church would ever be exposed to such. I have seen Kings, Princes, leading charges, being slaughtered and laying in pools of their own blood. I have heard the same voices from Popes, and wondered what it would take to get them to the field of battle. At least in Avignon they were too comfortable and not inclined to act personally. Yet.

I would bade Ockham farewell soon as I went forward to Prague. Spring was on its way and the Bavarian country side was just about to turn green. I wondered how I would tell Charles some of these things. Kings are not the best of listeners, and as we have found Popes are even less so. Thus far I have seen three Popes, and John XXII was clearly the most intransigent. A lawyer, Canon Lawyer, trained in the Justinian tradition with the Decretum of Gratian. Ockham, a Theologian, and Philosopher. Each talking past each other, each with strong egos. I knew enough to understand some of the moves, some of the games. As one would say, my main task was as a physician, and yet even there I could often do so little. I tried to follow Friar Bacon and his method of scientific proof, namely deal with facts, observables. I took it a bit further and tried to measure and quantify, compare and contrast, but always built upon observables. The metaphysician has no solid ground, no independent fact checker, the theologian in contrast has the Word of God, and the believer has but Faith.



Labels: [Commentary](#)

Thursday, December 14, 2017

[Net Neutrality: The Full Employment Act for Lawyers](#)

Beware of what you ask for. You see as a Common Carrier you received all types of protection. Since Elizabeth I you got lots of assurance that your liability was limited. Now that the big carriers got what they asked for, perhaps they may want to explore that a bit.

[I wrote an extensive piece](#) some ten years ago. It may really be worth looking at now! I also wrote a [draft book on the subject](#), including interconnection.

This may easily lead to a massive number of large class action suits. For example:

1. What the FCC in its wisdom did was remove Common Carrier protection. Under such a class, common carrier, your liability was limited to what you were paid for the transport. As no longer being a common carrier you become a party to any claim resulting from what the service being provided is used for and the damages resulting therefrom. Yep, send a noisy CAT of a mammogram and misread the lesion, you are now a party.
2. In classic common carriage, you sell access to your network according to standard prices. If you have a subsidiary that competes with some third party then you are safe from any antitrust claims. Both Sherman (criminal) and Clayton (FTC). But now you can compete with price discrimination, namely discriminatory pricing. Welcome to Clayton. This will keep antitrust

attorneys fully occupied, and it is a class.

3. I remember when I first started at Bell Labs in 1964. The turned Beverly Hills over with ESS No 1. It crashed at 12:45 PDT, which was 3:45 EDT and just before the Stock Market closed. Millions of lost trades. But too bad, as a common carrier your were safe. But now as a party to the transaction you become a party to the claim.

I can see this list just expanding! Having been an Expert at a few dozen trials, I just am amazed at how some folks just do not think, unless well I will just keep that one to myself.



Labels: [FCC](#), [Internet Neutrality](#)

Wednesday, December 13, 2017

[Healthcare in New Jersey](#)

[NJBIZ](#) reports on demands of the incoming Governor as to how to "improve" the State's Healthcare system.

Some observations:

Amend state law so that health care related state boards are not self-governed. Instead, require that at least half of any of these individual board's memberships be comprised of individuals whose professions are not directly regulated by that board, and who would be representative of consumers that utilize the services overseen by the board. In addition, the state should examine and issue a report on best practices utilized by other states for health care related state boards.

That would mean politically appointed and motivated individuals having no knowledge of or interest in medicine but promulgating a politically supported agenda.

Revise state law to allow for the electronic delivery of insurance materials and provide for such delivery as the default method, while allowing consumers to opt in to the delivery of paper materials if they wish.

Opt out seems to be pervasive in NJ. Especially with the Democrats. This would make every older person require electronic delivery and thus open it up to massive data fraud.

Amend state law (through the Division of Consumer Affairs) to expand the kinds of services nurses, physician assistants or therapists can perform without supervision and in general.

This is the Nurses full employment act. They are cheaper and even though not qualified they become your only choice!

That New Jersey adopt a standard that imposes requirements that providers offering services at hospitals participate in the same networks as such hospitals, and that providers and facilities publicly disclose the networks in which they participate.

If you are a specialist and the hospital at which you have privileges serves Medicaid then you must also! This will drive all specialists to private "clinics".

If you did not like Obama Care your will really thrill to Murphy Care! Another gift from Goldman Sachs.



Labels: [Health Care](#)

[Cancer Treatment and Unintended Consequences](#)

The recent explosion in immunotherapy targeting such elements as PD-1 or PD-L1 and others has demonstrated a significant positive step forward. However recent results indicate that there may also be a dark side to this process.

As Sarkizova and Hacohen have noted:

The T cells of the immune system have a key role in the identification and elimination of cells that pose a threat to the body, such as infected cells and cancer cells.(authors) propose a framework to assess how effectively tumours can be detected by T cells — a tumour property known as immunogenicity. The authors demonstrate that their models for assigning tumour-immunogenicity scores can be used to predict clinical responses to a type of cancer immunotherapy called checkpoint blockade.

Most cells in the body present peptide fragments known as antigens on their cell surface, which are generated from intracellular proteins. Each peptide is bound in a complex with a specialized receptor called an MHC class I protein (HLA class I in humans). T cells known as cytotoxic T cells police the body in search of cells displaying specific antigens, especially antigens from infectious organisms, or in the case of cancer, antigens known as neoantigens that have arisen as a result of a mutation. If the T-cell receptor (TCR) of a cytotoxic T cell recognizes and binds an antigen that is not normally present, the T cell will often unleash an attack that kills the cell displaying that antigen. TCRs are highly variable and have slightly different antigen-binding regions, enabling the immune system to recognize millions of antigens. Antigen binding to MHC proteins and TCR recognition of antigen–MHC complexes are key determinants of an immune response.

They continue with the discussion of checkpoints as follows:

Tumour cells often fight back against this immune-system surveillance by hijacking the natural mechanisms that dampen immune responses, which are normally intended to block autoimmune attacks against healthy tissue. Checkpoint-blockade therapies can block these immuno-inhibitory signals, such as those generated by the 'checkpoint' PD-L1 protein⁴. However, only a subset of tumours treated with such therapies regress. Therefore, approaches are needed to identify the tumours that are most likely to respond to immunotherapy.

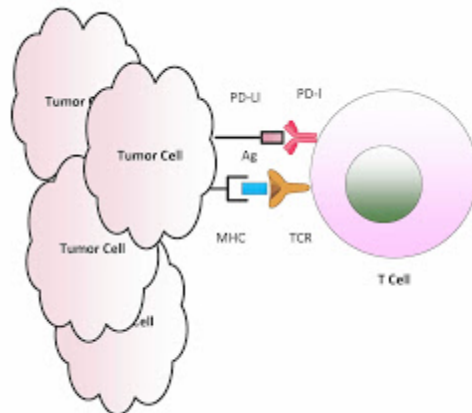
Current ways of predicting the effectiveness of checkpoint-blockade therapy rely on measuring the level of PD-L1 protein expressed by tumour cells, counting the number of T cells in a tumour, and estimating the number of different neoantigens that a tumour contains⁵. The work by Łuksza and Balachandran and their respective colleagues offers a new type of integrated model to predict whether a tumour will be attacked by T cells, a characteristic that they refer to as tumour fitness (low fitness being associated with a strong immune response against the tumour).

Thus in the best of worlds we see the result below. As Ludin and Zon note:

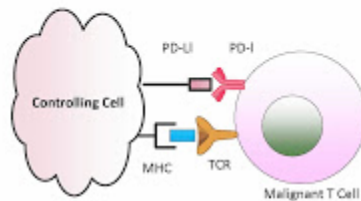
PD-1 is expressed on the surface of immune cells called T cells. When PD-1 is bound by a ligand produced by tumour cells, PD-1 signalling renders the T cell inactive, preventing immune responses that would destroy the tumour. Treatment with an antibody to PD-1 blocks ligand binding and so PD-1 signalling, instead promoting the PI3K signalling pathway, which is involved in T-cell activation. As such, anti-PD-1 treatment triggers an immune response,

Wartewig et al. have demonstrated that PD-1 signalling in a mouse model of T cell non-Hodgkin's lymphoma prevents proliferation of cancerous T cells (the source of the PD-1 ligand was not defined). In these mice, anti-PD-1 treatment can aggravate disease by reactivating the cancerous cells to enable then continuous proliferation.

Namely a tumor cell having a PD-L1 can be attacked by the T cells when we block this suppressor. We demonstrate this below. If PD-1 is matched with a PD-L1 then the T cell remains inactive. If we have an antibody used to block either PD-1 or PD-L1 then we can get T cell activation.



In contrast if the bad cell is the T cell, or if there is such a cell present in addition to the other tumor, then removing this block may activate the malignant T cell and off we go with a second malignancy. The example we show below.



As Wartewig et al note:

By contrast, a homo- or heterozygous deletion of PD-1 allows unrestricted T cell growth after an oncogenic insult and leads to the rapid development of highly aggressive lymphomas in vivo that are readily transplantable to recipients. Thus, the inhibitory PD-1 receptor is a potent haploinsufficient tumour suppressor in T cell lymphomas that is frequently altered in human disease. These findings extend the known physiological functions of PD-1 beyond the prevention of immunopathology after antigen-induced T cell activation, and have implications for T cell lymphoma therapies and for current strategies that target PD-1 in the broader context of immuno-oncology

Namely we have the potential that certain cells have managed to block malignant T cells from multiplying and thus keep a hematological cancer under control. When attacking another cancer with a blockade it may then allow this blocked cell to proliferate.

As Giladi and Amit note:

The cells of the immune system, which patrol the blood and dwell in tissues, have many functions. They protect the body from pathogens and cancer, and orchestrate metabolism and the formation of organs. They are involved in almost every activity that regulates the body's internal environment, from the development and remodelling of tissues to the clearance of dying cells and debris. So their dysfunction can cause many problems

This may be an obvious statement but it sets the path for what is to follow. The more one learns about the immune system the more we find a complexity of cells, not just T or B cells but T cells which perform different sets of functions. To understand this we need tools that allow us to ascertain what happens on a single cell basis. The authors continue:

First, it is clear that many of the current categories of immune cells, such as T cells or monocytes, encompass heterogeneous populations. To probe cellular complexity, researchers must therefore cast their nets wide, and try to collect all immune cells within a tissue or region of

interest. This is a very different approach from that used with methods based on cell-surface markers, which aim to obtain as pure a sample as possible.

Second, success will depend, in part, on the extent to which researchers preserve the states of cells and the original composition of a tissue. Cell stress or death should be minimized to ensure that tissue preparation does not favour specific cell types. ...

Third, bioinformaticians will need to develop scalable and robust algorithms to cope with greater numbers of cells, conflicting or overlapping programs of gene expression and fleeting developmental stages.

Fourth, after researchers have characterized all of the immune cells in a sample, they will need to find molecular markers that can be used to either enrich or deplete certain cell types in further samples.

The issue then is that it is essential to have in the "tool box" methods to carefully examine individual cells in situ. There are clear indications that cell interactions are complex, and also are extremely dynamic. The real question is: what level of depth of differentiation is essential for what level of patient care? As we noted above, there are cases where PD-1 blockage can on the one hand activate the immune system against the cancer and on the other hand suddenly activate dormant malignancies. Is this then just a "whack a mole" strategy against cancer, namely attacking one only to have then to attack a second resulting from the success of the first?

Fox and Loeb had previously attacked this issue from the perspective of breast cancer. They noted:

The total number of mutations that a tumour genome carries, including those present in only a small subset of cells, may in fact underlie the aggressiveness of different cancer subtypes. For example, the extent of genetic diversity within a tumour, and its divergence from normal tissue, probably influences the ability of the immune system to distinguish malignant cells from normal cells. Identifying the mechanisms by which cancer cells generate mutational heterogeneity may therefore present previously unexplored targets.

Single-cell sequencing will allow us to detect rare mutant subpopulations hidden within cancers that could expand and lead to drug resistance, and thus to avoid unnecessary and potentially harmful administration of ineffective, toxic therapies. Ultimately, the exceptional plasticity of the tumour genome may well prove to be a key characteristic of cancer¹¹ and a major, as yet untapped, therapeutic vulnerability.

There clearly is a growing need to perform a multiplicity of single cell analyses. However this is a complex spatio-temporal result, with a great deal of extraneous information. We should understand how cells genetic makeup changes as a function of time and of location. Location is itself complex because it refers to what cells are adjacent and even just close. Furthermore many gene expressions or suppressions are irrelevant, just chaff in an attempt to track a target. The desire to measure single cells is but a first step. A "model" or paradigm of what is essential for understanding the "system" is essential.

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Labels: [Cancer](#)

Monday, December 11, 2017

[The Accidental Suffragette](#)

Dorothy Day had a rather idiosyncratic life. She started out as a reporter on one of the many issue oriented papers in the early part of the twentieth century and that in New York managed to associate with a mix of the bohemian and left wing crowds of the day. She was involved with several different men, having first an abortion for a pregnancy and then giving birth out of wedlock on what may have been the second. After that she converted to Catholicism and aggressively pursued the Social Justice movement popular at the time. This included a focus on seeking better conditions for labor and immigrants.

[The book by Hennessy](#), her granddaughter, is a well written and somewhat balanced presentation of her life. Now for Day there have been a multiplicity of biographies as well as autobiographies so that one approaching Hennessy from that perspective will see a great deal of repetition of events. But Hennessy presents them in a fresh and readily readable manner.

One may ask why Day still plays an interesting role. First, it is the movement amongst Social Justice activists in the Catholic Church to seek Sainthood for her. Support is coming from many directions, such as Dolan in New York and Francis in Rome. This book by Hennessy is not a plea for Sainthood but a balanced presentation of her life. The second reason is that Day was a Social Justice advocate and as such one can examine her life and through it try to obtain a better understanding of just what that entails.

Now from my personal perspective I approached Day tangentially. In writing about my grandmother, Hattie Kruger, a Socialist in New York, a Suffragette, a woman who ran for Congress in 1918 and for New York State Office with Eugene Debs in 1920, I found that Hattie was arrested with Day and the two were in the first batch of women arrested in November 1917 by order of President Wilson and sent to Occoquan Prison where they were brutalized and force fed, again by orders of Wilson. Thus my grandmother spent time with Day and thus I wondered

what type of person she was. Furthermore Day lived three blocks from my Grandmother on State Island and my parents are buried a few grave sites from Day in the same Cemetery. So much for coincidences!

I was writing a piece on my Grandmother and her time as a Suffragette. I especially was focused on her time being arrested under the direct orders of Woodrow Wilson, that misogynistic, racist, anti-Semite, anti-Catholic, all around good guy. And we worry about Robert E. Lee, but I digress. Wilson hated these women walking around with signs asking for the right to vote. After all, he was a Virginian, a man, and more importantly the President. So off with their heads, or the next best thing was to arrest them and ship them off to prison. Get them past a friendly judge, and then to Occoquan Prison, now Lorton. Throw them in cells, host then down, let them starve! Yes indeed a real nice fellow Wilson was. After all he had just gotten us into WW I, sent a few hundred thousand to France, no uniforms though, but what the heck, let them figure out how to deal with the French snobs.

My Grandmother was in the first batch of women on that cold November day thrown into the back of the Black Marias, the police wagons. There were no Paddy Wagons in DC, not enough Irish. Along with her was a young lady called Dorothy Day. I had originally thought Day was there as a Suffragette. Not really. She was sent down as a reporter to cover the protest for her New York newspaper. She just happened to "be on the corner when the bus went by" so to speak. She became an "accidental Suffragette". Now Day recalls but one of the people with her and Day recalls that they joyfully discussed literature in the prison. Day at this time seems to have been more interested in the "adventure" of the moment and somewhat apart from the underlying cause, the right to vote for women. That surprised me, at least until I discovered a bit more about Day.

Days life during the teens and twenties was somewhat that of a libertine. In Day's writing and in that of Hennessy there are no holds barred regarding this period. One could surmise that this period is a bit like that of Augustine of Hippo, who took his concubine to Italy to study, abandoned her, then let his child loose, and then his son died. Augustine then returned to Hippo and had a career writing against the likes of the Donatists and Pelagians. The theme may have some parallel.

What did this "accidental Suffragette" do after her exposure to this world? It seems that she found God in the Catholic Church. Like many converts I have known, my mother having been one, they often move aggressively into their new found faith, and accept it in all its deepest dimensions. For Day it was a move which led to the founding of the Catholic Worker, a rather left wing but "Catholic" weekly. It focused on helping the oppressed, especially during the Depression period. Day indicates that the naming was in contradistinction to that of the Daily Worker, the paper of the Communist Party.

She then was accompanied by a French intellect and wanderer who convinced her to leverage this paper into a full blown mission, a mission to the poor and homeless, for which there were many in the 1930s. She soon found herself at the center of a movement, dedicated to this new found faith and its focus on human equality and justice.

By the 1940s she had also become an avowed pacifist and was strongly opposed the US entry into WW II, especially after Pearl Harbor. In the 1950s, she vehemently opposed the use of nuclear weapons and the execution of the Rosenbergs. By the 1960s she had a multiplicity of "farms" and similar places where people assembled and had what we called "Retreats", which were week-long "spiritual" get-togethers where they contemplated and listened to religious lectures. During this period she strongly opposed the Vietnam War, was pro-integration, and supported the farm workers actions and other similar equal rights movements.

She developed a wide cadre of admirers and fellow movement supporters ranging from labor leaders to religious figures such as Thomas Merton, the Trappist monk. By the 1970s, in her later years, she saw a slow reduction of many of these ventures, especially as she aged and was in poor health.

There is often comparison of Day to such figures as Francis of Assisi and others yet one can see Francis as the founder of a sustained Order of Friars who had a substantial impact on Catholic teaching. It is not clear what the sustained influence of Day will be. But it is worth the while to see through the eyes of her grand daughter what Day did, why, and to examine the consequences of her efforts.



Labels: [Books](#), [Politics](#)

Saturday, December 9, 2017

[Microbiome and Cancer](#)

We [wrote a piece a few weeks back on the Microbiome and Cancer](#). Some recent papers as summarized in [Nature](#) have discussed the progress in understanding this phenomenon. Now the Nature piece states:

Preclinical mouse models have shown that the gut microbiome can modulate therapeutic responses to cancer therapies. Yet, this has not been extensively characterized in humans. Two studies now propose that the gut microbiome is an important host factor that determines the response and primary resistance to anti-programmed cell death protein 1 (PD1) immunotherapy in patients with cancer. "the clinical response to PD1 blockade could be predicted by the composition of the gut microbiome" Both groups initially sought to determine whether the clinical response to PD1 blockade could be predicted by the composition of the gut microbiome. To achieve this, faecal samples were collected from patients with either melanoma, non-small-cell lung cancer (NSCLC) or renal cell carcinoma (RCC) before and after commencement of immunotherapy. Metagenomic shotgun sequencing was then used to quantify bacterial species. A common finding was that high diversity of the gut microbiome correlated with prolonged progression-free survival (PFS) following PD1 inhibition.

The papers are by [Routy et al](#) and the other by [Gopalakrishnan et al](#). [Routy et al note](#):

Immune checkpoint inhibitors (ICI) targeting the PD-1/PD-L1 axis induce sustained clinical responses in a sizeable minority of cancer patients. Here, we show that primary resistance to ICI

can be due to abnormal gut microbiome composition. Antibiotics (ATB) inhibited the clinical benefit of ICI in patients with advanced cancer. Fecal microbiota transplantation (FMT) from cancer patients who responded to ICI (but not from non-responding patients) into germ-free or ATB-treated mice ameliorated the antitumor effects of PD-1 blockade. Metagenomics of patient stools at diagnosis revealed correlations between clinical responses to ICI and the relative abundance of Akkermansia muciniphila. Oral supplementation with A. muciniphila post-FMT with non-responder feces restored the efficacy of PD-1 blockade in an IL-12-dependent manner, by increasing the recruitment of CCR9⁺CXCR3⁺CD4⁺ T lymphocytes into tumor beds.

There clearly are a multiplicity of dimensions in using the immune system to combat cancers. It is essential to view this as a systems problem, understanding that we are a bit ignorant of all of its dimensions.



Labels: [Cancer](#)

Thursday, December 7, 2017

[reCAPTCHA and Knowledge](#)

One should read Theaetetus a few times, even if Plato was a bit off, lacking any scientific basis. But then again these are techys I will be speaking of and worse they are millennials. But in trying to deal with reCAPTCHA, that device which says it can tell if you are a human, I suspect Plato would not agree.

Let me pose a simple example. The ask to show street signs. Then there is a photo with a street sign on a pole, and a bit overlapping another frame, just a wee bit. Now to me the pole is a part of the street sign. The sign would not function without the pole. But not to reCAPTCHA. So on to another picture asking the same question. How about that structure holding the sign above the highway? Nope, I guess not.

Language and meaning are complex, and despite the best efforts of those isolated mammals inhabiting some complex in California, I would guess, humans, the real kind, can understand the word "sign" in a multifaceted manner.

This is a simple but powerful example of the lack of human understanding, especially of others. Plato in his Socratic tales spent a great deal of time on this issue. Google seems clueless.



Labels: [Google](#)

Thursday, December 7, 2017

[Just an Observation](#)

From time to time I have bemoaned the USPS. Now, they look great compared to UPS! UPS seems to be sending its packages, no they are my packages, around the world a few times before they get where they are supposed to go. Perhaps someone in management could try to find out what is happening. After all they are a union shop and aren't they supposed to be better?



Labels: [Commentary](#)

[Remembering December 7th](#)



My father's crew mates at Manus in November 1944 after Battle of Surigao Straits. True Heroes!



Labels: [Commentary](#)

Wednesday, December 6, 2017

[Obesity and Cancer](#)

We have recently examined the issues of inflammation and cancer as well as the microbiome and cancer. A long standing relationship is with obesity and cancer. Obesity increases inflammation as well as altering the microbiome. [Science](#) notes:

Obesity-associated inflammation (OAI) can dramatically alter tissue composition, thereby creating a fertile soil for cancer development; it is conceivable that these changes may lower mutational and epigenetic barriers to tumorigenesis. For instance, in breast and pancreas, OAI is associated with altered extracellular matrix composition that facilitates transformation of premalignant cells. In the colon, epigenetic alterations that occur in cancer are observed in normal epithelial cells in the context of obesity, thus lowering the mutational threshold that is required for malignant transformation. These studies suggest that OAI “primes” both the tissue microenvironment and premalignant epithelial cells to facilitate oncogenic transformation. Indeed, obesity is often associated with specific molecular subtypes of cancer, which may reflect

a selective pressure exerted by the obese microenvironment resulting in the altered fitness of specific oncogenic mutations. Accordingly, tumors that evolve within an obese microenvironment may exhibit “obesity addiction” whereby they are driven by a dependency on hypernutrition and inflammatory cytokines.

It is interesting that fifty years ago we were all worried about the lack of food for humans. Now we have a massive explosion of obesity. Food seems no longer to be a global issue. But the sequellae from excess food may very well be more dire.



Labels: [Cancer](#), [Obesity](#)

Saturday, December 2, 2017

[Nuclear Buttons](#)

As of now, we have but a few students who may recall from their Second Year Latin:

Quo usque tandem abutere, Catilina, patientia nostra? quam diu etiam furor iste tuus nos eludet? quem ad finem sese effrenata iactabit audacia? nihilne te nocturnum praesidium Palati, nihil urbis vigiliae, nihil timor populi, nihil concursus bonorum omnium, nihil hic munitissimus habendi senatus locus, nihil horum ora voltusque moverunt?

The Oration Against Cataline by Cicero. Needless to say Marcus Tullius had less than an amicable ending. But Gary Wills interjects Marcus in his piece on Executive Power. It appears age creeps up on all of us. But I digress. [Wills](#) notes¹[1]:

The assumptions that Congress made about the conduct of President Eisenhower or President Reagan—that they could be counted on to act with humble precaution—no longer seem to apply. What can be done? There comes a time when, as Cicero put it, “The highest law should be preservation of the people,” Salus populi suprema lex esto. A crisis sufficient to justify use of this maxim cannot be predicted. It could be any first nuclear strike the president may order. Only extreme peril can justify an extreme remedy. It is said (I don’t know with what truth) that in 1974, Secretary of Defense James Schlesinger told the implementers that in the event of a nuclear order from President Nixon, who was in a massive drunken funk, they should clear it with him. We can only hope that there are high-ranking patriots who might act like that if Big Rocket Man went after Little Rocket Man. Even a soldier in the field must disobey a truly disastrous order from a manifestly disabled officer. The commander in chief has to be held to the same standard as his subordinate commanders, for the preservation of the people. It is reassuring to know that the current commander of the US Strategic Command, Air Force General John Hyten, as well as a former one, General Robert Kehler, recognizes this as a rule of international law.

¹[1] <http://www.nybooks.com/articles/2017/12/21/big-rocket-man/>

The problem here has in the past been one of neither side launching a nuclear attack, period. The sides were the US and the USSR. By the mid-1970s the consequences of a nuclear attack were seen by both sides as totally devastating making Mutual Assured Destruction, MAD, the only strategy to avoid. Back in the 60s we had [RISOP](#):

The U.S. military has canceled the Red Integrated Strategic Offensive Plan (RISOP), a hypothetical Russian nuclear strike plan against the United States created and used for decades by U.S. nuclear war planners to improve U.S. nuclear strike plans against Russia.

I recall one Plan, RISOP 9B, which assured the end of existence for all creatures on the planet! I recall when I was involved in the Comprehensive Test Ban Treaty negotiations in the late 70s having casual discussions with my Russian counterparts who also knew the consequences. There was a rational set of players on both sides. The very fact that we had the ability for a second strike, and a third if necessary, as did the Soviets, made both sides think. Clearly President Carter knew, as a Naval Officer on a Nuclear Sub, you had a key, and you also knew the consequences.

Does our current President know? Perhaps the question is; is there any parallel between the USSR and North Korea or Iran? The Russians and me and my colleagues could speak to our children and grandchildren. We saw a future, and despite differences we had them over politics, not religion or worse, not in the case of a putative mad man. Could we enter a nuclear war with Russia, doubtful, with China, doubtful, but the other two may readily launch a nuclear attack.

Thus, what do we do? One assumes that like RISOP 9B we have plans. A single nuke launched at San Francisco could be intercepted, hopefully. Then what? Or on the other hand do we consider a pre-emptive strike? If so, is it nuclear? We have a multiplicity of tactical nukes, some 1-5 KT yield with fairly clean radiation after effects, but if we did not use them after 9-11 then we would be hard pressed here. Nukes are nukes.

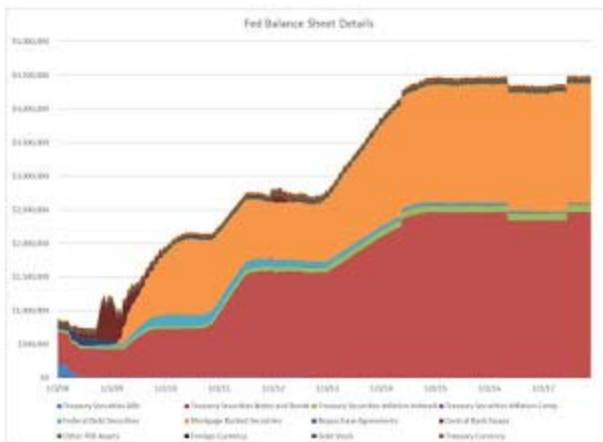
But one method of deterrence is uncertainty of the response by the other side, especially if the response could be overwhelming. Taking that uncertainty away then emboldens the adversary. That uncertainty is the most powerful of weapons. It costs nothing and does no damage short term. But what if it does not work? What if the adversary is just plain nuts? What if they do launch an attack? That is the real question.



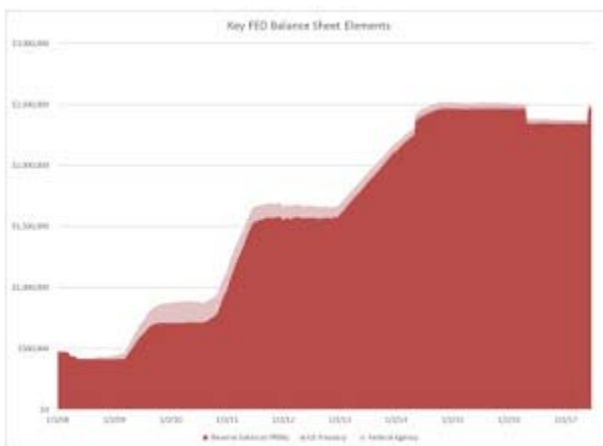
Labels: [Nuclear Weapons](#)

Wednesday, November 29, 2017

[FED Balance Sheet](#)



The FED Balance Sheet is shown above as of yesterday. Note that not much has changed.



Note the difference. Here we have removed the Mortgage Securities. Mostly Treasuries. Soon they must begin to unload this junk and at a much higher interest rate.

Based on this, the yield curve, the Trump Tax Plan, we expect significant inflation over the next three years. That will be one way to reduce the debt. I believe they did that in Germany in the 1920!



Labels: [Economy](#)

Tuesday, November 28, 2017

[Freedom of Speech?](#)

Just saw this on [China Daily](#). Worth thinking about.

The open trial of Peng and Lee will also help the public to know that the two defendants attempted to subvert State political power by forming online chat groups, and used them in a planned way to spread the idea of political subversion. Their activities violated China's Constitution and laws. And no country, let alone China, will tolerate such activities. The case

once again shows the judiciary's determination and ability to safeguard State security and maintain social stability in accordance with the law.

No other comments!



Tuesday, November 28, 2017

Yikes! Look at the Yield Curve!

Look at this yield curve. The short term is exploding and long term collapsing. That means in the long term there is no anticipation of growth but that short term there is great uncertainty!

The above clearly makes this point. Look at the spread, going to zero!

Labels: Economy

Sunday, November 26, 2017

More on Trump Tax

Dear Congressman Frelinghuysen,

I wish to bring to your attention two related issues. The first is the imposition of imputed income on Graduate students in the US. The second is Government funding of foreign students by various Government agencies. Both issues present clear and present dangers to the security of the United States. I base these conclusions on personal knowledge at academic institutions as well as my extensive international business experience in over twenty countries.

Permit me to lay out the details related thereto:

1 My background is a combination of academic and business actions. I hold a PhD from MIT in Electrical Engineering. I have been on the faculties of almost a half a dozen institutions including MIT, Columbia, GWU, and the Beijing University of Economics and Finance. I have personally started and operated companies in over twenty countries with offices in Moscow, Prague, Warsaw, and Athens. Most recently I returned to MIT from 2005 through 2012 to assist a half dozen Doctoral students. I also work with colleagues at Columbia Cancer Center in New York.

I have had extensive experience in major universities and also as an entrepreneur having started and/or financed some thirty-five companies. As such I have a somewhat unique set of experiences and expertise regarding the issue which I put before you in this correspondence. I also have been a resident of your District for nearly forty years.

2 The New House Tax Code materially changes the ability of Graduate students to finance their education

The new Tax proposal by the House makes some major material changes to various elements of the tax code. This correspondence refers mainly to that regarding the imposition of an imputed

income on Graduate students resulting from being a teaching or research assistant. My argument herein demonstrates that this change can and in my opinion will cause irreparable harm to the United States. Simply it will drive the remaining US citizen grad students out of Grad school, except for that small amount from families independently wealthy and capable of sending a student to such institution. However my experience is that most if not almost all students in Grad school for science and technology come from families of lesser means. In my own case I worked my way through MIT as an Instructor, and could not have done so under the proposed tax laws. In fact not being able to have done so would have resulted in thousands of lost jobs in our economy from the many companies I was able to start and/or finance.

3 Currently almost 80% of Graduate students in Science and Engineering are foreign.

The NY Times has a piece on the increasing percent of engineering graduate students who are foreign. They state:

At the undergraduate level, 80 percent are United States residents. At the graduate level, the number is reversed: About 80 percent hail from India, China, Korea, Turkey and other foreign countries.

This is a startling figure but one should ask; who is paying? Having spent an almost sixty years career in and out of Academia, I can make the following observations related thereto.

1. In the late 1950s the US Government made a major push to create more engineers and scientists. There were scholarships and institutions were incentivized to follow through. There were many scholarships and fellowships specifically for these types of degrees. Furthermore tuition was low, due mainly to the fact that overhead at Universities was minimal. Graduate fellowships were numerous, and were all performance related. If one did well in the right undergraduate curriculum then Grad school was effectively free. These graduates then went to the work force and created the technologies that underpin our national defense and competitive technologies. This is no longer the case.
2. Most of the grad students were first generation, coming from families that in many cases did not even graduate from a college. Frequently engineering and science was an entry point for the lower economic classes. Families with money often sent their children to exclusive schools and then in to banking or law.
3. Upon graduation jobs were available, especially for Graduate students with good degrees. Engineers and scientists entered areas such as solid state design, RF engineering, and the like. People during this period built things as compared to today's social media types who "code" screens which engage the users but one can argue has little value.
4. At that time places like Silicon Valley were inexpensive, allowing for a diverse group of workers. Housing was plentiful; and at reasonable prices. Startups made "real stuff", not just software enhancements.

In contrast, in today's world:

1. Almost all high tech grad students are funded by the U.S. Government. Yet 80% are foreign students who are also funded by the taxpayers. Those Chinese, Iranian, Syrian, grad students are funded by US tax dollars. They finish on our tax dollars and return home. In the case of the Chinese students they often bring this expertise back to Chinese companies and then these companies directly compete with the US. That is true in both for commercial and military entities.

2. US undergrads are often financially burdened when they finish their undergrad and thus are pressured to work and pay back the loans as well as taxes. As a side note the new Trump Tax Plan makes the student loan no longer deductible, another burden. The taxes taken from American students, and others, will then go to support the 80% of the grad students who are foreign.

3. What can be done? I believe it is simple; look back to the 1950s. Eisenhower may very well turn out to be our greatest President. His Administration saw the threat and at the same time the opportunity. They found ways to fund high performing undergrad tech students. Then make it a level playing field for US citizen students, especially if the taxpayer is footing the bill, the taxpayer should have preference. One should put a finger on the scale for US students.

4 Many, a great majority of truth be told, of the foreign Graduate students have their education funded by the US Government via Research Grants to Faculty members.

In my experience at MIT and other institutions, to this current day, Grad students are funded by research grants almost exclusively from US Government entities. Of the six doctoral students I assisted from 2005 through 2012 not one was an American citizen. Only one remained in the US after marrying an American citizen. All others returned to their country of origin. They took with them expertise vital to the success of the US. In addition without exception they were funded by DoD or DoD related research!

5 Moreover many of the foreign Graduate students in high tech such as Electrical Engineering and Computer Science are funded by DoD or similar national security sources.

The problem is not just that the foreign students are here and funded by US entities but that many of these in critical areas are funded by US DoD or related entities.

6 Graduating Foreign Students all too frequently return to their homes unable to remain productive in the U.S.

I had tried on multiple and repeated times to try and keep the students here. They wanted to stay. Yet Immigration Laws prevent this from happening. This results in the loss of intellectual capital paid for by the taxpayer and the transfer of this capital to risky if not outright hostile countries.

7 Many of the high tech foreign Graduate students returning to their countries after having been financed by DoD or related Government sources find their way into the home military or intelligence agencies. As a result many foreign Graduate students are being educated by US

Taxpayers via DoD or related Government sources and return to pose potential long term threats to the security of the United States.

I have seen many of these students returning to their home countries and finding positions in the defense or related industries. They have no choice since the U.S. will not accept them as potential citizens. This means that we really must re-examine our immigration laws regarding high tech and bio related graduate students. We must try to retain them, give them flexibility, no tie them to some work visa structure which benefits an employer but not eh U.S. If we are to invest them we then want the ability to gain the return on that investment.

8 The current Tax Code as noted below allows for US students to NOT include imputed tuition costs if they are Teaching or Research Assistants (TA or RA).

Namely Section 117 (c) allows for the exclusion of imputed tuition costs. That is highly acceptable. See Appendix A.

9 The new House proposal eliminates the student's ability NOT to include the imputed costs. In fact it makes the student include them which often dramatically increases the burden on US students making it impossible to attend Graduate School

Now quoting from the House Bill, on p 96 we have

SEC. 1204. REPEAL OF OTHER PROVISIONS RELATING TO EDUCATION. (a) IN GENERAL.—Subchapter B of chapter 1 is amended— (1) in part VII by striking sections 221 and tons in the table of sections for such part), (2) in part VII by striking sections 135 and 127 (and by striking the items relating to such sections in the table of sections for such part), and (3) by striking subsection (d) of section 117.

And on p 98 of the House Bill we see:

(e) CONFORMING AMENDMENTS RELATING TO SECTION 117(d).— (1) Section 117(c) (1) is amended— (A) by striking “subsections (a) and (d)” and inserting “subsection (a)”, and (B) by striking “or qualified tuition reduction”.

Namely the law is changed to allow for a imputed income resulting from an assistantship.

10 The combined results of funding foreign students and now taxing US students for unearned imputed income creates a clear strategic threat to the United States. In fact this is a clear and present danger. It strengthens our adversaries while debilitating the U.S to combat these adversaries.

The proposed taxing of Grad School tuition for Research Students would drive the 20% of American Grad students to 0% it is the "Make America Last" Act. We would be left with 100% Chinese, Iranian, Indian, Vietnamese etc students who will get all of our ideas paid by Government dollars and take it home to demolish our economy. Frankly this is one of the dumbest ideas I have ever seen. I managed to succeed due to Eisenhower and his innovations.

Remember Admiral Yamamoto went to Harvard, he then bombed Pearl Harbor. We do not want to repeat that! The proposed new Tax Plan has many destructive elements. It helps the rich but destroys our future. For example, the journal Nature states:

Graduate students, who receive the lion's share of tuition waivers, would be most affected. And 60% of the 145,000 students who get tuition reductions each year are working in science, engineering, technology and mathematics fields, the US Department of Education estimates. The amount of money that the government would reap from these taxes would be minuscule, given the \$20.5-trillion national debt. But it could weigh heavily on young scientists. Take a hypothetical PhD student at the Massachusetts Institute of Technology (MIT) in Cambridge, in receipt of a \$23,844 NIH stipend. Under the current system, she would pay very little in taxes. The new law would add her \$49,000 MIT tuition bill to her taxable income as though she were paid a \$73,000 salary — an amount she never actually sees. This would add thousands of dollars to her tax burden.

Thus, a student would get about \$24,000 plus an imputed say \$50,000. Under the old plan they paid tax on \$24,000. On the new plan it tax on \$74,000. Namely with a \$12,000 deduction it would be 15% of \$62,000 or \$9300. That is a 39% tax rate! Plus 3.5% for FICA plus 3% for Medicare plus in Massachusetts an added 8%. This is a 53.5% Tax Rate!

Now we already have 80% of the Grad students funded by their Governments, China and Iran. The remaining 20% are US and are paying the burden. So what will happen? Drug development, high tech development etc will all migrate to these countries. Not to mention weapons development. Eisenhower saw the need for a strong technology core. In contrast, Team Trump wants to destroy whatever future we may have had.

11 Some argue that the new House Bill has no true effect. They are grossly in error.

The recent House Tax Bill eliminates the ability of Grad students to not pay tax on a Teaching or Research Assistant-ship. Namely it means that they must pay tax on \$50,000 or more of money never received. Well they will destroy America as we know it. Perhaps that was the intent of the Republicans, I leave that to them. But Forbes has a writer who declares:

On the chopping block in House Republicans' bill is section 117(d) of the Internal Revenue Code, which exempts qualified tuition waivers from taxation. Many graduate students work as teaching or research assistance while completing their studies; universities often waive their tuition and provide a small living stipend as compensation. The House plan would treat these tuition waivers as taxable income, which graduate students fear could lead to annual tax hikes of several thousand dollars. Anxiety among graduate students and those considering graduate education is understandable. But what the narrative around this provision has missed is that the House bill does not touch another provision of the tax code: section 117(a). This section provides that scholarships used to pay tuition and fees are not considered taxable income. The catch is that universities which provide these scholarships cannot stipulate that students work as teaching or research assistants as a condition of receiving them. This is the main difference between scholarships and qualified tuition waivers: universities can require students to work as a condition of receiving the latter, but not the former. Under current law, both scholarships and

tuition waivers are not taxable. But the House bill draws a distinction between the two. Under the proposal, universities can still reduce their students' tuition bills without incurring tax consequences. However, if graduate students work as teaching or research assistants as a condition of getting that tuition help, then the amount of tuition reduction would be considered taxable income. Universities that wish to avoid saddling their graduate students with large tax bills therefore have an easy way out. They can reclassify their qualified tuition waivers as scholarships...

This is grossly false. The RA cost is charged to the research grant, usually a Government contract, and thus is netted to zero for the University. As a Scholarship it is not netted against the grant and thus comes out of the endowments or other similar funds. Perhaps for a TA this would work but there are fewer TAs and more RAs.

The main question is; who put this element in the Tax Bill and why? Now in my experience, Congress never really writes anything, Lobbyists do. So follow the money. Who did this?

12 To remedy this the US should promptly take the actions of: (i) removing the tax burden of section 117 as proposed by the House, and (ii) prohibiting the funding of students from hostile or potentially hostile countries by US agencies which research could be considered a threat to the US security or economy. Overall, Government should be looking out for the best interests of Americans. That means we need an understanding of the Eisenhower days, just after Sputnik. We managed to support the research areas and education of those most critical to our economy and security. The payoff lasted for decades. Now however is waning and just the opposite is occurring. Namely we are driving US students out with maniacal tax stipulations while funding the education and strategic capabilities of our adversaries, military and industrial.

I strongly recommend that the above recommendations be considered. I greatly appreciate your opposition to the Bill but after consideration this section can and I assure you shall cause irreparable harm to the United States! Its inclusion reflects a gross ignorance of what has allowed the US to be successful after WW II. This must be corrected promptly.

Very truly yours,

Appendix A

26 U.S. Code § 117 - Qualified scholarships

Qualified scholarships

(a) General rule

Gross income does not include any amount received as a qualified scholarship by an individual who is a candidate for a degree at an educational organization described in section 170(b) (1) (A) (ii).

(b) Qualified scholarship for purposes of this section—

(1) In general: The term “qualified scholarship” means any amount received by an individual as a scholarship or fellowship grant to the extent the individual establishes that, in accordance with the conditions of the grant, such amount was used for qualified tuition and related expenses.

(2) Qualified tuition and related expenses for purposes of paragraph (1), the term “qualified tuition and related expenses” means—

(A) Tuition and fees required for the enrollment or attendance of a student at an educational organization described in section 170(b) (1) (A) (ii), and

(B) Fees, books, supplies, and equipment required for courses of instruction at such an educational organization.

(c) Limitation

(1) In general Except as provided in paragraph (2), subsections (a) and (d) shall not apply to that portion of any amount received which represents payment for teaching, research, or other services by the student required as a condition for receiving the qualified scholarship or qualified tuition reduction.

(2) Exceptions Paragraph (1) shall not apply to any amount received by an individual under—

(A) The National Health Service Corps Scholarship Program under section 338A (g) (1) (A) of the Public Health Service Act,

(B) the Armed Forces Health Professions Scholarship and Financial Assistance program under subchapter I of chapter 105 of title 10, United States Code, or

(C) A comprehensive student work-learning-service program (as defined in section 448(e) of the Higher Education Act of 1965) operated by a work college (as defined in such section).

(d) Qualified tuition reduction

(1) In general Gross income shall not include any qualified tuition reduction.

(2) Qualified tuition reduction For purposes of this subsection, the term “qualified tuition reduction” means the amount of any reduction in tuition provided to an employee of an organization described in section 170(b)(1)(A)(ii) for the education (below the graduate level) at such organization (or another organization described in section 170(b)(1)(A)(ii)) of—

(A) Such employee, or

(B) Any person treated as an employee (or whose use is treated as an employee use) under the rules of section 132(h).

(3) Reduction must not discriminate in favor of highly compensated, etc.

Paragraph (1) shall apply with respect to any qualified tuition reduction provided with respect to any highly compensated employee only if such reduction is available on substantially the same terms to each member of a group of employees which is defined under a reasonable classification set up by the employer which does not discriminate in favor of highly compensated employees (within the meaning of section 414(q)). For purposes of this paragraph, the term “highly compensated employee” has the meaning given such term by section 414(q).

(5) Special rules for teaching and research assistants In the case of the education of an individual who is a graduate student at an educational organization described in section 170(b)(1)(A)(ii) and who is engaged in teaching or research activities for such organization, paragraph (2) shall be applied as if it did not contain the phrase “(below the graduate level)”.

Labels: Economy

Eric Ackerman and the Old World of Intelligence: UK Style

The book by Jackson and Hayson, *Covert Radar and Signals Interception*, is a well done presentation of the life and accomplishments of Eric Ackerman, one of the many brave and brilliant people who worked for R.V. Jones during WW II. Ackerman is a bit unique because of his brilliance in the ever developing electronic technologies combined with his daring in taking to the field at the time of war the systems used to penetrate and defeat the German systems. Eric grew up in somewhat humble beginnings and his schooling was in a technical school. Despite these limitations, he managed to become one of Jones's stars and an RAF officer, albeit not an active pilot.

The book covers Eric from his early life through the War and then into the Cold War. Eric was instrumental in a variety of signal intelligence and became almost a one man NSA, as the Americans would develop. Eric had the ability to understand enemy systems and techniques and then rapidly develop methods and systems to compromise them. Often he performed these tasks near or behind enemy lines and often at great personal peril.

The book provides full details on many of these exploits. It also provides a window to some of the personal elements of Eric's life, his marriage and his family.

I had the good fortune of working with Eric Ackerman from 1977 through 1980. I was his boss at COMSAT, but in many ways I was learning from him. I inherited Eric from his staff slot at COMSAT Labs. In 1977 I was at COMSAT Corporate, for two years since coming down from MIT. My experience was academic as well as in the military radar and Intel worlds. So unbeknownst to me Eric and I had somewhat a similar path, although during differing Wars. I had been approached by Government agencies to build a set of small earth stations and the related network of satellites and infrastructure for what was to be the verification systems on the Comprehensive Test Ban Treaty with the US, UK and USSR. I had done a preliminary system design and the "customer" was happy and wanted it implemented.

Thus I needed more folks and as luck would have it, Eric showed up at my office and said: "I was told to report to you. What do you want me to do?" Eric was then about 58, my father's age and I was mid 30s on my way to 40. Yet one thing I knew was, unlike so many of today's techies, I saw great deal of value to those who had come before me. Thus began my three years with Eric.

We assembled a team and designed the system in detail. Then we were awarded the contract to build it. That we did in record time, despite the massive political nature of COMSAT. Nearly everyone wanted a piece of it, and without the skill of Eric navigating the political and technical waters we would never have delivered the world's first VSAT, or very small aperture satellite system. It went out to our customer and passed all tests with flying colors. Then things got really interesting. I had no idea who Eric was other than a good Brit system designer and one who had fantastic people skills. So when I got a significant promotion, building all of COMSAT's equipment deliverables I chose Eric as my Chief Engineer.

Then Eric and I went out to meet our "customer". We were to discuss the details of full implementation and deployment. I had been seconded to U.S. Arms Control and Disarmament

Agency as part of the Comprehensive Test Ban Treaty team so I had become more involved in details, while keeping my ever expanding corporate duties. I relied on Eric more each day. On this visit to our “customer” we both had security clearances and I had a bunch more but when we got to the gate Eric was denied entry. We were told by Security at this “customer” that a Brit engineer was not allowed on the premises, period. Besides they asked: “Who is this Ackerman anyway?” I did not know even then of Eric’s background. We had traveled a long distance from Washington and here I had to leave Eric in the hallway all day! I felt mortified. After all, we had apparently done all we should have and here is some Government clerk telling us off.

After the meeting we took a flight back to Washington via Chicago. As luck would have it there was a massive blizzard and what would have been just a few hours of air flight ended up being half a day, waiting, in holding patterns, waiting etc. This is when I got to really know Eric. In those days I could bump to First Class on a 727 and smoking was allowed and Scotch flowed like water. Eric was in heaven. I apologized again for his rather shabby treatment and, after a few Scotches, Eric started telling me the past, and my “war stories” paled by comparison to his. I soon learned of R.V. Jones, then of his flights in and out of rather risky spots, his tricks played on the Germans, then his time doing the same on the Soviets. The tales in this book are but a few I became privy to. All in that half empty First Class cabin trying to get to Chicago. The worse the flight got, the more Eric had of the Scotch and the more detailed the stories. Eric was truly a hero in his own day.

I found that I had a group in my own Division doing what was, let us say, unsanctioned side work. Needing to find out what was going on I asked Eric if he had any ideas. Well, Le Carre step aside! I was invited to meet Eric and his colleagues at a small bar on Massachusetts Avenue, just a bit down from the British Embassy. It was a warm autumn day and at about 2 PM. I entered the bar. It was dark and near empty except for a cloud of smoke from the booth at the rear. I walked back. There was Eric with several of his old colleagues, all Brits. I now had a fully experienced Intel operation. Needless to say they did a splendid job solving my problem and keeping the results somewhere in the British Embassy. To this day I wonder if it is still in some archive in some part of MI whatever.

I left Washington in 1980 to go to New York, out of that world of electronic intel but kept in touch with Eric. I visited his farm and met his two sons and of course his wonderful wife. But unlike the depiction in book, the farm was a version of "Faulty Towers" with animals! We saw an old farm, with rather weathered barn, and rabbits, chickens, sheep and a mass of other animals just wandering around. You see, a farm is not something one retires to, it is something one retires from! As Keynes had noted in his famous test, “A man, who does well in life, may have the good fortune to retire and write books and do experimental agriculture” Keynes meant “gardening” not the establishment of a full agricultural complex! But Eric and his wife were happy, ecstatic to be exact, and their sons seemed to be prospering. We had our scotches reminisced about the old days, I was now in the movie business, and departed, regrettably not to meet again.

Thus the Eric I knew was a quiet but resourceful man, a gentleman in the best use of the term, one who knew how to approach and solve any problem, and one who was loyal to the best of extremes, and happy with his animals! I was honored to have spent a brief time with him and his help allowed me and others to move forward on our careers while remembering a good friend.

A couple of decades later I had started a telecom and fiber business in Central and Eastern Europe, with offices in Moscow, Prague and Warsaw. I chatted with my Moscow and Czech colleagues, all former technical people in the old adversary, and recounted my friend and colleague Eric. The US “customer” may not have heard of Eric but they clearly knew and respected him. The mere fact that I was associated with him gave me credibility well above anything else that I may have personally achieved.

Thus I was delighted to see and read this work about a dear old friend. It presents his life during his youth and during the War. Eric took technology to war on a personal basis. The book presents this exceptionally well and uses Eric as an example of some of the best of the best. Eric would take the work in Jones’ lab and test it out in true combat conditions. These tales are told again and again. In addition the book examines the post war Intel in the case of the Soviets.

Overall the book is good. It does suffer from several weaknesses which I shall relate here.

1. It really should have an editor to smooth out the flow of information. For the text tends to vacillate between historical reports and personal details.
2. The books by R. V. Jones displayed an ability to present the technology in a somewhat readable form. This seems in my opinion to be lacking in this book. The many systems that Eric worked on should be described so that the average reader could understand the issues at hand.
3. Eric’s personality did not come through as well as it should have. Then again since I spent three years with Eric toward the end of his life I have a view which may not be that of those who had known him earlier. In my above recollections I tried to demonstrate Eric as creative, supportive and especially loyal. Eric was one of those few friends who would go to the ends of the earth to help you.

I considered Eric a good friend and in many ways a superb teacher. Decades later when I returned to MIT I tried to explain to today’s students how “real engineers” function, and I used Eric as a prime example. In many ways we should really miss the Erics of the past. Today we have an overabundance of Internet “techys” whose egos and overblown self-worth belie the real engineering expertise of those who established the platforms upon which they build.

Labels: Commentary

Friday, November 24, 2017

How Not to Do R&D

I am always amazed when political figures opine on R&D. One can suspect that they can say whatever they want since their peers are equally clueless. Now a piece in Project Syndicate, that left wing blog for internationalists states:

A paradigmatic example is the American Telephone and Telegraph Company (AT&T) and its Bell Labs, a story meticulously recounted by Jon Gertner in his 2012 book *The Idea Factory*. The research, discoveries, and products that emerged from this single entity are astounding: not only reliable relays and switches for landline telephony, but also radar, lasers, the transistor, the integrated circuit, the fax machine, satellite communications, Shannon’s information theory, the

theory of computation, six sigma quality control, and even cosmic microwave background radiation. All of this happened inside a corporate behemoth, which could afford the lab thanks to its monopoly on local telephony and on the equipment used to provide the service, which was manufactured by AT&T's subsidiary, Western Electric. AT&T's monopoly position was always controversial in the competition-minded US regulatory system. So the company had to earn the right to be a monopolist by constantly improving its service and using its research power for national purposes such as military defense. To renew its corporate charter in 1956, it even had to agree to license all of its old patents royalty-free and to license all new patents at low cost. If AT&T had to be a monopoly, it had to be a monopoly that benefited society at large, not just its shareholders, through breakthrough research. ...As societies consider their R&D strategies, they must find ways to coax their largest corporations into a more AT&T-like bargain. If citizens are to tolerate or even support these companies' power, companies must use it in ways that bring outside benefits to the rest of society. Their R&D budgets, their patent history, and their innovations are part of what they should brag about in public.

I reviewed the book by Gertner and in that review detailed his many fallacies. AT&T ran Bell Labs to maximize the profits of the Bell System, NOT to advance technology. Remember that AT&T had profit based on a percent return on invested capital. Its operating costs were guaranteed in its rate base. Thus to maximize profit you built the most inefficient and capital intensive system possible! I know because I was there. As to Corporate R&D, the author should look. Corporations all too often "buy" new ideas, ideas generated in the cauldron of a free and open R&D environment. Look at the pharma business. Yes they do some R&D but they also but successful start ups. Look at immunotherapy and CAR-T cells as an example.

It is not surprising that a Harvard Prof would opine in this manner. One must have done something real to understand how the system functions. In my opinion, reading third hand material, and fallacious analyses, does not get you there. Socializing companies is not the answer.

Labels: Technology

Wednesday, November 22, 2017

The Stupid Stupid Press

The recent House Tax Bill eliminates the ability of Grad students to not pay tax on a Teaching or Research Assistant-ship. Namely it means that they must pay tax on \$50,000 or more of money never received. Well they will destroy America as we know it. Perhaps that was the intent of the Republicans, I leave that to them. But Forbes has a writer who declares:

On the chopping block in House Republicans' bill is section 117(d) of the Internal Revenue Code, which exempts qualified tuition waivers from taxation. Many graduate students work as teaching or research assistance while completing their studies; universities often waive their tuition and provide a small living stipend as compensation. The House plan would treat these tuition waivers as taxable income, which graduate students fear could lead to annual tax hikes of several thousand dollars. Anxiety among graduate students and those considering graduate education is understandable. But what the narrative around this provision has missed is that the House bill does not touch another provision of the tax code: section 117(a). This section provides that scholarships used to pay tuition and fees are not considered taxable income. The catch is that universities which provide these scholarships cannot stipulate that students work as teaching or

research assistants as a condition of receiving them. This is the main difference between scholarships and qualified tuition waivers: universities can require students to work as a condition of receiving the latter, but not the former.

Under current law, both scholarships and tuition waivers are not taxable. But the House bill draws a distinction between the two. Under the proposal, universities can still reduce their students' tuition bills without incurring tax consequences. However, if graduate students work as teaching or research assistants as a condition of getting that tuition help, then the amount of tuition reduction would be considered taxable income. Universities that wish to avoid saddling their graduate students with large tax bills therefore have an easy way out. They can reclassify their qualified tuition waivers as scholarships...

Well not really. You see as a RA the cost is charged to the research grant, usually a Government contract and thus is netted to zero for the University. As a Scholarship it is not netted against the grant and thus comes out of the endowments or other similar funds. Perhaps for a TA this would work but there are fewer TAs and more RAs.

So why did this brain child of American reportage get this? It is a secondary but key effect. It reflects the overall limited scope of recent American education, in my opinion, as exemplified in my opinion by this piece.

The main question is; who put this in the Tax Bill? Now Congress never really writes anything, Lobbyists do. So follow the money. Who did this? That should be the job of a reporter, not to try to act smart by reaching a putative false conclusion. I have no answer here but someone does.
Labels: Government

Sunday, November 19, 2017

[Russian Propaganda and Influence: New or Old?](#)



In early 1920, almost 100 years ago there was a Congressional Committee to investigate Russian interference with the US. The charge and conclusions were:

Resolved, That the Committee on Foreign Relations is hereby authorized Is/ directed, through the full committee or through any subcommittee thereof -? investigate as speedily as possible the status of said Martens; what aliiped government or power in Europe he represents; what, if any, recognition of any kind has been accorded him by this Government; whether or not li ns an alien enemy ; what propaganda, if any, he is carrying on for the overthrow of governments; and all facts and circumstances relating to his activities in this country and his alleged diplomatic representation, and all facts relative to the activities of any other party, parties, or organization bearing upon or relating to Russian propaganda in this country, and make report to the Senate of such findings.

The said committee is hereby empowered to sit and act at such time and place as it may deem necessary; to require, by subpoena or otherwise, the attendance of witnesses, the production of books, papers, and documents; to employ stenographers at a cost not exceeding \$T per printed page. The chairman of the committee, or unyjmember thereof, may administer oaths to witnesses. Subpoenas for witnesses shall be issued under the signature of the chairman of the committee or subcommittee thereof. Every person who, having been summoned as a witness by authority of said committee or any subcommittee thereof, willfully makes default, or who, having appeared, refuses to answer any question pertinent to the investigation heretofore authorized, shall be held to the penalties provided by section 102 of the Revised Statutes of the United States.

.....

In sum the committee finds in obedience to the instructions of the resolution of the Senate that—

- (1) Martens has no status whatever in this country in any diplomatic or other governmental representative quality.*
- (2) Martens assumes to represent the Russian Federated Soviet Republic—a regime established in Russia by revolution and functioning under a constitution which has been above summarized; a regime which has never been recognized by the Government of the United States and which in international law has no standing as a constituted authority.*
- (3) Martens has received no recognition officially or even provisionally by the Government of the United States.*
- (4) Martens, by the accepted practice of this Government or its treaty or other international obligations and usages, is a (man subject, and in consequence an alien enemy.*
- (5) Martens’s propaganda in this country for the overthrow governments is established by his own testimony, as shown in body of the report, that he has publicly associated and sympathy with those advocating such a course. He admitted to the committing his persistent revolutionary character, his desire to see the establishment of the “ dictatorship of the proletariat ” in all lands, his opinion that it would be better for this country if the soviet government were established here. It was also proved that he tinned to employ in the staff of his embassy persons who have publicly and in his presence advocated the bringing of bolshevism America and he admitted to the committee that “ any means w would produce this condition would be justified.”*

Namely the individual Martens was placed in legal limbo ultimately leading no where. So what is old is new again. It is worth reading this entire file if one is interested. This has been going on from the beginning.



Labels: [Russia](#)

Saturday, November 18, 2017

[Anchors Away!](#)

Well the boys in blue did it again. Another destroyer collision. As [USNI](#) reports:

The guided-missile destroyer USS Benfold (DDG-65) was hit by a Japanese tug during a towing exercise on Saturday, according to a statement from U.S. 7th Fleet. The forward-deployed destroyer was in the midst of a towing exercise in the Sagami Bay when the tug lost power and, “drifted into the ship.” “No one was injured on either vessel and Benfold sustained minimal damage, including scrapes on its side, pending a full damage assessment. Benfold remains at sea under her own power,” read the statement from 7th Fleet. “The Japanese commercial tug is being towed by another vessel to a port in Yokosuka. The incident will be investigated.” The incident comes as the Navy is struggling with the aftermath of two fatal collisions between merchant ships and the destroyers USS Fitzgerald (DDG-62) and USS John S. McCain (DDG-56) that claimed the lives of 17 sailors. The Navy found both incidents were preventable.

One wonders how many ships will be left if we ever need them. Having spent my youth in New

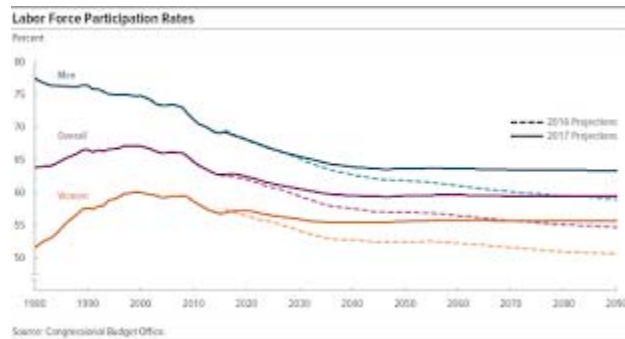
York Harbor, my grandfather was the Harbor Master for a while, and knowing the tug owners pretty well, double dated with a daughter of the Moran line, this type would close the harbor. Perhaps the Navy needs a big shakeup!



Labels: [Military](#)

Friday, November 17, 2017

[Labor Force Participation](#)



The above is the [CBO labor force participation rate](#) percents. This should be worrisome. There is a continual decline and thus we have fewer people capable of working actually working. The details behind this are nor complete but in the long term this must change. There are too few people bearing the total burden for those not working.



Labels: [Economy](#)

Thursday, November 16, 2017

[Show This to AMTRAK or NJ Transit, or MTA](#)

In Japan they take things seriously. As the [Guardian](#) notes:

t was an admission that would no doubt raise a sardonic smile among many commuters, and perhaps have them dreaming of relocating to Japan. The operator of a private railway firm that serves the Tokyo suburbs has issued an apology after one of its trains departed 20 seconds ahead of schedule. Passengers boarding Tuesday's 9.44.40am Tsukuba Express from Minami Nagareyama station, just north of Tokyo, were unaware anything was amiss when the train, which had arrived on time, pulled away from the platform at 9.44.20am. The train's operator, though, believed the foul-up was serious enough to warrant an apology. "We deeply apologise for the severe inconvenience imposed upon our customers," the Metropolitan Intercity Railway Company said in a statement.

Having gone through AMTRAK's closing of Penn Station, multiple failures of NJ Transit and the ever occurring delays and breakdowns of the MTA, this is amazing. One enters the NY City

subways and it is like entering Hell. Filled with various characters, filth, decay, collapsing infrastructure, and union employees perpetually delaying things, or worse AMTRAK, who could not get a watch to be correct twice a day, or NJ Transit who has the habit of stopping trains randomly and shoving all the passengers off to find their way home from some drug infested parking lot.

The new Tax Bill does not address any of this. In fact it makes the cost of living in this Dante like level of the Inferno just a bit more costly.

Thanks folks.



Labels: [Government](#)

[Ginkgo; Good or Bad](#)



I have a dozen or more Ginkgo trees, all from seed from the New York Botanical Garden trees, which were allegedly grown from seeds from the surviving Hiroshima ginkgo. The seed have just dropped and they do smell a bit rancid but after a month or two they disappear almost overnight, the squirrels. Now allegedly the ginkgo increases brain capacity. So am I allowing for the evolution of brilliant squirrels?

In a recent paper by [Oliveira et al](#) they note:

*Despite the ancient use in Chinese popular medicine and, more recently, in western modern medicine in many European countries, the biological effects of extracts of *G. biloba* (GBE) are still not clearly known. In modern medicine GBE has been used for tinnitus, to reverse memory loss, for dementia, and Alzheimer's and Parkinson's diseases in elderly people. Besides reports on improvement of blood circulation in the brain, there are a number of studies pointing to complex cellular effects, involving signal transduction pathways and epigenetic modifications. Evidence are presented from recent reports concerning genotoxic and antigenotoxic properties and the corresponding mechanisms underlying such activities, mostly regarding the prooxidant and antioxidant activities of the extract. However, several examples of direct interaction of the extract and its components with specific proteins are provided, especially for DNA damage repair, contributing for antigenotoxicity. Evidence of epigenetic effects of GBE are also presented from approaches involving transcriptomics, detection of activity of histone*

deacetylases, and screening of plant extracts with cell-based systems for detection of posttranslational modifications. The modulation of chromatin-remodeling enzymes by GBE and their interaction with proteins involved in DNA damage repair, apoptosis, and signal transduction are discussed in the context of neurodegeneration.

It is not clear what the implications are. But I have noticed my squirrels borrowing some books from my library. The works all related to editing human DNA. Should we be concerned?



Labels: [Genetics](#)

Wednesday, November 15, 2017

[Sent to Congressman](#)

The proposed taxing of Grad School tuition for Research Students would drive the 20% of American Grad students to 0% It is the "Make America Last" Act. We would be left with 100% Chinese, Iranian, Indian, Vietnamese etc students who will get all of our ideas paid by Government dollars and take it home to demolish our economy. Frankly this is one of the dumbest ideas I have ever seen. I managed to succeed due to Eisenhower and his innovations. Remember Admiral Yamamoto went to Harvard, he then bombed Pearl Harbor. We do not want to repeat that!



Labels: [Government](#)

Wednesday, November 15, 2017

[How to Destroy America's Future](#)

The proposed new Tax Plan as many destructive elements. It helps the rich but destroys our future. For example, [Nature](#) states:

Graduate students, who receive the lion's share of tuition waivers, would be most affected. And 60% of the 145,000 students who get tuition reductions each year are working in science, engineering, technology and mathematics fields, the US Department of Education estimates. The amount of money that the government would reap from these taxes would be minuscule, given the \$20.5-trillion national debt. But it could weigh heavily on young scientists. Take a hypothetical PhD student at the Massachusetts Institute of Technology (MIT) in Cambridge, in receipt of a \$23,844 NIH stipend. Under the current system, she would pay very little in taxes. The new law would add her \$49,000 MIT tuition bill to her taxable income as though she were paid a \$73,000 salary — an amount she never actually sees. This would add thousands of dollars to her tax burden.

Thus, a student would get about \$24,000 plus an imputed say \$50,000. Under the old plan they paid tax on \$24,000. On the new plan it tax on \$74,000. Namely with a \$12,000 deduction it

would be 15% of \$62,000 or \$9300. That is a 39% tax rate! Plus 3.5% for FICA plus 3% for Medicare plus in Massachusetts an added 8%. This is a 53.5% Tax Rate!

Now we already have 80% of the Grad students funded by their Governments, China and Iran. The remaining 20% are US and are paying the burden. So what will happen. Drug development, high tech development etc will all migrate to these countries. Not to mention weapons development. Eisenhower saw the need for a strong technology core. Team Trump wants to destroy whatever future we may have had.

Pity!



Labels: [Government](#)

Tuesday, November 14, 2017

[Night of Terror](#)



A hundred years ago today, my grandmother, Hattie F Kruger, and several other women petitioned the White House, Woodrow Wilson specifically, for the right to vote. Wilson in his classic manner had them arrested and jailed. It became what is known as the "[Night of Terror](#)".

My grandmother and six other women were placed in cells, hosed down in the freezing weather of the unheated prison, force fed by hose, and generally brutalized by command of Wilson. Yet today we still have Wilson "this and that" including a collection at Princeton. So we take down Lee, a person who I am not fond of since he defied his oath as a soldier, but Wilson remains at a pinnacle. Wilson, a man who was both a racist and anti-Semite, and who personally took a hand in torturing these women who asked for nothing more than the vote. They just asked, with a sign, and Wilson had them dragged and tortured well beyond Guantanamo.

Thus as we seem to be aghast at Hollywood, which should be no surprise if one looks at their products, we should also be aghast at this man. Woodrow Wilson.

Just a reminder of things past.



Labels: [Commentary](#)

Sunday, November 12, 2017

[Beards?](#)



For centuries Romans prided themselves on their clean faces and well groomed hair. Barbarians were also known as "barber rosa", red beards, scruffy unkempt and rather smelly creatures soon to be under the heels of the Romans. The exceptions were the Greeks, appreciated for their intellect and education as well as their beards.

Then along came Hadrian, the first Roman Emperor with a beard. Well and all, Hadrian managed to expand the empire. He was followed, with a few in between, by Marcus Aurelius, who was full bearded and wrote in Greek. Hadrian had his beard to hide a bad case of acne, Marcus to emulate the Greeks.

Thus one wonders the cause for the current phase of hirsute existence among the many. Razors invented as safety razors at the turn of the nineteenth century did away with a variety of facial hair, but today with a variety of facial cleaning methods we have not the beards of the 60s hippies but of the three day drinking binge.

Now Hadrian and Marcus Aurelius had good beards, they portrayed strength and vigor. One wonders what these half shaven par venues see in this presentation. What would Hadrian think?



Labels: [Commentary](#)

Remembrance

I just noticed that [Vanu Bose](#) passed away. I have known Vanu for many years and even named a Daylily for his wife, Miss Judy Lynn. Vanu was a brilliant engineer and his father was Amar Bose, of Bose speakers.

This apparently was sudden and Vanu was still a young man. He will be missed. He made many contributions to wireless as well as MIT. I greatly valued his friendship. His passing was all too early!



Labels: [Commentary](#)

Saturday, November 11, 2017

Happy Veterans' Day



In the Fall of 1943, I was off to work and he was off to War. Thanks to all the Vets!



Labels: [Commentary](#)

Monday, November 6, 2017

Busy Giddy Minds

From Shakespeare, Henry IV Part 2, Act 4, Scene 5, King Henry IV, the usurper, tells his son young Harry, Henry V:

*Therefore, my Harry,
Be it thy course to busy giddy minds
With foreign quarrels; that action, hence borne out,
May waste the memory of the former days.
More would I, but my lungs are wasted so
That strength of speech is utterly denied me.
How I came by the crown,
O God forgive;
And grant it may with thee in true peace live!*

Thus, as the King were to deflect problems at home, seek out foreign troubles.



Labels: [Commentary](#)

Sunday, November 5, 2017

[Graduate Students in the Engineering Fields](#)

The [NY Times](#) has a piece on the increasing percent of engineering graduate students who are foreign. They state:

At the undergraduate level, 80 percent are United States residents. At the graduate level, the number is reversed: About 80 percent hail from India, China, Korea, Turkey and other foreign countries.

True fact, but why? And who is paying?

Having spent an almost sixty year career in and out of Academia I can make the following observations.

1. In the late 1950s the US Government made a major push to create more engineers. There were scholarships and institutions were incentivized to follow through. There were scholarships and fellowships. My personal out of pocket fees were often low. If I recall, MIT annual tuition, both semesters, in 1960 was less than \$1,000. Grad school was free since you had some form of fellowship. Today there is no such advantage for Americans.
2. Most of the grad students were first generation types. Lots of fellow New Yorkers, most had little "family money" and many were even married with families. No longer the case.
3. Jobs were available, especially for Graduate students with good degrees. Programmers were not in demand, solid state engineers, RF engineers, and the like. People who built things not social media types.
4. Silicon Valley was cheap. Lots of housing and at reasonable prices. Start ups made stuff, not software. Millionaires came from oil and the like, not Wall Street and software.

Now in today's world there are major observations:

1. Almost all high tech grad students are funded by the Government. Yes, those 80% of the foreign students are funded by the taxpayers. Those Chinese, Iranian, Syrian, grad students are funded by US tax dollars. They finish on our dime and return home. In the case of the Chinese students they often bring this expertise back to Chinese companies and then directly compete with the US. That is true in both for commercial and military entities. One should always remember Yamamoto and Harvard and Pearl Harbor!

2. US undergrads are often broke when they finish undergrad and thus are pressured to work and pay back the loans as well as taxes. As a side note the new Trump Tax makes the student loan no longer deductible. The taxes will then go to support the 80% of the grad students who are foreign. This is the way Washington works.

So what can be done? Simple, look back to the 50s. Eisenhower may very well turn out to be our greatest President. Fund undergrad tech students. We really do not need more fine arts types. Political Science may be good but it just leads to more lawyers! Don't we have enough. Then make it a level playing field for US citizen students, if the taxpayer is footing the bill, the taxpayer should have preference. Put a finger on the scale for US students.



Labels: [Academy](#), [Taxation](#)

Thursday, November 2, 2017

[So Let's Look at a Typical Middle Class In Westchester County](#)

Take a simple example:

Husband and wife Income: \$120,000

Old Deductions:

State and NYC Taxes (12%) \$14,000

Real Estate on \$700,000 Home \$20,000

Health Care Insurance \$15,000

Medical Expenses Dental \$20,000

No Alimony

Charitable Deductions \$2000

Under old rules you go to deduct \$59,000

Under Trump Tax you lose:

State and Local Tax \$4,000

Real Estate \$10,000

Medical \$23000

or you lose \$37000!

If tax rate is say 15% you pay \$5500 MORE! If it is higher you pay even more!

This is back of the envelope but if you hated Obama Care you will truly despise this one! Of course if you are at Goldman and you donate in a nice tax plan a new medical facility you get a pyramid paid for by the schlubs above!

Yes Mr. President, the Middle Class will really thank you!



Labels: [Taxation](#)

[First Obama Care and Now Trump Tax! The Poor Middle Class.](#)

If one reads the new [Tax Bill](#) the following will be terrifying. Take the poor family facing massive healthcare costs from Obama Care and then a health crisis. Take a child with leukemia. Now not only are your insurance premiums exploding but you can no longer deduct the cost of trying to keep your child alive. This is about as evil as one can get. First they increase your healthcare then they tax you for it! This is Goldman Sachs at work! What middle class tax cut? This is a Bill which loads the middle class with the burden while allowing the 1% to get even more! This is H.R. 1 and good old Brady! Let's all kick the poor folks when they are down! Where is Robespierre!

4 SEC. 1308. REPEAL OF MEDICAL EXPENSE DEDUCTION.

5 (a) IN GENERAL.—Part VII of subchapter B is
6 amended by striking by striking section 213 (and by strik7
ing the item relating to such section in the table of section
8 for such subpart).

9 (b) CONFORMING AMENDMENTS.—

10 (1)(A) Section 105(f) is amended to read as foll1
lows:

12 “(f) MEDICAL CARE.—For purposes of this section—

13 “(1) IN GENERAL.—The term ‘medical care’

14 means amounts paid—

15 “(A) for the diagnosis, cure, mitigation,

16 treatment, or prevention of disease, or for the

17 purpose of affecting any structure or function

18 of the body,

19 “(B) for transportation primarily for and

20 essential to medical care referred to in subpara21
graph (A),

22 “(C) for qualified long-term care services

23 (as defined in section 7702B(c)), or

24 “(D) for insurance (including amounts

25 paid as premiums under part B of title XVIII
1 of the Social Security Act, relating to supple2
mentary medical insurance for the aged) cov3
ering medical care referred to in subparagraphs
4 (A) and (B) or for any qualified long-term care
5 insurance contract (as defined in section
6 7702B(b)).

7 In the case of a qualified long-term care insurance
8 contract (as defined in section 7702B(b)), only eligi9
ble long-term care premiums (as defined in para10
graph (7)) shall be taken into account under sub11
paragraph (D).

12 “(2) AMOUNTS PAID FOR CERTAIN LODGING
13 AWAY FROM HOME TREATED AS PAID FOR MEDICAL
14 CARE.—Amounts paid for lodging (not lavish or ex15
travagant under the circumstances) while away from
16 home primarily for and essential to medical care re17
ferred to in paragraph (1)(A) shall be treated as
18 amounts paid for medical care if—

19 “(A) the medical care referred to in para20
graph (1)(A) is provided by a physician in a li21
censed hospital (or in a medical care facility
22 which is related to, or the equivalent of, a li23
censed hospital), and

1 “(B) there is no significant element of per2
sonal pleasure, recreation, or vacation in the
3 travel away from home.

4 The amount taken into account under the preceding
5 sentence shall not exceed \$50 for each night for each
6 individual.

7 “(3) PHYSICIAN.—The term ‘physician’ has the
8 meaning given to such term by section 1861(r) of
9 the Social Security Act (42 U.S.C. 1395x(r))....

And if you like this one you will like the next!

19 SEC. 1309. REPEAL OF DEDUCTION FOR ALIMONY PAY20 MENTS.

21 (a) IN GENERAL.—Part VII of subchapter B is
22 amended by striking by striking section 215 (and by strik23
ing the item relating to such section in the table of section
24 for such subpart).

Perhaps the President did not see this part.

So what is worse. Forcing you to buy something you do not want or taxing you for the thing you had to buy that you did not want!



Labels: [Government](#), [Taxation](#)

Saturday, October 28, 2017

[Global Warming?](#)



Saw this guy today at Bronx Zoo! He has his own cot and toys. Somehow he liked the lounge chair and the sun.

Just for your information, he is at the top of the food chain.



Labels: [Climate Issues](#)

Tuesday, October 17, 2017

[Beware W10 Upgrade](#)

Like last years "upgrade" MS again messes everything up. Printers down, software needs re-configuring, and all the "goodies" must be manually disabled. In my opinion these are truly evil folks. All I want is my computer to run what I use it for. No games, just work. Is there any way that these demons can just stop it! An operating system is really simple, did one fifty years ago. Okay, a bit more complicated, but folks, stop it with all the crashes!

Hint: Stop any "upgrades". Unless you really like spending days fixing what they did.



Labels: [Microsoft](#)

Friday, October 13, 2017

[A Letter on Tax Proposals](#)

Senator Cory Booker
359 Dirksen Senate Office Building
Washington, DC 20510

Dear Senator Booker,

Congressman Rodney Frelinghuysen
2306 Rayburn House Office Building
Washington, DC 20515-3011

Dear Congressman Frelinghuysen,

As a constituent I would like to give my opinion regarding the proposed Tax Plan. Specifically as relates to deductions.

LOCAL TAXES AND REAL ESTATE TAXES ARE BY PERSONAL CHOICE

Despite the high tax burden in New Jersey for both income and real estate taxes, I and many people have made that choice. That is especially so for those in high income brackets for whom this tax is discretionary. If I do not like it I can move. Lower income people do not benefit from this deduction, especially given the proposed increase in the standard deduction. Thus, any elimination of this would not benefit the wealthier but the contrary.

CHARITABLE DEDUCTIONS BENEFIT THE WEALTHY. THEY ARE BY CHOICE AND ALL TOO OFTEN ARE GOVERNMENT SUBSIDIZED EGO TRIPS.

Charitable deductions are also discretionary. The new tax proposal allows them. They benefit the wealth. They allow for the pyramids built in the names of donors and via complex tax benefits allow near in write offs while sheltering significant incomes. Now I make substantial donations primarily to cancer research. However I do so anonymously and would continue to do so no matter what the tax situation is. Many however want their names in lights as well and benefitting from this deduction. Thus, charitable deductions benefit the wealthy much more than anyone else. The benefits are both financial and ego building. Ego gratification should not be subsidized by the tax payer. Especially the poorer ones who cannot even afford healthcare.

MEDICAL EXPENSE DEDUCTIONS DRAMATICALLY BURDEN THE POORER AND ARE HIGHLY REGRESSIVE. THEY ARE NOT BY CHOICE BUT ARE TRUE CALAMITIES.

As a result of the ACA I have seen healthcare costs explode for the middle class. Ballooning insurance and exploding deductions. Then along comes a medical crisis and the costs truly explode because none of the plans provide truly catastrophic coverage. People and families

suffering a health crises now face a financial crisis. I have seen many family and patients die of this disease and have seen the financial burden that they have had to bear.

Yes it happens that the new tax proposal will take this away from these poor people while allowing the rich to maintain massive healthcare plans paid for with tax deductible dollars at the corporate level and getting massive deductions for their "charitable" yet ego building deductions. Here the poor are truly underwriting the rich! Frankly this is grossly immoral and reflects in my opinion the total disconnection between the current administrations financial analysts and the real world. Goldman Sachs has not clue how a truck driver lives. A child gets Hodgkin's disease or leukemia and they are driven to bankruptcy. I have seen this again and again. While this is happening the rich and their "donations" go to fine dinners and tell each other how wonderful they are.

ENTREPRENEURIAL CAPITAL GAINS AND HEDGE FUNDS DO NOT EQUATE

I have spent several decades in venture capital. I have personally started and developed near a dozen companies and have invested in and overseen a total of thirty-five. In all cases I not only took the financial risk but conceived of the idea, structured the company, raised capital, operated the entity and monetized the result. Hedge funds are merely financial intermediaries. The entrepreneur is wedded to their concept and creation, twenty four hours a day. The hedge fund operator may at best attend a board meeting and collect a check. As such the tax code should incent the entrepreneur and tax the hedge fund operator as normal income.

Not only do we have the above problems in the Administration's proposal, but the wealthy would get the benefit of eliminating the Estate Tax. The poor would see no benefit there, nor would the middle class. The middle class clearly bear the burden of this proposal and those 1% folks get a massive tax cut, paid for by the Middle Class. I feel this to be grossly immoral.

I am asking that you consider my concerns as not just those of a single constituent but reflective of the many who cannot voice what they face. Medical Expense should be inviolate. It is the least that we as a society can do for those in need. The others are by choice. If you keep one, just one, keep the Medical Expense for the millions who will benefit during times of need.



Labels: [Health Care](#), [Taxation](#)

Thursday, October 12, 2017

[Programmers and Programming: Getting a Package](#)

There is this push to have everyone learn to code. Frankly that is wrong. The issue is to have everyone learn to think. Take as an example UPS and their on-line system. Now if you have a delivery and a number for tracking you can go on-line and hold the delivery, for a fee of course, until a later date. Sounds good? No.

What they do then is hold every delivery, not just the one you asked and paid for and they then

charge you this modest fee for each and every one. A massive amount you never thought about.

Then you try their on-line remedy. It comes back and says you cannot use them you must go back to the web page and use the command that got you there in the first place and thus an infinite loop.

The code is all correct. It does what some human told it to do. But, and this is the key issue, the human had no idea how other humans use the system. Namely the human did not think.

Coding is not what has to be inculcated in our students. Thinking is. That is the hard part. There are four parts to developing software.

First, the requirements. What do you want done and why.

Second, the design of the process to ensure it does what is required under all anticipated conditions and in the event it does not it hands the system to a human to remedy and then reiterates this back to the designers for a change.

Third, coding. That is the old typist role. Just type in the required steps.

Fourth, the fault checking. This is the hard part. You spend time finding all your mistakes; coding and logical. You seek all the things that can go wrong. Then FIX them.

Of course you then do this again and again. You need smart people, and it is often a burn out job. But if you want your business to succeed then you must do this. If you do not do this then you have a real problem. Look at UPS. In my opinion they are not only clueless but careless. Why the Post Office is even better, now!



Labels: [Commentary](#)

Wednesday, October 4, 2017

[Obesity and Cancer](#)

The [CDC](#) has released a report on obesity and cancer. In its [MMWR](#) they provide some details. They note:

Overweight and obesity are associated with increased risk of 13 types of cancer. These cancers account for about 40 percent of all cancers diagnosed in the United States in 2014, according to the latest [Vital Signs](#) report by the Centers for Disease Control and Prevention (CDC). Overall, the rate of new cancer cases has decreased since the 1990s, but increases in overweight- and obesity-related cancers are likely slowing this progress. About 630,000 people in the U.S. were diagnosed with a cancer associated with overweight and obesity in 2014. About 2 in 3 occurred in adults 50- to 74-years-old. The rates of obesity-related cancers, not including colorectal cancer, increased by 7 percent between 2005 and 2014. The rates of non-obesity related cancers declined during that time.

This is not a startling new fact. Ten years ago when discussing changes in Healthcare financing, [I wrote extensively about this](#). Obesity drives up free radicals and free radicals result in both methylation and BRCA and PARP repair defects. Thus massive DNA errors and in turn many malignancies. It would be of interest to see how many X rays would equal a certain BMI in terms of cancer risks. But that notwithstanding, we now accept the risk of cancer from obesity.

But the real problem is that we penalize pre-existing conditions but not obesity. Those who are obese will soon be costing us trillions. That is real money and money we do not have. The real-real problem is that many of these obese are young people. One need just walk into any shopping mall or airport and one sees them all over. Worse, in looking at hurricane relief efforts, there is massive obesity in those being rescued, and worse yet in many of the first responders. This will lead to massive healthcare burdens as time goes by. Furthermore these burdens can be chronic thus burdening the system for long periods.

To again reference the MMWR:

Overweight- and obesity-related cancers accounted for 40% of all cancers diagnosed in 2014, and varied substantially across demographic groups. Endometrial, ovarian, and postmenopausal female breast cancers accounted for 42% of new cases of overweight-and obesity-related cancers in 2014, which is reflected in the higher overall incidence of overweight- and obesity-related cancers among females. For cancers that occurred among both males and females, however, the incidence of most cancers was higher in males.

This problem demands some response. Now.



Labels: [Health Care](#)

Monday, October 2, 2017

[Nuclear Weapons](#)

Nuclear Weapons are a complex technology to assemble then add to it a delivery system such as an ICBM and you have a technology which takes expertise that exceeds what most nations have. Russia got its head start by use of spies in the Manhattan Project. China via Russia. Now we have North Korea and we wonder.

The tables below depict at a high level the elements of an ICBM nuclear weapon. It is a real high level but raises questions. The entries are based upon my assessment of the potentials and can be referenced back to multiple reliable sources. (For example see: The Los Alamos Primer, Serber, Univ. Cal Press, 1992) The entries reflect my personal opinion based upon my prior exposure during the CTBT discussions in the late 1970s.

| System | Subsystem | Requirement | Source | Status |
|--------------------------|----------------------|---|--------|--------|
| Launch Vehicle | | | | |
| | Rockets | High thrust solid fuel rockets | China | Active |
| | Fuel | High efficiency solid fuel | China | Active |
| | Shell | Thin metal sheathing for rocket. Must be reasonably hardened for potential adversarial attack | China | Active |
| | Thrusters | Dynamically controlled launch, ballistic and re-entry thrusters | China | Active |
| Inertial Guidance | | | | |
| | Strapped Down System | A fully operational strapped down system with integrated accelerometers and three axis ring laser gyros | China | Likely |
| | Ring Laser Gyros | High reliability and low drifting ring laser gyros | China | Likely |
| | Accelerometers | High reliability high accuracy strapped down three axis accelerometers | China | Likely |
| | Computers | Full complement of hardened CPU/memory and adjunct elements | China | Likely |
| | Software | Control software for full inertial guidance and mid stage terminal direction using Kalman filters | China | Likely |
| | Updating | On board inertial platform updating for terminal re-entry using look scanning or equivalent | US | Likely |

| System | Subsystem | Requirement | Source | Status |
|----------------|--------------------|--|---------------|--------|
| Warhead | | | | |
| | Metals | Metals sheathing for enclosure of fuze elements | USR | Likely |
| | Fluoride Materials | Fluoride materials such as enriched plutonium | US | Active |
| | Design | Complex design for assembly and integration. Also control for detonation at optimal height over target | US and others | Active |
| | Assembly | Complex assembly of the payload including optimal detonation | US | Active |
| | Misalignment | Reduction of payload to meet launch vehicle | US | Likely |
| | Activation | Activation requires the final compression of fluoride materials. Depends on type of weapon | US | Likely |
| | Detonation | Completion of activation | US | Likely |

| System | Subsystem | Requirement | Source | Status |
|-------------------------------|-----------------------|---|--------|--------|
| Targeting | | | | |
| | Location | Determination of target site and height of detonation | US | Active |
| | Re-entry Activation | Re-entry adjustments after ballistic phase and controls to re-entry the entry | US | Likely |
| | Re-entry Optimization | Adjustments | US | Likely |
| | Detonation Activation | Optimal detonation activation on target | US | Likely |
| Communications | | | | |
| | Launch Phase | Local Communications with missile | US | Active |
| | Ballistic Phase | Ongoing TT&C capabilities | US | Active |
| | Re-entry Phase | Final stage re-entry adjustments and activations | US | Active |
| Launch Sites | | | | |
| | Platforms | Physical structures and supports | US | Active |
| | Launch Supports | Stable launch structure platform | US | Active |
| | Stable Platforms | Establishment of launch location for targeting | US | Active |
| Launch Control Centers | | | | |

| System | Subsystem | Requirement | Source | Status |
|--------|------------------|---|--|--------|
| | Tracking | Tracking network for end stage deployment. | US | Active |
| | Telemetry | Telemetry during various phases. | US | Active |
| | Command | Command and control system and software. | US | Active |
| | Control | | US | Active |
| | Communications | All communications. | | Active |
| | Materials | | | |
| | Titanium | | | Active |
| | Vanadium | Vanadium is essential in metal hardening and enclosures. | Russia is a primary source. | Active |
| | Rare Earths | The rare earth elements are used extensively in onboard electronics and hardening of materials. | China is currently the only open source. | Active |
| | Composites | There may be a complex set of composites employed to minimize weight and increase strength. | UK | Active |

These Tables depict the high level elements of such an integrate system. I have not done work in this since the late 70s on the CTBT with the Soviets but one suspects that not a great deal has changed.

The question is; has our Government entities performed such an analysis and if so then one suspects that the threat can be mitigated by asserting who supplied what. North Korea is incapable of many of the elements needed. Just not enough people or lacking in fundamental elements. Thus a threat from them is athreat from those facilitating them.

It is worth an analysis. So where is the press on this one?



Labels: [Nuclear Weapons](#)

Saturday, September 30, 2017

[New Jersey Gets No Respect](#)

As usual, the [NY Times](#) has a piece degrading something, this time it is New Jersey. The writer states:

Anyone who has ever driven on the New Jersey Turnpike knows that, at a certain point in the road, the entire Manhattan skyline appears to rise from the surrounding marshland like a close-yet-so-far Land of Oz, both tempting and terrorizing with its mysterious jutting cutouts. To traverse this roadway, as ... surely did as a young man, was undoubtedly to exist in a constant state of aspiration and alienation. No matter one's personal glories, for those who call New Jersey home, and especially those who reside in Northern New Jersey, it's difficult to forget that one is still not from "the city," as the landmass across the river is known. Overcompensation tends to follow. Blind arrogance is an occasional byproduct.

Now I was not born nor bred in New Jersey. It was Staten Island, and yes for those in the rest of NY City Staten Island is a Borough and is NYC! Thus I was born and bred, whatever that means, in New York City. I did spend time in New Jersey, riding my bike across the old Goethals Bridge, down to Route 1 and out to the old Newark Airport, Lockheed Constellations and all. We did have a ferry to NYC, and a ferry to Brooklyn. No one really ever went to Brooklyn, it was also a little ferry, and an ugly one at that, not the grand ferry to Manhattan.

Residing in Northern New Jersey is also interesting. You see that from the Morris County line to the California border, county by county, it voted Republican. Not saying that it was all Republican but it is interesting to note the dramatic difference.

The above mentioned article, an ad hominem attack on someone allegedly born and bred in New Jersey, Livingston I believe, it is an adjacent town but a different county, all Democrats, is also an attack on anyone in New Jersey. Now New Jersey is not that bad, in fact it can be very livable. The people are generally friendly, similar to Staten Island. We had our notables on Todt Hill, "death" hill if you read Dutch, and in my town we had a similar family, if you get my gist. So it was like home.

The only problem in New Jersey is taking a train to New York City. It was easier to travel from St Petersburg to Moscow during the Russian Revolution than getting from my town to NYC. But then they had a Communist Revolution we have Amtrak and New York State. Go figguah.

For the many who may have never been in New Jersey, or for those limited to the Turnpike or Newark Airport, try a trip west. The Delaware river, the rising hills, the forests and preserved lands, go south to the pine lands. Not too bad. And unlike NYC, one can escape from New Jersey quite easily. We have roads. At one point the Turnpike has a total of sixteen lanes, yes eight in each direction. Road maintenance is at night so as not to slow traffic. That is the opposite of Connecticut, where two lane roads are closed at random times to trim a tree, resulting in hours of delay. Or the same in Pennsylvania.

So to the writer who seems to have an inferiority complex of birth in New Jersey, give it a rest! You had no choice, I did. It sure beats Connecticut!

Oh yes, "blind arrogance", it seems that the arrogance is on the other foot, the one who wrote this piece.



Labels: [Commentary](#)

Friday, September 29, 2017

[The Microbiome and Cancer](#)

The microbiome is that collection of stuff we carry around in our guts. Most of us never really think much about this but it turns out to have significant impacts on cancers. After a bit of thought it becomes clear why.

In a recent paper by [Fullbright et al](#) they have done a wonderful job on describing some of these effects. They conclude:

The densest populations of endogenous microbes are found within the intestines and are in close proximity to the epithelium and underlying mucosal immune system. As a result, the earliest observations linking the microbiota with the hallmarks of cancer have primarily focused on gastric cancers and CRC. Nonetheless, more recent studies have also implicated the microbiota

in cancers at distal sites as a potential predictor of successful response to cancer therapy and as a means to augment the efficacy of existing anticancer therapeutics. Furthermore, the well-established link between several viruses and human cancers (i.e., Human papillomavirus and cervical, genital, anal, and oral cancers; Epstein-Barr virus and lymphomas; hepatitis C virus and hepatocellular carcinoma; Kaposi's sarcoma-associated herpesvirus and Kaposi's sarcoma) provides a strong rationale to investigate the role of nonbacterial members of the microbiota (virus, fungi, and archaea) in modulating the hallmark capabilities and cancer development. Finally, the cancer microenvironment itself can enhance the procarcinogenic activities of the microbiota, which further demonstrates the importance of the crosstalk between host and microbe in modulating cancer progression. In summary, because of the extensive capacity of the microbiota to influence many hallmarks of cancer, treatment for a variety of cancers may soon involve personalized medicine targeting the microbiota.

This is definitely worth following as we understand more regarding this complex environment.



Labels: [Cancer](#)

[Trump Care?](#)

Just a note on Taxes and Healthcare. So you thought Obamacare was bad. Try Trumpcare. Not the failed plans but the tax proposals. You see they want to eliminate deductions for medical expenses. So not only do you pay Medicare, on everything, that 3% of every transaction, selling your house etc, but no God forbid you get slammed with medical bills, you must pay the new taxes on top of that! Yep, you sick folks will really get soaked this time. If they can't fix it then tax it! Good luck in 2018!

Just an observation. The poor old folks paying high real estate taxes and state income taxes, and medical expenses will pay through the roof, but the advantage is their heirs will not have to pay tax on whatever is left! So I guess the solution is to die broke! That is one way to eliminate the estate tax. Middle Class tax cut? What moron thought this one up. Karl Marx!



Labels: [Health Care](#), [Politics](#)

Monday, September 25, 2017

[CBO Latest Proposal](#)

The [CBO released their latest estimates](#). They contend:

Over the 2017–2026 period, CBO and JCT estimate, the legislation would reduce the on-budget deficit by at least \$133 billion, the projected savings from the House-passed reconciliation bill. (The effects on the deficit were estimated relative to CBO's March 2016 baseline, as has been done for all legislation related to the 2017 budget resolution.) Those savings would occur mainly because, under the legislation, outlays from new block grants between 2020 and 2026 would be smaller than the reduction in net federal subsidies for health insurance. Funding would shift

away from states that expanded eligibility for Medicaid under the Affordable Care Act (ACA) and toward states that did not. The number of people with comprehensive health insurance that covers high-cost medical events would be reduced by millions compared with the baseline projections for each year during the decade, CBO and JCT estimate. That number could vary widely depending on how states implemented the legislation, although the direction of the effect is clear. The reduction in the number of insured people relative to the number under current law would result from three main causes. First, enrollment in Medicaid would be substantially lower because of large reductions in federal funding for that program. Second, enrollment in nongroup coverage would be lower because of reductions in subsidies for it. Third, enrollment in all types of health insurance would be lower because penalties for not having insurance would be repealed. Those losses in coverage would be partly offset by enrollment in new programs established by states using the block grants and by somewhat higher enrollment in employment-based insurance. Many of the new programs would probably cover people with characteristics similar to those of people made eligible for Medicaid by the ACA. The decrease in the number of insured people would be particularly large starting in 2020, when the legislation would make major changes to federal funding for Medicaid and the nongroup market. CBO and JCT expect that market disruptions and other implementation problems would accompany the transition to the block grants created by the legislation—despite the availability of funding specifically designated to assist with that transition—given the short time for planning and making changes between now and then.

This is a lot of effort for nothing. The major problems are:

1. Central Government control of everything.
2. An absurd Electronic Health Record system designed by people who seem in my opinion to have no clue as to how medicine functions.
3. Excess reporting of details that are useless.
4. Lack of change in key sectors such as torts etc.
5. Funding of absurd entities like PCORI.

I let you all be the judge.



Labels: [Health Care](#)

[Humans?](#)



As the hurricanes swirl about the Atlantic and the under tow pulls and then throws one back upon the massive rocks the sea gulls watch as one rather dumb human sets out to surf among the waves. Now who is the smarter? Or is there a reason why there are more sea gulls than humans?



Labels: [Commentary](#)

Saturday, September 23, 2017

[Improved CRISPR](#)

The use of [CRISPR techniques](#) to cleave and cut/add DNA sequences is a two step process. First the use of a CRISPR or equivalent to target the sequence and then the CAS9 to cut it. Target and cut. However there are problems. The target may appear at multiple locations and the DSB, double stranded break cut, is often subject to faulty repairs. Thus, although CRISPER can be an elegant approach, its errors can have massive defects.

Doudna and her team have announced some improvement in [Nature](#). They state:

The RNA-guided CRISPR–Cas9 ... has been widely repurposed for genome editing. High-fidelity (SpCas9-HF1) and enhanced specificity (eSpCas9...) variants exhibit substantially reduced off-target cleavage in human cells, but the mechanism of target discrimination and the potential to further improve fidelity are unknown. Using single-molecule Förster resonance energy transfer (smFRET) experiments, we show that both SpCas9-HF1 and eSpCas9... are trapped in an inactive state when bound to mismatched targets. We find that a non-catalytic domain within Cas9, REC3, recognizes target complementarity and governs the HNH nuclease to regulate overall catalytic competence. Exploiting this observation, we designed a new hyper-accurate Cas9 variant (HypaCas9) that demonstrates high genome-wide specificity without compromising on-target activity in human cells. These results offer a more comprehensive model to rationalize and modify the balance between target recognition and nuclease activation for precision genome editing.

As [The Scientist](#) notes:

To minimize the off-target effects of CRISPR-based genome editing, researchers have designed a version of Cas9, the enzyme that cuts DNA, that avoids mistakes with unprecedented precision. Mutating one piece of the nuclease, called REC3, reduced off-target effects to below that of other high-fidelity Cas9 enzymes....namely, eSpCas9(1.1) and SpCas9-HF1—are more specific to their target sequences and make fewer off-target cuts than the natural version. That's when they identified REC3's role in sensing the accuracy with which the enzyme binds to an intended stretch of DNA: in the event of a mismatch, the team found, REC3 would keep Cas9 inactive. ...When they tested this new HypaCas9 on six target sites, the researchers found that at two sites the nuclease made no mistakes, at three sites it made one error, and for one site it hit 18 unintended loci. In comparison, wild-type Cas9 only had a perfect score once, and otherwise tallied between eight and 134 off-target effects, depending on the intended site. The two more-specific Cas9 variants performed just as well as HypaCas9 for five sites, but had a few additional errors at the sixth.

This may be a significant step forward in improving CRISPR usage and safety.



Labels: [CRISPR](#)

Tuesday, September 19, 2017

[News and Fake News](#)

In a piece in the [NY Times](#) an Irish born former Administration official bemoans the explosion of "fake news". The author states:

What exactly has changed since then to make foreign propaganda far more dangerous today? During the Cold War, most Americans received their news and information via mediated platforms. Reporters and editors serving in the role of professional gatekeepers had almost full control over what appeared in the media. A foreign adversary seeking to reach American audiences did not have great options for bypassing these umpires, and Russian dezinformatsia rarely penetrated. While television remains the main source of news for most Americans, viewers today tend to select a network in line with their political preferences. Even more significantly, The Pew Research Center has found that two-thirds of Americans are getting at least some of their news through social media. After the election, around 84 percent of Americans polled by Pew described themselves as at least somewhat confident in their ability to discern real news from fake. This confidence may be misplaced.

Now let's go back a bit. Remember Hearst and the Spanish American War? You don't you say, well you should. Had it not been for his papers we most likely would never have had the hill climbing Teddy. Strange how events turn out.

Now one should also remember Radio Moscow. I do. In 1952 I had a Hallicrafters Short Wave receiver. I listened to the BBC, to Radio Moscow, and a slew of other stations. Even at a young age one could tell Radio Moscow was propaganda, I did not need the Nuns to tell me that. But they did offer a free magazine, Soviet Life. So like a good young Catholic student I wrote a letter asking for my free subscription, doing so on my lined note paper using my best Waterman Blue

Ink pen and placing the cross and "JMJ" atop the letter ans mandated by the Nuns. I unfortunately never got my Soviet Life then, perhaps it was the JMJ or perhaps it was intercepted before ever getting out of the US. But that did not stop my listening to what, even at that age, I knew was fake news. It was comedic, the Soviet exaggeration. Then of course there was Voice of America and Radio Free Europe. The list went on.

You see a rational person can readily identify "fake news". We see it everywhere today. It starts with advertising and then fills the cable news channels. Newspapers all have their own slant on what they consider news. As for social media, I have no use for it.

Proper education is the solution. A Civics class, a real History class, reading from what the Founders based their decisions on, ie the Federalist Papers and their opposition. Then rely upon educated reason. "Confidence misplaced" is a rather snarky way to say. "I know the truth and you have no clue" Rather in a democracy people are bombarded with "facts", many contorted, many twisted and bent to meet some other objective. But that is life.

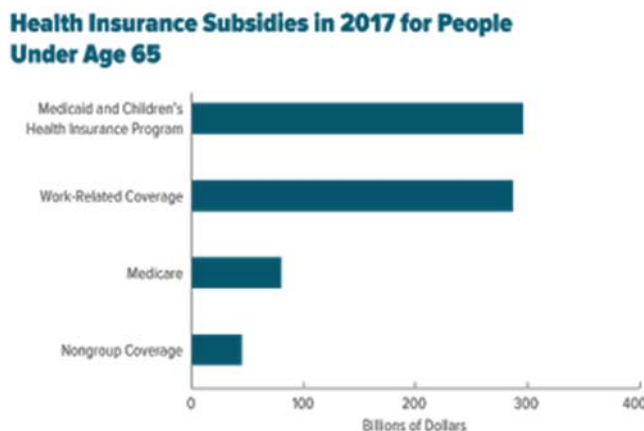
Oh, by the way, if anyone in Russia is monitoring this, any chance I can get my Soviet Life subscription? I liked the pictures and it was free. Thanks.



Labels: [Politics](#)

Thursday, September 14, 2017

[CBO Healthcare Costs for those Under 65](#)



The [CBO published a report indicating the 2017](#) costs of Healthcare for those under 65. Note Medicaid is \$300 billion plus and Medicare, for those disabled, is \$100 billion plus. The dominant driver is the expended Medicaid from the ACA.

They continue:

According to CBO and JCT's estimates, a monthly average of about 244 million noninstitutionalized civilians under age 65 will have health insurance in 2017. Almost two-thirds of them will have coverage through an employer, and about a quarter will be enrolled in

Medicaid or the Children's Health Insurance Program (CHIP). A smaller number will have nongroup coverage, coverage that is provided by Medicare, or coverage obtained from various other sources. On average, about 28 million people—10 percent of all noninstitutionalized civilians younger than 65—will be uninsured in 2017, CBO and JCT estimate (see Figure 1). Between 2017 and 2018, the number of uninsured people rises by 2 million in the agencies' projections, mainly because premiums in the nongroup market are expected to be higher. From 2018 through 2027, the number of people with coverage is expected to grow from 242 million to 247 million. But the number of uninsured people is also expected to grow, from 30 million to 31 million, keeping the uninsured share of the under-65 population stable at 11 percent.

Now under Medicare we have an annual cost of \$10,000 per person. Thus Medicare for all at 330 million people is \$3.3 trillion a year! Yep, a large number.

At least when Thomas Paine made his suggestions in the 1790s, he had the courage to estimate the costs as well as the source of payment. Where are Thomas Paines when we need them?



Labels: [Health Care](#)

Thursday, September 7, 2017

[AI and the Academy](#)

In a [Press Release MIT](#) announces that it has entered into a \$240 million dollar effort with IBM to establish a joint AI Laboratory. They state:

IBM and MIT today announced that IBM plans to make a 10-year, \$240 million investment to create the MIT-IBM Watson AI Lab in partnership with MIT. The lab will carry out fundamental artificial intelligence (AI) research and seek to propel scientific breakthroughs that unlock the potential of AI. The collaboration aims to advance AI hardware, software, and algorithms related to deep learning and other areas; increase AI's impact on industries, such as health care and cybersecurity; and explore the economic and ethical implications of AI on society. IBM's \$240 million investment in the lab will support research by IBM and MIT scientists. The new lab will be one of the largest long-term university-industry AI collaborations to date, mobilizing the talent of more than 100 AI scientists, professors, and students to pursue joint research at IBM's Research Lab in Cambridge, Massachusetts — co-located with the IBM Watson Health and IBM Security headquarters in Kendall Square — and on the neighboring MIT campus.

This comes after much criticism of the IBM Watson venture as more hype than reality. But it does raise many major questions.

1. MIT is an academic institution and what research which is done there has always been of a public nature. MIT Lincoln Lab is an exception but that Lab, as was the Draper Instrumentation Lab, considered an off shoot, not on the main campus and not an academic department.

2. IBM one would assume is investing \$240 million and expects a return to shareholder value. That must mean that IBM has not only first dibs on whatever is developed but also there is some

form of proprietary ownership which seems to be antagonistic to normal academic freedom.

3. If one does a study in this "Lab" then can one take what expertise one has created and take it to a competitor?

4. Why IBM. Is IBM desperate to get something out of Watson that they would dump a quarter of a billion into this effort? Motives count.

5. MIT was a Land Grant School, and as a result had an obligation to support US industry and interests as a goal if not a primary goal. Does this enhance or subrogate that goal?

Needless to say this makes for good PR but is it good science and engineering? I wonder.



Labels: [Academy](#)

Wednesday, September 6, 2017

[Over Rated?](#)

There is an explosion of AI related products. One of the most significant is Watson, the IBM entry which continually gets great praise. [STAT](#) has published an excellent piece worth reading by anyone concerned.

The article concludes:

While not specific to Watson's health care products, the report said potential clients are backing away from the system because of significant consulting costs associated with its implementation. It also noted that Amazon has 10 times the job listings of IBM, which recently didn't renew a small number of contractors that worked for the company following its acquisition of Truven, a company it bought for \$2.6 billion last year to gain access to 100 million patient records. In its statement, IBM said that the workers' contracts ended and that it is continuing to hire aggressively in the Cambridge, Mass.-based Watson Health and other units, with more than 5,000 positions open in the U.S. But the outlook for Watson for Oncology is challenging, say those who have worked closest with it. ...the lead trainer at Memorial Sloan Kettering, said the system has the potential to improve care and ensure more patients get expert treatment. But like a medical student, Watson is just learning to perform in the real world. "Nobody wants to hear this," ... said. "All they want to hear is that Watson is the answer. And it always has the right answer, and you get it right away, and it will be cheaper. But like anything else, it's kind of human."

Medicine is complex, and especially cancer care. No patient is the same. It is not only the pathology but the patient's approach to the disease. Even in such centers such as MSKCC there are a multiplicity of treatments. Also even the current immunotherapy treatments may work 40% of the time. Why the 40% and why not the 60% is the question without an answer.

IBM used to be a service company, selling hardware and software services. It then morphed into a consulting company, a real service business. One wonders just what business they are in now.

This is an article well worth the reading.



Labels: [Health Care](#)

Monday, September 4, 2017

[We Told You So!](#)

In a [just released re-study of the PCa mortality and PSA tests](#) the authors note:

Screening was estimated to confer a 7% to 9% reduction in the risk for prostate cancer death per year of MLT. This translated into estimates of 25% to 31% and 27% to 32% lower risk for prostate cancer death with screening as performed in the ERSPC and PLCO intervention groups, respectively, compared with no screening...After differences in implementation and settings are accounted for, the ERSPC and PLCO provide compatible evidence that screening reduces prostate cancer mortality.

And the reasons are what he had noted when these, in my opinion fatally flawed, trials were performed.

Perhaps they could now calculate how many men died as a result.

As [Eureka](#) notes:

After differences in implementation and settings were accounted for, two important prostate cancer screening trials provide compatible evidence that screening reduces prostate cancer mortality. These findings suggest that current guidelines recommending against routine PSA-based screening may be revised. However, questions remain about how to implement screening so that the benefits outweigh the potential harms of overdiagnosis and overtreatment.

It is a shame!



Labels: [Cancer](#)

Saturday, September 2, 2017

[The FCC and Net Neutrality](#)



It appears as if the current FCC management is about to undo what is called Net Neutrality. A while back I wrote a long piece in [Internet Neutrality](#) while still back at MIT. My point was simply that a carrier is just that, a carrier, and since the days of Elizabeth I this concept was accepted and became the element which led to the dominance of England in world trade. Now comes the FCC and the incumbents. The FCC has never been known for much more than a political equivocator depending on whose party is in charge. So one should not expect anything more than an expression, nay and echo, of what the powers to be or those in charge really want.

[Wired](#) magazine has a piece that somehow thinks this is all new. They state:

This past April, the Federal Communications Commission invited the American people to weigh in on whether the federal government should roll back the rules currently in place to protect net neutrality. By the time the online comment submission period ended last Wednesday, the agency had collected 21.9 million comments, an astounding level of participation on what at first glance appears to be a rather esoteric telecommunications policy issue. (For comparison, when the FCC received around 500,000 postcards and emails about its media ownership rule changes in 2003, it was considered a big deal. Even Janet Jackson's wardrobe malfunction at the 2004 Super Bowl garnered only about 1.4 million comments.) So what did the people say? The industry group Broadband for America, which opposes the FCC's current rules, recently commissioned an analysis of the comments from a company called Emprata. The study determined that a majority of the comments—about 60 percent—favor keeping the FCC's current rules, which classify internet service providers as "Title II" common carriers like mobile and landline phone companies and ban them from blocking or interfering with lawful content. If you look only at unique comments, as opposed to form letters using boilerplate text, those in favor of keeping the Title II rules outweigh those who want to jettison the rules 1.52 million to 23,000. The only hitch: the commenting process was such a debacle that the legitimacy of the entire body of comments is now in question.

Should one be surprised that the FCC's system is so let us say reckless? Hardly. It is a Government controlled process. Some Beltway Bandit probably wrote the specs, then another Beltway Bandit did the software. And in the midst of this no one is really responsible for anything. So one expects rational actions from these folks.

In my experience and in my opinion I saw the FCC up close. If I went in with some issue, my opponent was in the waiting room after I finished to rebut my position. How did they find out?

Simple, the Sunshine rule, the FCC tells everyone everything. In those days one filed a paper document. Yes it was cumbersome and yes form was important. But it meant that someone had to give some thought to the process and multiple filings were difficult. The on line approach allows for slamming of various types not to mention the system allows the uploading on anything, yes folks anything.

These then are the people who will control our information flow. One should understand that the main ISPs, such as Comcast, Verizon, AT&T are also in the media business and promulgate their own interests. They carry a big stick, and they also have great carrots for FCC officials when they go out in the world. Just look at the heads of major industry lobbying groups!

So what will happen with Net Neutrality; ask the largest bidder!



Labels: [Internet Neutrality](#)

Thursday, August 31, 2017

[A Modifier of a Verb is Called an Adverb](#)



In the [NY Times](#) there is a piece recounting the alleged work ethic of Silicon Valley. They start by stating:

Silicon Valley prides itself on "thinking different." So maybe it makes sense that just as a lot of industries have begun paying more attention to work-life balance, Silicon Valley is taking the opposite approach — and branding workaholicism as a desirable lifestyle choice. An entire cottage industry has sprung up there, selling an internet-centric prosperity gospel that says that there is no higher calling than to start your own company, and that to succeed you must be willing to give up everything.

First, grammatically it is "thinking differently" if one wants to modify how one thinks. If however if it is used as a predicate then "I think different." means somehow that this thing called different is "what" you think.

Now in the 14th Century all students took the Trivium, Grammar, Logic, and Rhetoric. Why you may ask. To express themselves to each other clearly and correctly. Now Scholasticism was ending with Ockham and minimalism but this use of language correctly and unambiguously allowed for the development of English Law which may be one of the greatest creations of Mankind. I am not a lawyer for full disclosure.

Now back to the work ethic. Just being busy for 24 hours is meaningless unless you are

productively doing something. I managed for a decade to work more than 24 hours a day, traveling to beat the sun to my some two dozen countries. I have seen lawyers book more than 24 hours in a day the same way. But that is a trick.

The question is; what are you producing during that time. Writing code is not "producing", it is effecting and idea. Creating a new system architecture is "producing", whereas writing code to do what you were told to do is akin to typing a Tolstoy novel. You are not Tolstoy, you are a typist. Thus the content of what is produced is critical. It begs the question of a Post Doc performing hundreds of tests for some Principal Investigator. Is that also akin to programming or is value added? Or is that why they are just a Post Doc.

The article continues:

Good grief. The guy is developing an app that lets you visualize how a coffee table from a catalog might look in your living room. I suppose that's cool, but is it really more important than seeing your kids? Is the chance to raise some venture-capital funding really "the ultimate reward"?

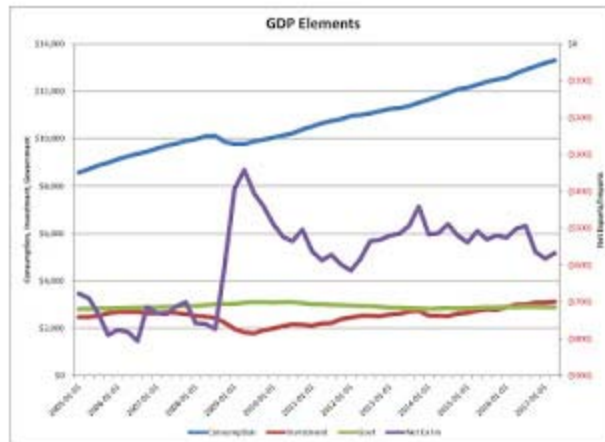
There are two issues in this statement. First, is another App of any value, period! Fifty years ago one built a better communications system, an improved medical imaging system, an innovative therapeutic, or any other thing that was real, advanced humanity as a whole. But a new App, get real. Second is the issue of who is doing what. In my experience the true start up is one , perhaps two people. There is a visionary, a Founder, and that person assembles a team. That person is the "dream merchant" selling the vision, laying out its implementation, convincing customers, and yes raising money. For the most part every one else is an employee, a follower. Thus this begs the question; do all people have to hustle, or just the leader?

Recently while trying to sort through some possible start up ideas at MIT we had one where the alleged CEO disappeared. I finally found him and the reason was because his wife had a baby and he was taking his Paternity Leave as she was taking her Maternity Leave. My daughter was delivered by me and the Resident and I went back to the Institute and picked my wife and daughter up the next morning between classes. That was fifty years ago. Did not skip a beat. No leave anywhere, and that is truly a Hustle. Today I guess we all get leave, paid and all. Unless you are not in Silicon Valley of course!



Labels: [Academy](#), [Commentary](#)

[GDP April 2017](#)



Here is the current GDP. It is growing, albeit still slowly. The above is each element, not the total. Consumption shows good growth and Investment is increasing. Net ExIm has come back up again however. Overall things are not that bad.



Labels: [Economy](#)

[Sister Rosita](#)

In the 5th Grade I had Sister Rosita. A short rotund Sister of Charity whose sole purpose in life was to get me to spell correctly. This was well before the age of Dyslexia and special needs students such as myself. Sister Rosita would shout at me, "McGarty, when will you ever spell correctly!" And I would reply, "I will have people to correct my errors Sister." Then "WHAM", the good old three foot (or should it be feet?) ruler across the knuckles.

Now Sister Rosita is a thing of the past and I have Microsoft Word. It always spells the word correctly, unfortunately it is often the wrong word. No matter how I look at it the word always looks correct, at least for a month or so. Then I read it and see the error.

Now add to this mess such things as Twitter. I tried Twitter for a few months, found it useless. Also as some may note I cannot say much with few words. I think through something, write a draft, with mis-spellings and all, then post it. Some folks actually read this stuff. Now along comes the NY Times and spelling²[1]. They note as follows:

Actually, we should lay off everyone's spelling. In a digital age of autocorrect and electronic publications that can be edited from afar, not to mention social media platforms that prize authenticity and immediacy over polish, misspelling has become a mostly forgivable mistake. You simply do not need to be able to spell as well as people once had to, because we now have tools that can catch and correct our errors — so it's just not a big deal if, on your first draft, you

²[1] <https://www.nytimes.com/2017/08/27/technology/donald-trump-twitter-spelling.html?hp&action=click&pgtype=Homepage&clickSource=story-heading&module=second-column-region®ion=top-news&WT.nav=top-news>

write “heel” instead of “heal.” People are very attached to spelling, of course. When I first floated the idea that politicians’ misspelling was a forgivable sin, I was dragged over the coals for it on Twitter. My wife got so upset that she quit talking to me for most of a day. When I emailed my editor to say I wanted to defend Mr. Trump’s misspelling, she wrote back, “You should listen to your wife.” So I did what I normally do when confronted with people who are wrong on the internet: I researched the subject. I looked at the history of standardized spelling and what misspelling says about you cognitively. I uncovered a rich history of political misspelling. And I read a book by an Oxford professor on the shifting cultural attitudes toward spelling and then talked to him for a long time. Yet there is an even deeper sort of elitism underlying the criticism of spelling mistakes. It stems from people correlating accurate spelling with a good education and outsize intelligence, which is actually incorrect. There is not much scientific evidence to suggest that spelling well is connected to high intelligence. In the same way that some people are naturally better at arithmetic than others, some are naturally better spellers than others (and some people have lexical disabilities, like dyslexia, that make spelling even more difficult). But if you spell well, you can still do lots of dumb things, and if you spell poorly, you can still be very smart. Standardized spelling has been with English for at least a few hundred years, and it has mostly served us well. So I understand that the idea of abandoning it, or at least relaxing our adherence to it, may sound frightening, like the first step on a short march to civilizational decline...Second, there’s little evidence that how one types on electronic media has much to say about how one functions otherwise. One study, in fact, showed that kids who frequently used “textese” tended to be better at grammar than those who didn’t. All of this suggests that we are simply giving too much weight to spelling and other typographical mistakes. Focus on what people say, not how they spell it.

So is the art of spelling lost at last? It is akin to the "other left" syndrome where some says turn left when they mean turn right and correct it by saying the "other left".

Spelling counts. But not on Twitter or even Facebook.



Labels: [Commentary](#)

Wednesday, August 30, 2017

[Look to the Left, Look to the Right](#)

In the old days, when you started class at the University, there was a sense of terror of not succeeding. The old adage of looking Left and then Right and saying that one of them will not be graduating in four years left you with a sense that you had to press on from day one.

Now the [Institute President](#) states:

“We are very lucky to have you!”

I guess so. But why are the students very lucky to be there?

Then it states:

"MIT is a unique crucible, where you will be faced with challenges you didn't quite expect, at an important time of your life," she said. "My advice here is quite simple: Embrace failure! If you haven't already, you'll soon realize that failures frequently, and I might say usually, allow you to learn far more than your successes." Failure, she said, "lets you know that your knowledge lacked depth, or your understanding was incomplete, or maybe your expectations were a little unrealistic. Filling in those gaps adds to your knowledge base, and how you go about recovering from those failures will teach you lifelong lessons."

I would gather that this is not something you would espouse at the Med School! Yes, we make mistakes, and yes we learn from these mistakes. But in life, Failure is often not an option. Prior Planning Prevents Poor Performance, a dictum my father embedded in my thinking from day one. Experiments fail, but in so doing one hopefully understands why.

But embracing failure should not be an option. You don't drive eighty miles per hour on black ice, failure there can be severe!



Labels: [Academy](#)

[What is in a Change?](#)



Back in the early 1960s, Walker Memorial at MIT was a meeting place at lunch time and even for dinner. It was as close to High Table in an English University one could get, but no High Table. It was a watering hole, a meeting ground, a place to trade ideas, a eat food which was lower in carbs than what is there today.

Walker Memorial is now 100 years old and [MIT is celebrating](#). They note:

For many of those who have passed through Walker Memorial over the past 100 years, the most

enduring images remain the [murals](#) in Morss Hall, which were painted by Edwin Howland Blashfield of the Class of 1869. Created and installed between 1923 and 1930, their allegories of alma mater receiving homage from scientific and academic disciplines have watched over countless MIT community functions, from dining hall breakfasts to the Assembly Ball and more. For most MIT alumni and students, Walker Memorial holds indelible memories. A century after its completion, the tribute to President Walker has been realized in the best possible way — with the building continuing to serve as a community gathering place.

However it is currently planned to be turned a building for the Music Department. [MIT notes](#):

Walker Memorial Hall is a significant campus building that has served many roles on the MIT campus over its nearly 100-year history. Currently in need of substantial renovation, Walker appears to be a good match with the programmatic needs of the Music and Theater Arts Department – a community in search of a new home. MIT is currently studying the possibility of renovating Walker to co-locate the Music and Theater Arts Department with its teaching and extracurricular activities. The new center would allow MIT to explore new frontiers of artistic and technological discovery.

Now I am not against music, but the loss of this "watering hole" is significant. It has been replaced by Starbuckian hang outs featuring high carb feasts and uncomfortable seating. I think that it is a loss.. Just a thought.



Labels: [MIT](#)

[A Statue, per chance, A Lesson](#)



Now with all the fuss about statues perhaps there is one which is acceptable. This is Thomas Paine, in a small park down the road from the center of Morristown, not far from the Inn that Washington and Hamilton would hang out from time to time.

Paine one could say was sinless, at least as per the current standards. He donated what little money he made from his publishing to the Revolutionary cause, he then moved to France to assist that Revolution. He did get crosswise with Robespierre, but one could say anyone would have done so. He understood Liberte, Equalite, Fraternite as simple, freedom, individualism as per de Tocqueville, and the freedom of associations. He did not especially like Jefferson, and Adams found him even more strident than he was, but his words resonated.

His social views ring clearly even today. So perhaps we should look for the statues of those whose insight has lingered in a positive sense. Good old Tom!



Labels: [Commentary](#)

[CAR-T Cell Approval by the FDA](#)

A year ago [we wrote extensively about the developments in CAR-T cells](#). We have been following this work for several years and it has finally reached a clinical level with [FDA approval](#) today of a Novartis therapeutic.

The FDA notes:

Kymriah, a cell-based gene therapy, is approved in the United States for the treatment of patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse. Kymriah is a genetically-modified autologous T-cell immunotherapy. Each dose of Kymriah is a customized treatment created using an individual patient's own T-cells, a type of white blood cell known as a lymphocyte. The patient's T-cells are collected and sent to a manufacturing center where they are genetically modified to include a new gene that contains a specific protein (a chimeric antigen receptor or CAR) that directs the T-cells to target and kill leukemia cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient to kill the cancer cells. ALL is a cancer of the bone marrow and blood, in which the body makes abnormal lymphocytes. The disease progresses quickly and is the most common childhood cancer in the U.S. The National Cancer Institute estimates that approximately 3,100 patients aged 20 and younger are diagnosed with ALL each year. ALL can be of either T- or B-cell origin, with B-cell the most common. Kymriah is approved for use in pediatric and young adult patients with B-cell ALL and is intended for patients whose cancer has not responded to or has returned after initial treatment, which occurs in an estimated 15-20 percent of patients.

ALL is a deadly childhood cancer, most often, and I recall see my first case in March 1968. Cold rainy day and a ten year old had a fever and malaise and we ran the blood work and it was a leukemia. Death was then a certainty. Now with this therapeutic survival is a viable option.

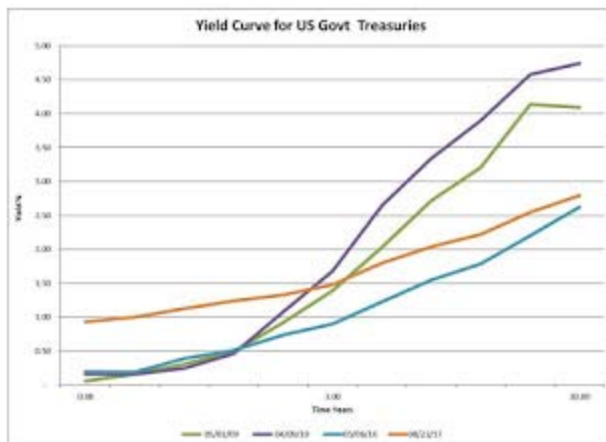
It should be interesting to see how this can be applied to other cancers. Cell markers must be available for the differing malignancies.



Labels: [CAR-T Cells](#)

Wednesday, August 23, 2017

Yield Curves August 2017



The above shows the ever closing gap on the Yield Curve. The short term rates have been growing rapidly but long term have not moved. One suspects a built up delay in the long term but the short term action is the Fed rolling over its holdings and the buyers demanding more return. This has yet to be seen on the long term because there is much less of it in proportion to turnover.



The above is the spread. It is lower than any time since we started tracking after the Banking Crash.



The above is a similar demonstration but it shows the explosion of the short term rates. One expects long term explosion in the coming year.



Labels: [Economy](#)

Sunday, August 13, 2017

[Programming and Programmers](#)



My first computer was a used IBM 709 and the language was FAP, or Fortran Assembly Programming. The input was a paper tape! Yes, boys and girls, there were such things. I used it to analyze acoustic feedback instabilities in public address systems.

Does this talent make one better? In my opinion, not really. Programmers today are labor and VCs are capital. One should go back and read Marx.

Everything is divided into labor and capital

The software engineers are labor and the VCs and management are capital

Capital needs labor, especially in Silicon Valley, to think they are paid lots so that the value of capital's assets increase, such as real estate

Capital demands labor be compliant and not rebel

However there is a natural dialectic, labor vs capital, and this is just the beginning of that Hegelian dialectic, there will be more.

Thesis is the current model of the allocation of capital and labor.

Antithesis is the recognition by labor that they are being manipulated.

Synthesis will be the revolutionary change that is inevitable in this industry.

Strange that quasi Marxists, namely the current Capitalists, are in reality playing our Marx in real life, as capitalists!

Just a thought.



Labels: [Commentary](#)

Friday, August 11, 2017

[Ontogeny Recapitulates Phylogeny, or What Comes First, the Chicken or the Egg](#)



In [Nature](#) there is an article where they are applying the AI world's approaches to plant systematics. Namely the process of sorting and arranging plants. They note:

There are roughly 3,000 herbaria in the world, hosting an estimated 350 million specimens — only a fraction of which has been digitized. But the swelling data sets, along with advances in computing techniques, enticed computer scientist ... and botanist ..., to see what they could make of the data. ... team had already made progress automating plant identification through the Pl@ntNet project. It has accumulated millions of images of fresh plants — typically taken in the field by people using its smartphone app to identify specimens. Researchers trained similar algorithms on more than 260,000 scans of herbarium sheets, encompassing more than 1,000 species. The computer program eventually identified species with nearly 80% accuracy: the correct answer was within the algorithms' top 5 picks 90% of the time. That, says Wilf, probably out-performs a human taxonomist by quite a bit.

Now having done this a few decades ago, and still proceeding to do so with *Hemerocallis*, the answer is not form but simple genetics. Sequence the genes, then using a mutation hypotheses base determine how the genes evolved. The use the shapes to see the effect. As is well known this process has been around since Linnaeus and it suffers from substantial defects. Just because a form looks close to something says nothing about the genetic evolution.



Labels: [Botany](#)

Sunday, August 6, 2017

[Those in Glass Houses Should Not Throw Ginkgo Nuts](#)



I grow Ginkgo trees. This is a view of this year's Ginkgo nuts, ready to drop and then off to the cooling off period before potting for next season. [Ginkgo trees](#) are ancient, one of the gymnosperms or naked seed plants. Surviving for millions of years, amongst multiple climate changes and assaults. [They line the streets of New York](#) because they thrive on pollution. Good friends for humans. I have a few dozen on my land alone.

Now seventy two years ago today my father and his shipmates were in the North Pacific preparing for an invasion of Japan. They were the survivors of the battles at Leyte, Saipan, and other places in the Pacific. They had already been given their winter gear in preparation of the invasion. They knew how bloody Okinawa was and were preparing for even worse.



The above is what they found in Manila. The Japanese did this. Thus they truly feared what they would be up against in the invasion of the islands.

Then late in the day of the 6th of August they heard about Hiroshima. They did not cheer, they cried. For they knew this was the true beginning of the end and that they would now have a chance of seeing their children.

Thus when revisionist "historians," such as the one in the [New York Times](#), bemoans:

The Hiroshima ginkgos, the tenacious older siblings of the tender green trees in front of our

North Carolina house, were able to resist the most devastating outcome of science and technology, the splitting of the atom, a destructive power that could turn the whole planet into rubble. Those trees' survival was a message of hope in the midst of the black rain of despair: that we could nurture life and conserve it, that we must be wary of the forces we unleash.

They fail to understand that this plant had managed a survival of even greater proportions. Referring to the Japanese curator who introduced this writer to the tree the author states:

By then middle-aged, his body was a testament to that war crime and its aftermath. One ear was flat and mangled, his hands were gnarled, and from a finger on each grew a black fingernail.

One can vehemently object to the use of the pejorative term, "War crime", as if war itself is not the very crime he detests. The Pacific was strewn with bodies. My uncle was riddled with Japanese machine gun bullets on Okinawa, yet survived, along with his men, and awarded the Distinguished Service Cross. The devastation on Okinawa was just a prelude to what would have happened on the main islands. I would take umbrage to the term "war crime". Neither the survivors nor the tree deserve such.



Labels: [Commentary](#)

Saturday, August 5, 2017

[Guess Who Is Coming to Dinner?](#)

Yep, it is that MIT Professor who thinks all of us out here in the real world are so stupid...[Now he wants to teach us economics!](#)

He tells us:

I'm excited to announce the launch of a new course on edX that covers Introductory Microeconomics. I've wanted to do a course like this for years. I have always found economics provides a terrific way to think about the world. Economics principles explain so much of what drives our everyday life: how people decide which goods to buy and how to spend their time; how firms set prices and hire workers, and whether the outcomes of markets are fair and efficient. These economics principles were inspirational to me when I first learned them as an undergraduate. I have gone on to apply to them to a set of topics I am passionate about, both as a Professor at MIT and as a policy expert for both state and local governments. Whether in the classroom, in Washington D.C., or in state capitals, I have found that basic economic principles never lead me wrong in terms of explaining important aspects of the world.

But wait, I thought we were beyond the pale, uneducateable, devoid of any intellectual merit. I guess it is like all those Shark movies, a shark can attack in any form, Zombie Shark anyone!



Labels: [Academy](#)

SATURDAY, JULY 29, 2017

HEALTH CARE, ECONOMISTS AND REALITY

The Health Care market is complex, and to understand it one must drop back and ask two questions. First, just what are we trying to accomplish with Health Care. Second, are there other examples of “insurance” that people buy which seems to work?

Let us answer these two questions quickly. First we want Health Care so that people who are sick can be treated in the best reasonable manner. Note I did not say best possible manner. It should be reasonable based on resources available. However if someone can afford more than they can personally buy more. Second, we have many examples of such an approach apart from Health Care. Namely home, auto, liability insurance.

What makes the other insurance factors work? Simple:

1. They are bought as an individual not through companies as a benefit. Every buyer gets to make their own choice.
2. Minimum levels are coverage are mandated but they really are minimal to protect third parties such as liability limits.
3. Added coverage is optional and can be purchased.
4. It is not tax deductible.
5. There is an un-insured motorist pool which can be made akin to the high risk medical pool.
6. Insurance companies are many and compete aggressively for customers.

Thus we have thousands of examples of such coverage. Then why is Health Care so crazy. Well there are many people who think they know.

In a recent [NY Time](#) article by an often self-proclaimed top economist the author states:

In Econ 101, students learn that market economies allocate scarce resources based on the forces of supply and demand. In most markets, producers decide how much to offer for sale as they try to maximize profit, and consumers decide how much to buy as they try to achieve the best standard of living they can. Prices adjust to bring supply and demand into balance. Things often work out well, with little role left for government. Hence, Adam Smith’s vaunted “invisible hand.” Yet the magic of the free market sometimes fails us when it comes to health care. There are several reasons.

Namely he contends:

1. Externalities abound. In most markets, the main interested parties are the buyers and sellers. But in health care markets, decisions often affect unwitting bystanders, a phenomenon that economists call an externality.

Now the externalities are also the unintended consequences. All too often whenever Government gets into the fray we see unintended consequences. Why? Simply because almost all legislation is written by lobbyists who serve the interest of their employers. The more legislation the more externalities. Externalities rare a result of the way legislation is created not inherent in Health Care.

2. Consumers often don't know what they need. In most markets, consumers can judge whether they are happy with the products they buy. But when people get sick, they often do not know what they need and sometimes are not in a position to make good decisions. They rely on a physician's advice, which even with hindsight is hard to evaluate.

Well consumers do not know what fender will get crushed by some moron trying to squeeze between you and an eighteen wheeler. You need coverage not specificity. That is the nature of insurance. When my car gets hit I do not know how to repair the fender or how to price it out. Same for dozens of other insurance markets. I am buying a policy to cover the unknown. Thus this reason is without merit.

3. Health care spending can be unexpected and expensive.

Same as the above. I cannot tell you when that moron in the black pickup tries to squeeze between me and the 18 wheeler. I was stopped to allow the 18 wheeler to safely turn. The moron in the pickup is just that, a moron! So his policy pays but mine increases my fee, perhaps because I did not have wings on my care to fly away. Why says insurance is logical.

4. Insured consumers tend to overconsume. When insurance is picking up the tab, people have less incentive to be cost-conscious.

Auto insurance customers do not, frequently. This is insurance fraud. They have adjustors for that. Now there is a corollary. Namely many people abuse themselves via obesity, alcohol, tobacco, and what we get is self-induced disease. That is the equivalent of a person having a multiplicity of moving violations. We have seen and addressed this element.

5. Insurance markets suffer from adverse selection. Another problem that arises is called adverse selection: If customers differ in relevant ways (such as when they have a chronic disease) and those differences are known to them but not to insurers, the mix of people who buy insurance may be especially expensive.

If everyone who drives must have insurance, actually it is the vehicle, then why not the same with Health Care. No exceptions. You may just have the minimum liability policy or you can get

the top of the line. But you have it. Perhaps the bottom minimum is covered by a tax deductible. If people do not have the funds they great a tax credit to pay for it. But no free riders.

We had [developed the details of such a plan](#) some eight years ago. It is not hard and not overly costly. It goes a lot of oxen. From fat people charged a surcharge to companies getting rid of the benefit. It also get the Government out of telling me when to get a colonoscopy.



Labels: [Health Care](#)

[LEARNING TO TALK \("TAWK"\) LIKE A NEW YORKER](#)

I grew up on Staten Island. Now I gather that some folks grew up "in" Staten Island but grammatically that would make them a worm or gopher but I gather one must leave Grammar behind in the new Century. Now in my Senior Year of Secondary School after the Christmas break since I had already gotten into college, had my scholarships etc. I began to get a bit reckless. My father, in order to see that I stayed the straight and narrow decided I need some focusing. Now to put this in context my father was in the NYPD Youth Division and my degree of reckless behavior amounted to what today would probably make one a Saint, especially under the current management back in Rome, but I digress.

Thus my father with the agreement of the Headmaster sent me for the month of January to the NY Department of Sanitation, the Garbage folks for simplicity. Thus each day I arose at 4 AM and got the 110 Bus to another bus, and then to the NYDS garage with some 40-50 other folks. My first day I forgot my long underwear and wore chinos. It was 20 F and snowing. Needless to say I soon learned that looking "cool" was not an option.

Then out to shovel snow and collect trash. Twelve hours a day, from 6AM to 6PM, with an hour for lunch at some greasy spoon diner. I brought my own peanut butter sandwich.

What did I learn? The first was the use of the most famous profanity in New York, the one making the rounds in the current White House. After 4 years of Latin, through Virgil, I knew Grammar but I have never seen a single word which could be a noun, verb, adjective, adverb, gerund, preposition, etc ever. But I learned its usage like a pro. It made me a member of Good Fellas, I could F word with the best.

Now back to Virgil in February I learned several things. First, do not try these words out in Virgil, and do not try them in Chaucer, you see after Latin was Middle English. Where could I use my new found language. I had a good hold of street Spanish, Italian, academic French, and Latin, a smattering of classic Greek, but my Sanitation Department linguistic capabilities were homeless.

But alas, they now have a home! Doors have been opened by the literati in DC, by the very political lights that leads us forward. I have my skills fine tuned to take on any position in Government!



Labels: [Commentary](#), [Politics](#)

TUESDAY, JULY 25, 2017

GOING TO THE MOVIES

For over a hundred years when one wanted to go to the movies one saw a film that was of interest, found a theater that was showing it and then went to buy a ticket, arriving early if it was popular. The one sat through 30-40 minutes of painful video from ads to previews, oftentimes breaking eardrums.

Now it has changed. Really. You must go on line, choose your seat, choose your time, buy your ticket, and then off to the theater you go. There is no first come first served at the ticket counter, and in fact there is no ticket counter, just a scanning device that allows you entry into massive seats and still the same boom box.

But I suspect that one can now arrive respectfully late, avoid all the promos, and just see the film. This is a cultural change and I wonder where it may take us.



Labels: [Commentary](#)

THURSDAY, JULY 20, 2017

MOST INFLUENTIAL SCIENCE BOOKS

What can be influential in science, what books for example. The Guardian has run a piece and Richard Dawkins's *Selfish Gene* comes out on top. They note^{3[1]}:

*Debates about the most influential science book of all time habitually settle into a face-off between Darwin's *Origin of Species* and Newton's *Principia Mathematica*. But a poll to celebrate the 30th anniversary of the Royal Society science book prize returned a more recent winner: Richard Dawkins's *The Selfish Gene*. Dawkins took a decisive 18% of the vote, while Darwin was jostled into third place by Bill Bryson's *A Short History of Nearly Everything* in the Royal Society poll of more than 1,300 readers. As interesting as the votes on the 10 books shortlisted for contention was the often passionate championship of titles that were left off the list. They were dominated by physics and cosmology. Silly not to include David Deutsch, sniffed one of many, who cited a range of works by the Oxford-based quantum physicist. Carl Sagan's "mind-blowing" 1980 TV tie-in *Cosmos* garnered a clutch of votes from fans who described it as life-changing.*

Now I thought about some of the works I have read over the years and especially the ones I have re-read, some several times. My most favorite is the two volume auto biography of Norbert Wiener. Each time I go through it I see more and more. It is the mind of a mathematician, a

^{3[1]} <https://www.theguardian.com/books/booksblog/2017/jul/20/dawkins-sees-off-darwin-in-vote-for-most-influential-science-book>

brilliant mind. Many think Norbert as a bit of an odd duck and in the Engineering world the folks like Shannon much more, but there is nothing like Wieners autobiography. It is a snapshot in time and a time when one could roam across the world and share ideas.

Now on to my list:

1. Bell, Men of Mathematics
2. Einstein, Relativity
3. Einstein, The Meaning of Relativity
4. Feynman, QED
5. Feynman, The Character of Physical Law
6. Gamow, One, Two, Three...Infinity
7. Schrodinger, What is Life?
8. Shannon and Weaver, The Mathematical Theory of Communications
9. Watson, Double Helix
10. Watson, Molecular Biology of the Gene
11. Wiener, Cybernetics
12. Winograd and Flores, Understanding Computers and Cognition

Just some thoughts.



Labels: [Commentary](#)

WEDNESDAY, JULY 19, 2017

[CBO NUMBERS](#)

The [CBO](#) issued a report on the savings when eliminating Obamacare. They state:

CBO and the staff of the Joint Committee on Taxation (JCT) have completed an estimate of the direct spending and revenue effects of the Obamacare Repeal Reconciliation Act of 2017, an amendment in the nature of a substitute to H.R. 1628, which would repeal many provisions of the Affordable Care Act (ACA). According to the agencies' analysis, enacting the legislation would decrease deficits by \$473 billion over the 2017-2026 period

Yet if you look at what they reported a day ago the savings would be almost \$600 billion per-year! How can anyone believe these folks! What number is ever real! Well it is Washington after all.

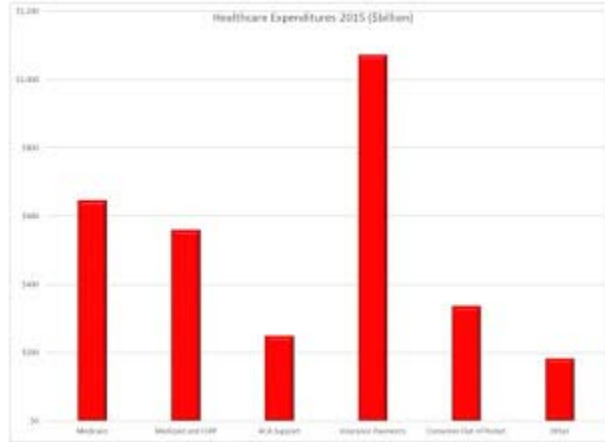


Labels: [Health Care](#)

TUESDAY, JULY 18, 2017

HEALTHCARE EXPENDITURES

The [CBO](#) published a report containing the data below.



Let us examine the above:

1. Medicare is a paid for insurance plan. eight years ago we showed that any middle class person contributing for their 50 years would have paid into he plan, assuming interest at the FED rate in excess of any benefits. Thus Medicare is a paid up benefit. In addition Medicare still charges for participation and still one needs extra coverage. Thus for those who have never held a reasonable job and paid little into Medicare it is a free ride, for all others we pay well more than any benefit!
2. Medicaid is a free plan. The ACA double Medicaid coverage adding \$250 billion to this plan. BUT, it was to stop and fall upon the states. As some [Governors try to allege](#), falsely so, we are not expected to keep filling up their trough.
3. ACA Support is the \$250 billion being spent for Obamacare payments on the Exchange. Add that to the Medicare expansion and we have \$600 billion we never had before!
4. Insurance is what the working folks pay!
5. Out of Pocket is again the working folks.
6. Other is the working folk.

Thus almost \$600 billion is added to our deficit and growing. The folks who pay their own way, including Medicare, will ultimately have to pay for this excess free riders!



Labels: [Health Care](#)

MONDAY, JULY 17, 2017

RUSSIAN INTELLIGENCE

In the old days when the Soviets had a KGB and other intel agencies they were pervasive and managed to keep themselves well hidden from Western intel agencies. The classic example was the Philby clan who managed to keep themselves out of the MI6 and CIA radars. The Russians are quite intelligent and sophisticated and somewhat unlike Chinese intel have well established western outlets. There were thousands of fellow travelers in the old Soviet days and in today's world the need for promulgating a Soviet world view are no longer necessary. The interest is establishing a strategic advantage to maximize whatever Russia may have.

Unlike China which has an economic dependence on the West, Russia sells its extraction elements, oil and minerals. You really can't buy any "Made in Russia" stuff at Walmart. So why doe Russia do what it does? Simply it is the Russian mindset of having a presence, a seat at the table. It is doubtful that Russia wants to overthrow the United States. Frankly they have enough problems at home without taking on more. International influence, yes, international "respect", yes, recognition, yes.

Now as to Russian Intelligence Operatives. What do they seek? Sources of information, strategic advantages, weaknesses of the other side. If a target can be compromised then a target can be manipulated. Yet to compromise one must know something the target wants kept secret and then let the target know that they are vulnerable. Classic extortion. To work, the Operative must be invisible, yet present to the Target.

What are the rules for an Intelligence Operative?

There are three simple rules:

1. Never put it in writing

What does this mean? Simply never leave a discoverable trail. Clearly when one enters Trump Tower or any other major building in New York one is captured on video hundreds of times and one must register to enter the building, one is photographed, one must submit valid IDs etc, pass through Secret Service filters. Thus, any meeting at Trump Tower is a major violation of Rule 1! Let us assume that the Trump folks were just naive. They took a meeting which may after the fact have poor optics. Let us assume they were smart. They took a meeting knowing that any operative would never appear in such an open venue. Operatives meet in obscure locations like forests, mountain paths, under bridges, or anywhere where they chance of being seen is as near zero as possible. Operatives do not meet at a location under Secret Service control, like Trump Tower. Unless the Secret Service has also been compromised in toto! That is a tale going too far.

2. Trust no one

As an Operative you must trust no one, not even your father (or mother as the case may be). Anyone can be anything at any day. Trust is a non-entity. Counter Intelligence relies of building trust with a target. If the target is themselves an Operative then the target knows enough not to

trust anyone. In fact any attempt to build trust may be a sign of a Counter Intel Operative. I have seen Counter Intel Stasi and Cuban Operatives, very attractive but they scream beware!

3. Always have a second exit.

This is a critical one. It covers a lot of ground. From that of a simple Plan B to the use of third parties to do messy jobs and seeing that they are expendable. Never hold the knife, you may get caught. Have plausible deniability, be transparent. Have another identifiable as the Operative, always have a delaying plan while escape can be made.

Is Russia a Major Threat?

In the old days we worried about a Soviet nuclear attack, really! There were plans for various options such as the RISOP plan^{4[1]}. We still live on a remnant of RISOP. Russia has ready nuclear forces, and the US maintains its triad forces. The past Administration let the weapons remain un-updated, but there are still more nuclear weapons to destroy the earth many times over. Russia likewise has active capabilities. But both Russian and American key players understand the end game of any nuclear engagement and would thus mitigate against any. China is a bit uncertain but its focus has been on economic warfare. Thus Russia may at the extreme be a threat but not in any day to day environment. One may then ask why they are acting as they do? The answer is simple. It is the tale of the frog and the scorpion. The scorpion walks to the edge of a raging river and seeks to cross. He asks a frog who at first refuses, after all it is a scorpion. The scorpion promises not to sting. The frog agrees and halfway across the raging river the scorpion stings the frog, now both will die. The frog asks in his last breath; why? The scorpion replies: I can't help it, I am a scorpion. Thus one understands the Russian mind.

Is Russia more of a threat than China?

Now here we have a concern. This is an economic player. A large military but one suspects to keep peace at home. But a massive player in world economies and growing. Perhaps more time on this issue would be better spent than on the scorpion!



Labels: [Russia](#)

SUNDAY, JULY 16, 2017

[PROSTATE CANCER MORTALITY: FACT OR WHAT?](#)

In a recent paper by Wilt et al the authors state:

^{4[1]} <https://fas.org/blogs/security/2008/07/risop/>

After nearly 20 years of follow-up among men with localized prostate cancer, surgery was not associated with significantly lower all-cause or prostate-cancer mortality than observation. Surgery was associated with a higher frequency of adverse events than observation but a lower frequency of treatment for disease progression, mostly for asymptomatic, local, or biochemical progression.

Put aside the adverse events since it is well known that any surgery has such a risk. We would focus on survival alone. The authors continue:

In conclusion, radical prostatectomy was not associated with significantly lower all-cause or prostate-cancer mortality than observation through 20 years of follow-up among men with localized prostate cancer that was diagnosed during the early era of PSA testing. Absolute differences remained below 6 percentage points. Death from prostate cancer was very uncommon among men with low-risk disease who were assigned to observation. Surgery may be associated with decreased mortality among men with intermediate risk prostate cancer, depending on the pathological classification. Surgery resulted in substantially greater long-term urinary incontinence and erectile and sexual dysfunction than observation and was associated with a significantly lower risk of disease progression and additional treatments, most for local or asymptomatic biochemical progression.

The problem with this analysis is as follows:

1. It is clinically well known that a small percentage of all PCa is of a highly aggressive form.
2. The highly aggressive form almost always results in death.
3. The highly aggressive form occurs early in the onset of the disease and metastasis is almost immediate.
4. The specific genetic makeup of this highly aggressive form is currently undetermined. Moreover there may be a pleiomorphic genetic presentation.
5. However, whenever it is suspected, such as presented in the above paper, the detailed genetic makeup of the cancer cells should and must be determined. It was not apparently done here. Not all PCa is the same.

Thus we examine the data from the perspective of the putative existence of a highly aggressive form.

The Press does take this report to arguable extremes as is usually the case. Science Daily states^{5[1]}:

^{5[1]} <https://www.sciencedaily.com/releases/2017/07/170712201146.htm>

Prostate cancer surgery offers negligible benefits to many men with early-stage disease, a major 20-year study demonstrates. In such men, who account for most cases of newly diagnosed prostate cancer, surgery did not prolong life and often caused serious complications such as infection, urinary incontinence and erectile dysfunction...In men with early prostate cancer, the study compared surgery with observation. With the latter, men only were treated if they developed bothersome symptoms, such as urinary difficulty or bone pain. Such symptoms may indicate progression of the cancer.

Many men in the observation group received no treatment at all because early-stage prostate cancer often grows slowly and rarely causes symptoms. To evaluate any potential benefits of surgery, the researchers randomly assigned 731 men in the U.S. with localized prostate cancer to receive either surgery or observation at one of 44 Department of Veteran Affairs Health Care Centers or eight academic medical centers, including Washington University. The average age of men in the study was 67 at the time of enrollment. Of the men who had prostate cancer surgery, 223 (61 percent) died of other causes after up to 20 years of follow-up, compared with 245 men (66 percent) in the observation group -- a difference that is not statistically different. Further, 27 (7 percent) men in the surgery group died of prostate cancer, compared with 42 men (11 percent) in the observation group, but that difference also is not statistically significant.

However, the data show that surgery may have a mortality benefit in some men, particularly those with a long life expectancy and intermediate-risk prostate cancer. (Such men generally have PSA scores of 10-20 ng/ml and a Gleason score of seven. The latter score signifies tumor aggressiveness.)

One of the major concerns here is that there is a limited amount of data on each patient. Since the progression of PCa can be dramatically different depending upon a plurality of factors at presentation, it is essential that such details be incorporated in such an analysis. Moreover, if such an incorporation were included then the size of the sample is easily an order of magnitude larger than what was done here.

Herein we examine some of the elements of this paper and consider critiques which require some attention. All too often papers like this end up as significant elements of policy and limiting care to men who require it. The definitive conclusions are in my opinion at best speculative.

Let us begin with several definitions used and referred to in the paper. Namely the definitions of risk. The Table below is from Rodrigues et al and presents a list of Low, Intermediate and High risk criteria.

The D'Amico specific criteria are summarized below.

| <i>Institution/ organization</i> | <i>Low risk</i> | <i>Intermediate risk</i> | <i>High risk</i> |
|--------------------------------------|---|--|---|
| D'Amico | T1-T2a, Gleason less than 6, PSA less than 10 | T2b, Gleason equal to 7, PSA between 10 and 20 | Greater than T2c, Gleason between 8 and 10, and PSA greater than 20 |

Note that for the low case we have Gleason score of less than 6 which is quite low and no Mets and a PSA less than 10. Most urologists are aware that even here there may be a small number, say 5%, who despite this favorable set of measurements go on to an aggressive cancer.

Let us also briefly summarize the issue of Staging^{6[2]}. This we do below:
 Primary tumor (T)

- TX: Main tumor cannot be measured.
- T0: Main tumor cannot be found.
- T1, T2, T3, T4: Refers to the size and/or extent of the main tumor. The higher the number after the T, the larger the tumor or the more it has grown into nearby tissues. T's may be further divided to provide more detail, such as T3a and T3b.

Regional lymph nodes (N)

- NX: Cancer in nearby lymph nodes cannot be measured.
- N0: There is no cancer in nearby lymph nodes.
- N1, N2, N3: Refers to the number and location of lymph nodes that contain cancer. The higher the number after the N, the more lymph nodes that contain cancer.

Distant metastasis (M)

- MX: Metastasis cannot be measured.
- M0: Cancer has not spread to other parts of the body.
- M1: Cancer has spread to other parts of the body.

We summarize these in the following Table. Note that for th prostate HG PIN is considered CIS. This is despite the fact that some HG PIN resolve uneventfully to a benign state. This has been noted in other cancers as well such as breast and melanoma.

^{6[2]} <https://www.cancer.gov/about-cancer/diagnosis-staging/staging>

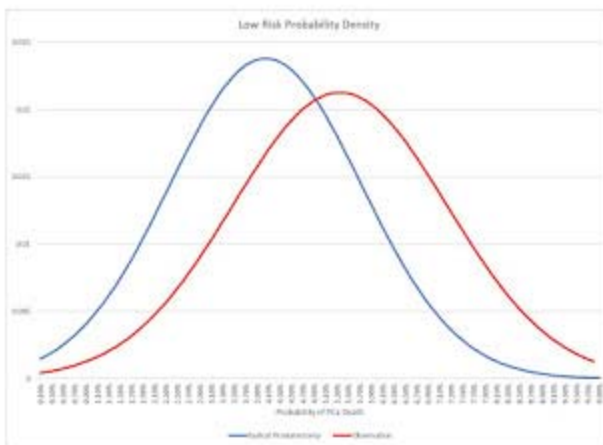
| Stage | What it means |
|----------------------------------|--|
| Stage 0 | Abnormal cells are present but have not spread to nearby tissue. Also called carcinoma in situ, or CIS. CIS is not cancer, but it may become cancer. |
| Stage I, Stage II, and Stage III | Cancer is present. The higher the number, the larger the cancer tumor and the more it has spread into nearby tissues. |
| Stage IV | The cancer has spread to distant parts of the body. |

Let us begin by examining the Wilt et al data. Our focus is on Table 2. Cumulative Incidence of Death from Prostate Cancer through 19.5 Years. The data for that Table can be summarized as below:

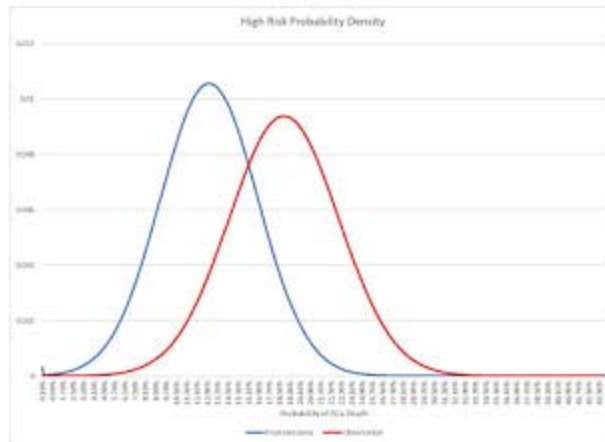
| | Radical Prostatectomy | | | Observation | | |
|--------------|-----------------------|--------|--------|-------------|--------|--------|
| | Low | Medium | High | Low | Medium | High |
| Total | 148 | 129 | 77 | 148 | 120 | 80 |
| Mean | 4.100 | 8.500 | 13.000 | 5.400 | 15.800 | 18.800 |
| Low | 1.900 | 4.800 | 7.200 | 2.800 | 10.400 | 11.700 |
| High | 8.600 | 14.600 | 22.300 | 10.300 | 23.400 | 28.700 |
| Sigma | 1.675 | 2.450 | 3.775 | 1.875 | 3.250 | 4.250 |

We have added percent numbers to the data for clarity. They are percent mortality.

Let us examine a simple case. First for the Low Risk we have a mean death from PCa as 4.1%. In the Observation class the death was 5.4% The probability density for these are shown below:



There clearly is a greater risk in just Observation. Now consider the High risk case. This we show below:



Again there is a substantially high rate of death.

Assume there are two distinct types of PCa. In each generic class there are these two genetic classes. We first limit to one class of patients, say the Low Risk Class. This can be readily generalized to include all. Our goal is to try to determine how large a sample we need to determine the two means from a sample containing a mix of the two. We further assume we do not know the genetic difference that makes one in a class.

A Simple Example

Thus consider the following simple thought experiment. Let us assume we have 100 cases of Low Risk PCa. Let us assume that 5% of these or 5 cases are of the highly aggressive form. Namely no matter what one does they will lead to death. Let us further assume that we can perform a prostatectomy or observe.

Then if after some period, say 20 years, we find the following:

- a. Prostatectomy yields 5 deaths.
- b. Observation yields 8 deaths.

Then we could say that even if we were to remove the tumor, in the 5 cases after prostatectomy the patient would still die of the disease.

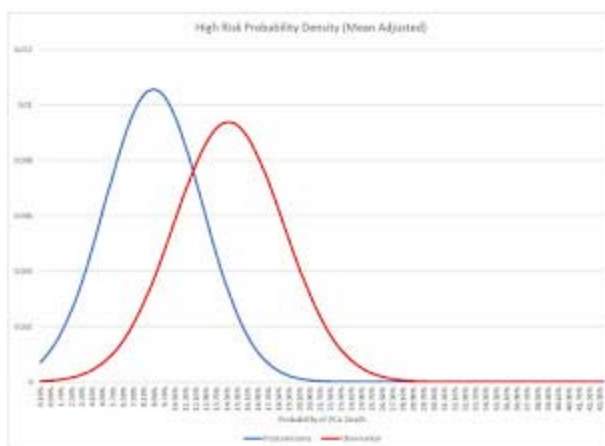
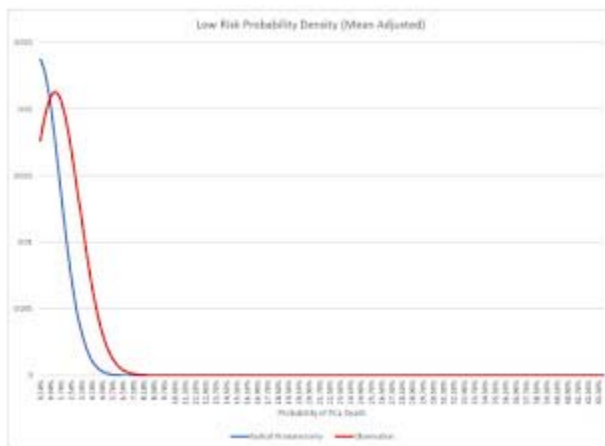
In contrast in observation, in a similar 100 cases, 5 also would die of the disease as well as an additional 3 because of non-treatment.

The question then is; can we use the data to examine such a hypothesis? Secondly; how does the inclusion of such a hypothesis change the results from the NEJM paper?

Thus let us consider the data as follows. Assume that in the Low Risk Prostatectomy case we have a percent death caused by PCa as given but assume that is due to a genetic only risk of

highly aggressive tumors. Then remove that from the samples and consider what remains. The data we show below.

| | Radical Prostatectomy | | | Observation | | |
|---------------------|-----------------------|--------|--------|-------------|--------|--------|
| | Low | Medium | High | Low | Medium | High |
| <i>Total</i> | 148 | 129 | 77 | 148 | 120 | 80 |
| <i>Initial Data</i> | 4.100 | 8.500 | 13.000 | 5.400 | 15.800 | 18.800 |
| <i>Mean</i> | 0.000 | 4.400 | 8.900 | 1.300 | 11.700 | 14.700 |
| <i>Low</i> | 1.900 | 4.800 | 7.200 | 2.800 | 10.400 | 11.700 |
| <i>High</i> | 8.600 | 14.600 | 22.300 | 10.300 | 23.400 | 28.700 |
| <i>Sigma</i> | 1.675 | 2.450 | 3.775 | 1.875 | 3.250 | 4.250 |



The conclusions from the above seem to be:

1. If you do not have a genetically aggressive form, then the risk of dying from a Low Grade PCa is about 2.5%
2. If, however, you have a High Grade form at presentation, and not an aggressive form, then you have a 7% chance of dying from PCa versus an 18% chance with Observation alone.
3. The question is; are you willing to forego a 2.5:1 risk while avoiding surgical issues?

Observations

The data presented in the paper raises more questions than can be answered. For example:

Mortality is Lower

If we examine the data as presented and look at Prostatectomy vs Observation, for each of the three risk categories there is a clear advantage in lowered mortality in a prostatectomy. The authors further state:

Reducing overtreatment is needed. Men with low-risk and PSA based screening–detected disease can safely avoid harms and costs of early radical intervention or of biopsy-guided active surveillance with delayed radical treatment. Observation, PSA-based monitoring, and active surveillance with delayed radical intervention remain infrequently used, even among older men, despite a frequency of metastatic progression of less than 3%, prostate cancer mortality of 1% or less, and cost-effectiveness that is superior to that with early radical intervention. PSA-based monitoring and biopsy based active-surveillance programs should reduce the frequency of surveillance biopsies and increase biopsies and PSA thresholds that trigger radical interventions.

We now comment on this conclusion.

It is not at all clear that the data makes any sense.

Let us examine total mortality, namely from any cause, over the 20 year period. This is summarized below:

| | Prostatectomy | | Observation | |
|---------------|---------------|------------------------|-------------|------------------------|
| | Events | Percent | Events | Percent |
| Low (Local) | 82/148 | 55.4 (47.4 to 63.2) | 83/148 | 56.1 (48.0 to 63.8) |
| Intermediate | 77/129 | 59.7 (51.1 to 67.8) | 89/120 | 74.2 (65.7 to 81.2) |
| High | 55/77 | 71.4 (60.5 to 80.3) | 59/80 | 73.8 (63.2 to 82.1) |
| Low (Central) | 58/111 | 52.3 (43.0 to 61.3) | 67/122 | 54.9 (46.1 to 63.5) |
| Intermediate | 97/155 | 62.6 (54.7 to 69.8) | 99/139 | 71.2 (63.2 to 78.1) |
| High | 55/78 | 70.5 (59.6 to 79.5) | 63/85 | 74.1 (63.9 to 82.2) |

Note that almost 75% of the High Risk patients died of something in the 20 year period. Not knowing the age data and normal mortality data this is relatively meaningless. In contrast these

deaths in the High Risk cohort due solely to PCa are between 19% and 26%. Thus the other causes of death are 3 to 4 times greater. One wonders what that means. The Table below is the PCa death only data.

| | Prostatectomy | | Observation | |
|----------------------|---------------|-----------------------|-------------|------------------------|
| | Events | Percent | Events | Percent |
| <i>Low (Local)</i> | 6/148 | 4.1 (1.9 to 8.6) | 8/148 | 5.4 (2.8 to 10.3) |
| <i>Intermediate</i> | 11/129 | 8.5 (4.8 to 14.6) | 19/120 | 15.8 (10.4 to 23.4) |
| <i>High</i> | 10/77 | 13.0 (7.2 to 22.3) | 15/80 | 18.8 (11.7 to 28.7) |
| <i>Low (Central)</i> | 1/111 | 0.9 (0.2 to 4.9) | 8/122 | 6.6 (3.4 to 12.4) |
| <i>Intermediate</i> | 14/155 | 9.0 (5.5 to 14.6) | 12/139 | 8.6 (5.0 to 14.5) |
| <i>High</i> | 10/78 | 12.8 (7.1 to 22.0) | 20/85 | 23.5 (15.8 to 33.6) |

Here one wonders that those with High Grade at presentation have a disease cause mortality of such a small rate over this period. It is a large Gleason grade plus Mets! One knows that PCa Mets rapidly to the bone and from there one all too often sees IDC occurring which is fatal.

Moreover, if a patient presents with >T2c, or PSA >20, or GS 8-10, then one would expect a rather dire result from the PCa. Instead we see after 20 years a modest death rate. This data does not conform to certain realities.

There is clearly a complex underlying dynamic at play here and it clearly demands a deeper analysis.

How Big is Big

The size of the samples is small, just over 100 patients. In view of the potential for an even smaller size of the subset of aggressive types which would be as small as 5%, then frankly a much larger sample is demanded.

What is the Genetic Makeup?

The results are totally devoid of any genetic makeup of the cancers. Not only is the nature of the spread missing but the genetic makeup is now considered as an essential element of any analysis. What genetic flaws were in the cells of the patients who died of PCa and what in those who survived.

Dynamics of Survival

There is a somewhat complicated analysis on survival or mortality. If as this study states, for example, only 20% of the patients died of PCa but 80% died of any cause, then depending when this occurred, the percent of PCa deaths could be misrepresented. Namely if the 80% occurred short term, then the size of the sample is reduced by that number and if the 20% died when the 80% were dead then the death rate would be much higher. The denominator would be lower. Without such dynamic data one is hard put to understand the results.

A Bayesian Analysis

Any analysis of PCa must include a Bayesian analysis. Namely one must consider disease caused death subject to underlying facts. First important fact is that not all PCa is identical. There are genetically different classes and any analysis that disregards this fact is fundamentally flawed. Namely if we have several classes then we need to have mortality by class. This has been grossly neglected in this analysis and it thus provides results which are fatally flawed.

For example. If for each patient one had; family history, PSA velocity, previous biopsy history, and the like, then one could segment the results to ascertain some reasonable a priori risk factors. Secondly the same would be the case if the tumors were sequenced for a set of reasonably well know genetic markers. Third, the time to death, that is from diagnosis to death is essential. Fourth, the tumor status of those surviving, over time, is also essential.

Devoid of any of this data the results are in my opinion of questionable use.

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SUNDAY, JULY 16, 2017

MORE ON US HEALTHCARE

[NEJM](#) has an article reporting on the Commonwealth report. As we have noted previously, Commonwealth is both a left wing entity promoting single payer systems like the NHS in the UK and that its head was a major player in the ACA development. This player now seems to be decrying the system he was part of creating. But I leave that till later.

The NEJM article notes:

The first challenge the U.S. health care system must confront is lack of access to health care. The high-income countries that are top-ranked according to the most recent Fund report (the United Kingdom, Australia, and the Netherlands) offer universal insurance coverage with minimal out-of-pocket costs for preventive and primary care. Affordable and comprehensive insurance coverage is fundamental.

As has been noted again and again the socialized NHS has one of the worst records in treating cancers. Why? They delay in seeing a specialist and the delay in obtaining any remedial care. In the US if one wants there is a wealth of immediate care for almost any problem. Take MSKCC in New York. The doors are always open. The problem there however is not access but knowledge of what must be done. We also have a multiplicity of Trials allowing for leading edge access.

The second challenge is the relative underinvestment in primary care in the United States as compared with other countries. Other countries make primary care widely, and more uniformly, available. In contrast to the United States, a higher percentage of these countries' professional workforce is dedicated to primary care than to specialty care, and they enable delivery of a

wider range of services at first contact, even at night and on weekends.

This is one of those; on the one hand and on the other hand, issues. Primary care should be able to deal with the up front issues that lead to specialty care. For example, obesity, Type 2 Diabetes. Primary care physicians are all too uncomfortable confronting an obese person. They would rather hand out medication and wait for the inevitable heart disease or kidney failure and then hand the disaster of a patient to a specialist. Drug abuse is the same. If we allowed and educated primary care physicians to deal bluntly with the up front problems then perhaps we could reduce the need for some specialists.

The third challenge is the administrative inefficiency of the U.S. health care system. Both patients and professionals in the United States are baffled by the complexity of obtaining care and paying for it. Clinicians and their staff spend countless hours completing documentation to prove that insurance coverage is active, that benefits and services are covered, that services were delivered, and that payment or reimbursement occurred. Coping with the byzantine layers of administration results in high levels of burnout for doctors and other professionals, which can reduce the quality of care. The complexity also affects patients, who receive confusing benefit descriptions, limited information about doctors and hospitals, unintelligible and often unexpected (or "surprise") bills for services, and unpredictable copayments at labs and pharmacies.

On this I agree. But the problem here strangely is the making in some small way of the efforts of the CEO of Commonwealth while in the previous Administration as well as decades of Government interference. So the solution is more Government? The logic is not only compelling but reeks of insanity!

The fourth challenge is the pervasiveness in the United States of disparities in the delivery of care. People with low incomes, low educational attainment, and other social and economic challenges face greater health risks and worse health in all countries, but especially in the United States, which has a less robust social safety net than other high-income countries. Other countries achieve better population health by spending relatively more on social services than on medical care.

Again the suggestion is to spend more. Frankly the US safety nets have exploded over the last twenty years. The problem is life style that is supported by those safety nets. Obesity is explosive in this population because the "free lunches" supplied are carbohydrate rich and excessive. BMIs have exploded from 20-22 to 30-42! What safety nets are these folks demanding? Is this something where we are to hold the hand of every person, spoon feed them?

Overall the report has in my opinion severe drawbacks. The very questions seem to pose the answer they present. The structure is highly subjective and lacks any substantial set of measurable metrics of value.

But alas, if the more Government we gave in the last eight years did not work, well just add more of that again, until it works.



Labels: [Health Care](#)

SATURDAY, JULY 15, 2017

[WHY IS AMAZON SO BAD AT DELIVERY?](#)

Amazon used to employ the service of UPS a great delivery service. They switched to the USPS, generally OK. They then switched to AMZL, their own service. The latter is akin to putting a message in a bottle to send to Moscow and throwing it from the Verazzano Bridge hoping it will get there. Namely is just plain out does not work.

Thus for a company which seems to have its act together everywhere else why are the so grossly incompetent in doing their own deliveries? Simple answer; incompetent management. In my experience someone most likely got the job for reasons unconnected with competence. After-all who could not figure out delivery?

Well Amazon could. It is a shame that they are so grossly incompetent. Added to this no one really cares. Cracks in the wall like this often lead to a total collapse. Perhaps someone should notice. Doubt it however, egos always get in the way!



Labels: [Amazon](#)

FRIDAY, JULY 14, 2017

[LATEST HEALTH CARE PROPOSAL](#)

It is worth looking at the "new" [health care bill](#) proposed today. Frankly it is a minor set of amendments to the ACA. It is NOT a repeal, it is at best an editing. One should remember that the core of the ACA remains.

This Bill:

1. Keeps the near confiscatory Medicare Tax on everything an over-65 person has. Sell a house, sell some stocks, sell a car, get taxed 3.75% on the gross. Where does it go? To support some Millennial who wants to follow their dream!
2. It continues to squander money on entities such as PCORI
3. It continues to allow the USPSTF to dictate what is allowable medical care and practice.

The list goes on!

The Senate and the House have accomplished nothing! Wait till November 2018!



Labels: [Health Care](#)

STRANGE ANALYSIS

In a recent report by one of the left wing [Washington Health Care think tanks](#) they state:

The U.S. ranked last on performance overall, and ranked last or near last on the Access, Administrative Efficiency, Equity, and Health Care Outcomes domains. The top-ranked countries overall were the U.K., Australia, and the Netherlands. Based on a broad range of indicators, the U.S. health system is an outlier, spending far more but falling short of the performance achieved by other high-income countries. The results suggest the U.S. health care system should look at other countries' approaches if it wants to achieve an affordable high-performing health care system that serves all Americans.

The [New Scientist](#) reports on this result:

A comparison of health systems in 11 wealthy nations has found the US falling short by multiple measures, while the UK's National Health Service leads in several categories. "We measured performance quality across five domains, and the USA fell short in all five," The domains were ease of access to healthcare, how equal access is to people of different incomes, administrative efficiency, how well the care process works for people who use it, and how good the health outcomes are.

Now the CEO of this think tank was a prominent figure in the development and deployment of the ACA, Strange that his work has led to this disaster.

However if one looks more objectively we have the NHS in the UK depriving parents of their rights and also having the highest death rate from cancer in the developed world due to the rationing of care. Thus if you chose your criteria to meet your desired conclusion I guess the US can be considered the worst!

Ironically it was, in my opinion, the think tank CEO's role in the EHR space that led to the massive administrative inefficiencies! So who to blame?



Labels: [Health Care](#)

THE VATICAN AND POLITICS

Over the last two thousand years the Vatican, or the Papal forces wherever they may have been located (like Avignon), have ventured into politics. Each time they do so they seem to strike a multiplicity of hornet nests. Add to this mix the Jesuitical philosophy and sophistic speculations on various individuals and you have a rather messy mix. John Paul II was on the verge of banning the Jesuits with their extreme proponents of Liberation Theology (see Gutierrez, A Theology of Liberation, Orbis, 1996).

Now comes the current Bishop of Rome and his minions declaring that major portions of American Religious groups are Manichean. To be a Manichean one must believe in gods of good and gods of evil and they are at war with one another.

Along comes the [Vatican](#) noting as follows:

Religion has had a more incisive role in electoral processes and government decisions over recent decades, especially in some US governments. It offers a moral role for identifying what is good and what is bad. At times this mingling of politics, morals and religion has taken on a Manichaeism language that divides reality between absolute Good and absolute Evil. In fact, after President George W. Bush spoke in his day about challenging the “axis of evil” and stated it was the USA’s duty to “free the world from evil” following the events of September 11, 2001. Today President Trump steers the fight against a wider, generic collective entity of the “bad” or even the “very bad.” Sometimes the tones used by his supporters in some campaigns take on meanings that we could define as “epic.” These stances are based on Christian-Evangelical fundamentalist principles dating from the beginning of the 20th Century that have been gradually radicalized. These have moved on from a rejection of all that is mundane – as politics was considered – to bringing a strong and determined religious-moral influence to bear on democratic processes and their results.

There is no basis for this set of conclusions. Frankly it is sophistic and polemical and lacking of the slightest scholastic insight. Then they state:

A third element, together with Manichaeism and the prosperity gospel, is a particular form of proclamation of the defense of “religious liberty.” The erosion of religious liberty is clearly a grave threat within a spreading secularism. But we must avoid its defense coming in the fundamentalist terms of a “religion in total freedom,” perceived as a direct virtual challenge to the secularity of the state.

The authors grossly misunderstand the concept of religious freedom in the United States. Unlike France, which proclaims itself to be totally secular, ironically a result of the extensive interference of the Jesuits against the Government and even the people of France, in the US we have an express right of religious freedom devoid of any interference of the state.

Then the authors make the following statement:

There is a shocking rhetoric used, for example, by the writers of Church Militant, a successful US-based digital platform that is openly in favor of a political ultraconservatism and uses Christian symbols to impose itself. This abuse is called “authentic Christianity.” And to show its own preferences, it has created a close analogy between Donald Trump and Emperor Constantine, and between Hilary Clinton and Diocletian. The American elections in this perspective were seen as a “spiritual war.”

Humorous, yes, but reflective of all Americans, hardly! Now they also note:

Pastor Rousas John Rushdoony (1916-2001) is the father of so-called “Christian reconstructionism” (or “dominionist theology”) that had a great influence on the theopolitical vision of Christian fundamentalism. This is the doctrine that feeds political organizations and

networks such as the Council for National Policy and the thoughts of their exponents such as Steve Bannon, currently chief strategist at the White House and supporter of an apocalyptic geopolitics.

Guilt by association? Possibly.

One wonders why the Vatican has taken up a battle against the U.S. Not really if one truly understand South American Jesuits!



Labels: [Church](#)

THURSDAY, JULY 13, 2017

[CAR-T CELLS](#)

Last year [we wrote an extensive analysis of CAR-T cells](#). In [Nature](#) this week there is a piece on the FDA progress on approving them. They note:

External advisers to the US Food and Drug Administration (FDA) have thrown their support behind a therapy that genetically engineers a patient's own immune cells to target and destroy cancers. In a unanimous vote on 12 July, the panel determined that the benefits of CAR-T therapy outweigh its risks. The vote comes as the agency considers whether to issue its first approval of a CAR-T therapy, for a drug called tisagenlecleucel, manufactured by Novartis of Basel, Switzerland. The FDA is not obligated to follow the recommendations of its advisers, but it often does...Studies have shown that CAR-T therapies can produce lasting remissions in such cases. In one key trial of tisagenlecleucel, which started in 2015, 52 out of 63 participants — 82.5% — experienced overall remissions. The unpublished trial had no control group, so investigators cannot yet say with certainty how much effect the treatment had. But many participants of such trials have remained cancer-free for months or years.

These are most likely the first of many therapeutics that are customized to attack specific individual cancer cells of an individual patient. Simply stated:

1. Immune System is Used to Attack
2. Targets on the cancer cells are identified
3. Chimeric cells are created to use the patients immune system but modified to attack the specific cancer cell
4. The cells are individually customized and then reinserted into the patient.
5. This is a very powerful approach! It may actually be akin to carpet bombing, turning the immune system against itself. There seems to be no way to turn it off.

However, ALL was a deadly disease. One of the first cases I saw was in 1967 when a classmate

was sent home from Marine Corps training with a high and uncontrolled fever. It was ALL and he was dead in a couple of weeks. If this approach works it may very well stop this disease and more.



Labels: [CAR-T Cells](#)

THURSDAY, JULY 13, 2017

[OBESITY VS SUGAR](#)

There has been an ongoing war, more than just a battle, over what causes obesity and then the issue regarding its sequellae. Namely such things as Type 2 Diabetes, then heart disease, kidney failure, and a significant number of inflammatory disease including cancers. Obesity leads to inflammation and inflammation leads to cancer. That is well established.

But people seem to focus on the wrong things. Some call it a disease, namely obesity. Thus one could call anything a disease, it is a way to hide the fact that it is done by choice. Some seek a single cause, carbohydrates, and even down to sucrose, plain white sugar.

Now white sugar is known to be a major cause of tooth decay. Yes it can add to obesity and is rather dangerous when one has diabetes.

Now there is an article in the [Guardian](#) that states:

I am now a member of the zipper club. I know, I thought it sounded rude too. But apparently it's the club name for those of us who have a scar right down the middle of our chest. I have one down my leg too, from groin to ankle. And as I spend time recovering from a heart bypass operation – mostly doing very little, watching the cricket, reading the paper – I have started to reflect on my condition. How did it come to this? How did the arteries of my heart become so clogged with gunk that I may have been just weeks from meeting my maker? “Diabetic,” they said. “Pah,” I thought. I don't feel any different. I just get up to pee a bit more at night. Some biochemical medical problem just seemed a bit too elusive, abstract, distant. I mean, who really took that seriously? Earlier this year, I was sent on a diabetes awareness day and spent the time looking out of the window, bored. They tried to explain it to me but I wasn't concentrating. Well, now that someone has sliced through my breastbone as they might a Christmas turkey, the whole thing doesn't seem quite so distant. And suddenly – and unsurprisingly – I am concentrating. All ears to, and pretty evangelical about, the evils of sugar.

This person knew or should have known that he was potentially a walking time bomb. The chest crack is perhaps just the beginning. He appears to have been obese for quite a while. How does one stop this? Good question. I have tried to tell folks what the problem is. When a teenager has a BMI in excess of 30 the mother says he is just a bit chubby and will out grow it. Doubtful.

The long term costs are explosive. Any new health care plan must somehow include a set of incentives regarding this issue. Otherwise the ongoing 3.75% Medicare tax on us older folks will go towards these chronic diseases, not to what it is supposed to go towards.



Labels: [Health Care](#)

THURSDAY, JULY 6, 2017

[GOVERNMENT DOES NOT SEEM TO BE ABLE TO DO ANYTHING](#)



The [NJ Transit](#) announced:

Jul 06, 2017 09:48:41 PM Train service is suspended in and out of Penn Station New York due to a minor NJ Transit train derailment. All mid-town direct trains will be diverted To HOB

Yes indeed, another train fell off the track. Our outgoing Gov spends time on closed public beaches, only God knows what the Secretary of Transportation does for a living, and the trains keep falling off the tracks. Metaphor anyone?

Next Monday they close Penn Station. That's 600,000 people per day. Go where? We need a new Dante!

And yes, there is zero chance that the work will be done on time or correctly. It is after all the Government folks are doing it. The only thing it will do is pad Pensions for these folks, Sad!



Labels: [Government](#)

SUNDAY, JULY 2, 2017

[HEALTH CARE STRATEGY](#)

Eight years ago as the former Administration and Congress pushed the existing ACA, the media and the "think tanks" aligned with the Administration extolled the advantages and disadvantages of the collection of plans and how they finally morphed into what became the ACA.

In reality it was a massive Potemkin Village attack. While the focus was on trivial issues, the hidden agenda of control and taxation received no coverage. For example Medicare on all capital gains was never discussed, EHR mandates never discussed, and such flawed entities such as the USPSTF and PCORI were never discussed.

Bottom line, we all focused on the Potemkin Village while not seeing the armed vehicles come down the back road and add \$400 billion to our annual deficit! Only half of that is excess

Medicaid.

Now what have the Republicans done. Nothing. They have no voices out there with tables and charts, not specifics on anything, and they never even built a Potemkin Village! In fact they do not even have fuel for their tanks! The Senate head seems as lost as his spouse who seems to be fiddling while Penn Station, well euphemistically at least, "Burns".

Eight years ago I could read the Bill, make my nasty comments and bemoan our fate. Now we can read nothing and in fact our fate is now being cast in concrete.

It is a shame that we cannot reach some agreement. But alas, it is Washington!



Labels: [Health Care](#)

WEDNESDAY, JUNE 28, 2017

[WHAT IF AMAZON RAN HEALTHCARE?](#)

Amazon is a great company. Really. I now get almost all personal and business purchases from them.

Now compare them to almost any health care entity, insurer to nurse. Amazon sees me as a customer. The current health care folks see me as an interruption to their personal world. I pay Amazon for service, in health care that nexus is gone.

If I have a problem with an Amazon transaction, I even get a call within a hour to remedy it! Try that with any healthcare provider.

For example I have a health care intermediary selected by a company bought by that man in Omaha who thinks he knows everything. This intermediary has a Better Business Profile that is just a step above Satan! One reads tales of poor old lady retiree taking forever to even get the phone answered and their claims denied for no reason.

Amazon and of course Bezos likes its customers and treats them with dignity. So why not get into healthcare. Get your medical care insurance from Amazon, choose your urologist from Amazon, look at the number of stars for your choice, compare prices.

This could be a great improvement! OK so Bezos and the WaPo are a bit wacky, the rest of what he does is fantastic. There is 18% of the economy just sitting there. Whole Foods is a millennial hangout, but everyone needs health care sometime.

So Mr. Bezos, I could set this up in a heart beat for you. Just give me a call!



Labels: [Health Care](#)

[CODING:PROGRAMMER AS TYPING:SECRETARY](#)

Back in the 1970 the old Bell Telephone Companies were under pressure to have more women in management. The solution was simple. Make them programmers. Take them out of the typing pool and make them Cobol programmers.

Silicon Valley types are too young to remember Cobol but it was the business language of the 60s. Fortran was scientific. C was just starting to be thought of. I first learned FAP, Fortran Assembly Programming where we loaded registers with bits.

Now the wizards of Silicon Valley have a new Trojan Horse. Instead of training young folks in typing and shorthand, we will train them in coding. See the trend? Katherine Gibbs graduates of the new millennium.

Thus the [NY Times](#) notes:

Computer science is also essential to American tech companies, which have become heavily reliant on foreign engineers. Mr. Trump's efforts to limit immigration make Code.org's teach-Americans-to-code agenda even more attractive to the industry. In a few short years, Code.org has raised more than \$60 million ..., along with individual tech executives and foundations. It has helped to persuade two dozen states to change their education policies and laws... while creating free introductory coding lessons, called Hour of Code, which more than 100 million students worldwide have tried. Along the way, Code.org has emerged as a new prototype for Silicon Valley education reform: a social-media-savvy entity that pushes for education policy changes, develops curriculums, offers online coding lessons and trains teachers — touching nearly every facet of the education supply chain.

Is this just a Trojan Horse for the "training" of cheap labor. Or is it just another way for the NY Times to insert Trump in every paragraph?

But really, the algorithm to optimize train flow into and out of Penn Station is NOT programming and those being trained to "code" will not have the skills to develop such optimization. They will become the typists of the 21st century. The more we have the cheaper they become.

I always remember the NYNEX VP of MIS, a tough Irish woman, who when hearing Bob Kahn speak of the Internet and its potential in 1990 told me that I and Bob were fools, and why did we waste her time! That was an example of "training".



Labels: [Commentary](#)

TUESDAY, JUNE 27, 2017

[PLANTS AND CRISPR](#)

So much of the CRISPR wars have focused on human intervention. However the impact in the plant world is extraordinary. After all we have to eat.

[Dupont Pioneer](#) had announced a major effort worth the look.

DuPont Pioneer today announced waxy corn hybrids as its first commercial agricultural product developed through the application of CRISPR-Cas enabled advanced breeding technology. This next generation of elite waxy corn hybrids is expected to be available to U.S. growers within five years, pending field trials and regulatory reviews. "We're applying our 90 years of knowledge of corn biology to develop the next generation of high-quality waxy corn hybrids for the benefit of the entire value chain from growers to processors and end users," said Neal Gutterson, vice president, research and development for DuPont Pioneer. "Starting with an identity-preserved product as our initial CRISPR-Cas offering allows us to lay a solid foundation for success of future larger volume products from this plant breeding innovation." Pioneer is the leading supplier of waxy corn hybrids globally. In the United States, about a half-million acres of waxy corn are grown each year; however, they traditionally yield less than non-waxy corn hybrids. Waxy corn produces a high amylopectin starch content, which is milled for a number of everyday consumer food and non-food uses including processed foods, adhesives and high-gloss paper. Waxy corn is typically grown on contract through a closed-loop production system commonly referred to as "identity-preserved." "The next generation of waxy hybrids developed with CRISPR-Cas will represent a step-change in how efficiently we bring elite genetic platforms of high-yielding waxy corn to our customers," Gutterson said. The United States Department of Agriculture (USDA) recently ([USDA](#)) recently published its response to Pioneer's "[Regulated Article Letter of Inquiry](#)" stating that it does not consider next-generation waxy corn developed with CRISPR-Cas enabled advanced breeding technology as regulated by USDA Biotechnology Regulatory Services.

This is worth following.



Labels: [CRISPR](#)

TUESDAY, JUNE 27, 2017

[HAPPY ASTEROID DAY!](#)



Yes, today is Asteroid Day. [NASA](#) has announced this event. Look up....it will distract you from Washington!



Labels: [NASA](#)

MONDAY, JUNE 26, 2017

[CBO HEALTHCARE AND FACTS](#)

The current debate in Healthcare is again filled with junk "facts". The [CBO](#) claims:

The Senate bill would increase the number of people who are uninsured by 22 million in 2026 relative to the number under current law, slightly fewer than the increase in the number of uninsured estimated for the House-passed legislation. By 2026, an estimated 49 million people would be uninsured, compared with 28 million who would lack insurance that year under current law.

Now the [Census Bureau](#) notes:

The total U.S. population is projected to increase by 98.1 million between 2014 and 2060. As shown in Figure 1, the population is expected to increase from just under 319 million in 2014 to just under 417 million in 2060. This corresponds to an average increase of 2.1 million people per year.

This means that we will be well over 350 million by 2026. We just reached 325 million as of this week! Thus 22 million of 350 million is 6% of the population who will be off Medicaid! This is less than what the ACA put on Medicaid.

These numbers are utter nonsense. I expect the Press in all its ignorant glory will spin this nonsense with no reference to the facts!



Labels: [Health Care](#)

SATURDAY, JUNE 24, 2017

[SCIENCE AND POLITICS?](#)

There seems to be an almost explosive growth of using "science" as a tool for politics. The [NEJM](#) has an article by a member of the former Presidents Transition Team berating alleged new participants in the current Administration.

NEJM facilitated the following rant:

Reasonable people may disagree about how to interpret data, but they do not ignore scientific method by giving credence to flawed, fraudulent, or misrepresented studies. They may disagree about the moral significance of fertilization, but they do not delete implantation from the stages of pregnancy and do not confuse the public debate by conflating opposition to abortion with opposition to contraception. They may disagree about the morality of using cadaveric fetal tissue for research, but they do not claim that it is useless. Ignoring, denying, or reimagining reality

has real consequences for public policy and human health. Whether in the debates regarding climate change, evolutionary theory, or human reproduction, alternative facts are just fiction, and alternative science is just bad policy.

Now this person, the writer, a Law Professor somewhere out West, argues against some current appointees regarding birth control. I do not know any of the parties but I do claim a bit of logic. All of the references she uses are from the left wing press, not a single one from one of her alleged offenders. Frankly any attorney knows that you use the words of the alleged offending party, at least somewhere!

All her claims are without merit unless she can spell out in the words of the alleged offenders. Lawyers do not make scientists but at least lawyers use facts. This article seems to me to be totally devoid of any facts substantiating directly her claims.

The other dimensions are also the presence of and domination by former elected politicians now holding the mantle of scientific hierarchy, like that of the AAAS, and using that position in my opinion as a means to position their political views.

Eight years ago the battle was over poor economics and shaky healthcare, now we seem to be battling over made up religions, holding the other party out to be Satan! Grow up folks.



Labels: [Health Care](#)

[PROPAGANDA](#)

It is worth re-reading [Bernays on Propaganda](#), one of the many Wilson employed as Government workers to press his cause for War. As Bernays starts:

The conscious and intelligent manipulation of the organized habits and opinions of the masses is an important element in democratic society. Those who manipulate this unseen mechanism of society constitute an invisible government which is the true ruling power of our country. We are governed, our minds molded, our tastes formed, our ideas suggested, largely by men we have never heard of. This is a logical result of the way in which our democratic society is organized. Vast numbers of human beings must cooperate in this manner if they are to live together as a smoothly functioning society. Our invisible governors are, in many cases, unaware of the identity of their fellow members in the inner cabinet. They govern us by their qualities of natural leadership, their ability to supply needed ideas and by their key position in the social structure. Whatever attitude one chooses toward this condition, it remains a fact that in almost every act of our daily lives, whether in the sphere of politics or business, in our social conduct or our ethical thinking, we are dominated by the relatively small number...

The Government, either the elected or the "Deep State" has mastered the means to control, not just influence, the opinions of the masses. What is especially interesting is that scientists, whose life is supposedly dedicated to questioning, all too often fall into the line of the echo chamber, the desired propagandist focus. Kuhn in his work on Scientific Revolutions looked at this as the paradigm trap.

One should spend more time reading Alice in Wonderland and question the Rabbit Holes, and that nothing is necessarily what it appears to be.

Propaganda is a trade craft practiced by nations, the US as well as Russia, China, and even ISIS. One should always question, especially scientists. Yet there seems to be a lemming effect at play.

Suggestion: step back and examine the "facts", and ask if they are even the true "facts".



Labels: [Commentary](#)

SATURDAY, JUNE 17, 2017

[PSA TESTING](#)

I bought my first copy of Scientific American in early May of 1960 on a news stand on Lexington and 52nd Street. I had just returned from my NYC Lifeguard course, and also awaited my being sent to Coney Island. But now I had this window to science. Each article was an opening to some new state of the art discussion. Written by the best of the best and in a manner which assumed you had some reasonable basis to understand. I worked really hard to meet the demands of the authors. I read and reread each article to understand it. I took what little money I had from being a Lifeguard and bought a subscription. I kept it until the magazine turned into something just worse than Time. It became, about in the year 2000, a rag, at least in my opinion. Too bad, it was a window to science, but along came the Internet so who really needed it anyhow.

So I ran across a rant by some person in [Scientific American](#) bemoaning the PSA test. He states:

I recently had an awkward conversation with my doctor. I was getting a routine physical, and he recommended that I get a PSA test for prostate cancer. I'm 63. I told him the PSA test harms more men than it helps. He acknowledged that PSA tests produce false positives, but he insisted that follow-up tests and biopsies will determine whether you really have a life-threatening cancer. He knew someone whose life had just been saved by the test. When I still declined to get tested, he looked as though he felt sorry for me. He should feel sorry for the millions of men who have gotten unnecessary biopsies, surgery and radiation as a result of taking the PSA test.

Having written and done work in this area, yes go check me out if you don't believe me, I see that the PSA has substantial merit. The harms are all too often in ones head. A bit of hematuria, some slight discomfort, but overall not that bad. My dentist is worse! Really worse.

He continues:

Just to be clear: you are 240-120 times more likely to misdiagnosed as a result of a positive PSA test and 80-40 times more likely to get unnecessary surgery or radiation than you are to have your life saved.

I do not know where this came from. It seems to imply that of the 240 high PSA tests and PSA

velocities done only one in 240 yields a positive PCa. Not in any tests I have seen, and no basis for the claim.

He also states:

In 2012, the U.S. Preventive Services Task Force, a federally funded panel of experts, recommended against the PSA test, saying the cons outweighed the pros. The decision was based primarily on data from two large studies, one done in the U.S., which found that screening did not reduce mortality, and the other in Europe, which showed a modest reduction.

Well first, the two trials had fatal flaws which we and others have discussed at length. Second, the USPSTF is NOT a panel of experts on PCa. They are what I would call a "fishing, drinking and smoking" club of some physicians and others politically connected who have been allowed to opine and now control our health care! There was not a single urologist on the panel.

I would suspect that some sixty years ago Scientific American would have had some set of experts opine. Now they have some fellow with an attitude. Good luck young man!



Labels: [Cancer](#)

[SUR LE PONT D'AVIGNON, TOUT LE MONDE Y DANSE, DANSE!](#)

It is most likely the case that any child who learned French also learned this little ditty. All the world danced across the bridge in Avignon. And at the heart of the dance was John XXII, the Bishop of Rome, And at the heart of the juristic proceedings coming from Avignon, the New Babylon, were those that inspired William of Ockham and Marsilius of Padua. It was the arrogance of the then Bishop of Rome which led to the development of Individualism and the ideas that lent substance to Montesquieu.

For some reason the current Bishop of Rome is celebrating the 700th anniversary of this event. As the [Vatican](#) notes:

Pope Francis has appointed Cardinal Paul Poupard as his special envoy to the celebrations of the 700th anniversary of the enclave of the Popes in Avignon, France. Cardinal Poupard is the president-emeritus of the Pontifical Council for Culture. He will be accompanied at the 23-25 June event by Msgr. Jean-Marie Gérard, vicar general of Avignon, and Rev. Canon Daniel Bréhier, rector of the Cathedral of Avignon.

Celebrating this event is rather strange since it precipitated the revolt of Luther and all that followed.

What is even more ironic is that it was John XXII who attacked the Franciscans and the Spirituals who felt a need for poverty. After all how could John live in such a lavish castle while the Franciscans alleged the Apostles owned nothing.

This is a celebration of the Papacy leaving Rome and commencing its accumulation of massive

wealth and its persecution of the Franciscans and other intellectuals. I would have thought that this would be a time for reflection and not one of celebration. Especially for one named Francis.



Labels: [Papacy](#)

TUESDAY, JUNE 13, 2017

[YOU DON'T NEED INSTRUMENTS IN YOUR CAR \(AIRPLANE, WHATEVER\)](#)

I noted a piece today about monitoring blood sugar for people with Type 2 Diabetes. Frankly it can be "cured" in almost 90% of the cases by losing weight and keeping BMI less than 23. But who cares, most physicians send the patient off with meds, and let the patient think that if they take the meds they are fine. High blood glucose causes inflammation and inflammation is a major cause of cancer. Thus pushing down the HgA1B is a bit deceptive. The weight is still there. The fat is the inflammatory cause, and off we go.

In a [WebMD](#) piece the author states:

People with type 2 diabetes who aren't taking insulin don't necessarily need to check their blood sugar levels, a new study contends. Many of these patients use "finger prick" blood sugar monitors, but "testing blood sugar didn't have any impact on their blood sugar," said study author "The best way to control blood sugar is to take your medication the way your doctor asks you to and to take good care of yourself," she said. "The key is really taking your medications." Monitoring might be helpful when starting a new medication or changing doses, Young said.

Monitoring blood sugar should be the best early warning sign. Even before one starts taking meds. Fasting blood sugar is a red light for improper diet. Those late night cookies, ice cream, soda, cake, etc drive up the FBS. So why not start before one needs meds. It tells you if your oil pressure is dropping, if you are running out of gas, or the altitude is too low.

Pilots make mistakes when they do not pay attention to instruments. The instrument is an early warning signal. Meds are just wearing blinders and hoping for the best. It does not happen.



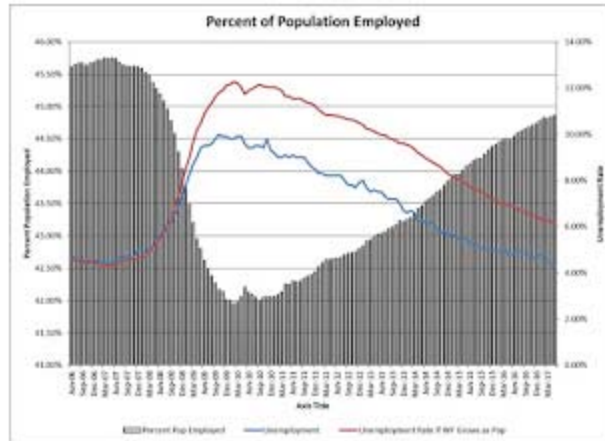
Labels: [Diabetes](#), [Health Care](#)

MONDAY, JUNE 12, 2017

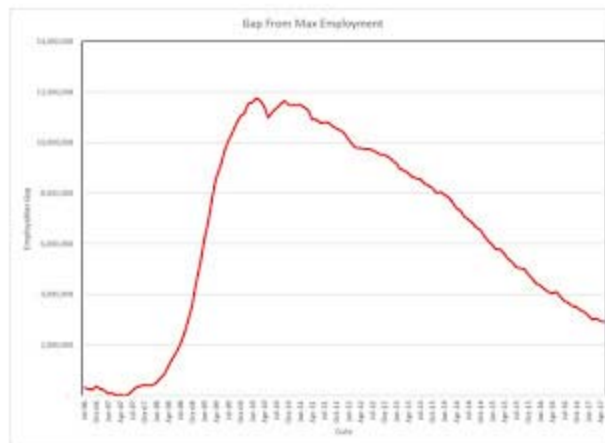
[FED BALANCE SHEET](#)

Every once in a while it is worth looking at the FED Balance Sheet. Here is the core values.

EMPLOYMENT



The above is a summary of the recent employment. The following curve is of interest.



It says that based on 2006 stats we have some 3 million plus still not even counted! The actual unemployment using 2006 base of workers is 6.5%. The decrease is constant but we have a long way to go.

Next we will look at the mix.



Labels: [Economy](#)

SUNDAY, JUNE 11, 2017

SCIENCE AND ENGINEERING VS RELIGION?

Carbon dioxide is emitted by a variety of natural and man made systems. Energy generation as currently deployed uses a great deal of CO₂ producing sources such as coal. In a recent [Science](#) piece there is an alternative proposed to recycle the CO₂ for zero emissions.

They state:

In contrast, NET Power, the startup backing the new plant, says it expects to produce emission-free power at about \$0.06 per kilowatt-hour. That's about the same cost as power from a state-of-the-art natural gas-fired plant—and cheaper than most renewable energy. The key to its efficiency is a new thermodynamic cycle that swaps CO₂ for the steam that drives turbines in conventional plants. Invented by an unlikely trio—a retired British engineer and a pair of technology geeks who had tired of their day jobs—the scheme may soon get a bigger test. If the prototype lives up to hopes, NET Power says, it will forge ahead with a full-scale, 300-megawatt power plant—enough to power more than 200,000 homes—which could open in 2021 at a cost of about \$300 million. Both the company and CCS experts hope that the technology will then proliferate. “This is a game-changer if they achieve 100% of their goals,” says John Thompson, a carbon capture expert at the Clean Air Task Force, an environmental nonprofit with an office in Carbondale, Illinois.

If this works it is a great step forward and involves no Carbon tax or belief in world ending events.

I guess something else will come along. Some people need to have an event to end the world and somehow scientists and engineers always burst their balloon. Who was that guy who said population would end life as we know it?

The only real ender is a bunch of nuclear weapons...remember that!



Labels: [Global Warming](#)

WEDNESDAY, JUNE 7, 2017

[PUBLIC PRIVATE PARTNERSHIPS](#)

I have considered these several time with ultimately no positive results. The mindset of the civil servant is orthogonal to that of the business person, especially an entrepreneur.

An entrepreneur will take risks, their own time and money, and seek a return on that investment if possible. A civil servant is risk averse. They want to get as much as they can for nothing and never want to endanger their pensions. An entrepreneur has no pension and does not get paid.

A decade ago I tried this with a town in New Hampshire and the result was a loss of many dollars and time. The town could never agree to anything. In fact the Board demanded free service for its "poor" residents, and my comment was "show me one and I will pay personally for their service". Needless to say it went no where.

The [NY Times](#) discusses this concept and the article states:

Whether through fees like parking meters and tolls on a road, or through government payments to the contractors, such projects are ultimately supported by taxpayers.

Now read this statement very carefully. Taxpayers support it even if there are tolls or

meters! Now just think, yes think, what the words mean and are saying. If the user is paying, which is what we see in a real economy, then the taxpayer pays only as a user, NOT as a taxpayer. That is basic logic. But somehow the writer states the opposite, namely the statement is at face wrong! The writer in my opinion must be clueless!



Labels: [Government](#)

HUGS?

The [Guardian](#) has an interesting piece in "hugs". They note:

When will Jerry Seinfeld learn about hugging? Given that his celebrated sitcom's unsentimental tone was based on their "no hugging, no learning" writers' room maxim, possibly never. And, clearly, time is running out if a recent encounter with Kesha is anything to go by. Seinfeld was being interviewed by US radio host Tommy McFly at an event in Washington DC on Tuesday, when the pop star interrupted them to announce: "Oh my gosh, I love you so much." "Oh, thanks," said Jerry.

"Can I give you a hug?" asked Kesha. "No, thanks," Seinfeld said.

This is interesting since I spent last weekend at one of my grandson's graduations where the Episcopal, read Church of England, Oxford educated, headmaster hugged each and every graduate! It would have been child abuse a decade ago!

Now I am from the older generation where even "kissing" was frowned upon, germs I was told. Hugs! Why the other fellow could stab you in the back, especially if you were in Washington. Professional full time GS-12 backstabbers all over!

The first time I came to this hugging thing was a friend who lives in San Francisco who came to New York and greeted me with a hug, in the middle of Manhattan. Yes the crowd around look at bit askance, it was an investment bank after all. But in San Francisco one is expected to do the extreme. New York on the other hand is truly a social conservative holdout. We do not even acknowledge others on an elevator!



Labels: [Commentary](#)

WEDNESDAY, JUNE 7, 2017

ASCO AND PCA

In an [ASCO](#) report commenting on the USPSTF D rating for PSA testing the report states:

In 2012, PSA screening for prostate cancer (CaP) detection was given a "Grade D" recommendation for all men by the USPSTF. Recent U.S. studies report declines in PSA screening with concomitant increases in advanced CaP at diagnosis. This study examined the association between PSA screening history and CaP aggressiveness in a racially diverse, military cohort with equal health care access.... In this RP cohort, higher risk stratum, increased

GU, and poorer BCR-free survival were associated with no PSA screening history. BCR-free survival was incrementally worsened by less PSA screening. A complete absence of PSA screening may lead to more aggressive disease at presentation and poorer clinical outcomes.

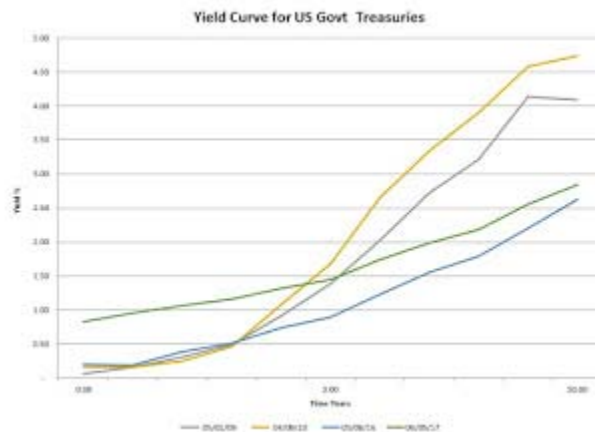
This was a Government conducted study, by people apparently competent in the field. This is just another study confirming the deadly results of following USPSTF.



Labels: [Cancer](#)

TUESDAY, JUNE 6, 2017

TREASURY SPREADS JUNE 2017



Treasury spreads are flattening out again. Look at the one above for yesterday and it seems to be as flat as one can get before the FED increases the short term rate. Note if the FED does increase the short term we may eventually get to an inverted curve again. The concern should be the long term and the fact that the FED is trying to unload the \$4 trillion of junk on its books!



The above provides a good look over the past ten years. Worth thinking about!



Labels: [Economy](#)

MONDAY, JUNE 5, 2017

[IN THE OLD DAYS, OR "WHEN I WAS YOUR AGE"](#)

The [NY Times](#) has posted a piece from a Campus Security Guard in England. Now my first cut at undergraduate school was in New York City, not London and it was decades ago. My two grandsons are off to college, one going as far as the nearest stop light, the other going halfway cross country. It really is different for them than it was for me.

Back in 1960 I had three roommates, O'Malley, Driscoll, and Gallagher, we could have been an Irish Law Firm, but each was different. We rented a two bedroom apartment on Broadway, nice, new, and \$120 per month! That was \$30 each per month. Then food was what you collected, and security? There was none. The closest I got was the fact that my father was in the NYPD as was my grandfather and so I had a "cop network" if necessary.

We walked to class and took the subway at odd hours, the Broadway line. One night I met Malcolm X on the train with his group. Said hello, and he got off at 42nd Street. Sort of a Forest Gump moment.

The Brit notes:

Before I started in the job, I had the same image of the campus guard in my head as you did: a bloke too fat for the cops, or a mixed martial-arts nerd. Guards like that exist, but they don't tend to last. Once they realize you do more talking in this job than throwing punches, and take one look at the salary, they check out. It's true, the money's not fantastic, but I wouldn't want to do anything else. The buzz I get from helping people is up there with scoring a football goal, or perhaps, remembering a password I thought I'd forgotten. Plus, I get to see people shaping their futures every day. Who'd want to swap that for breathing office air?

When I spent a decade or so at MIT, during the Viet Nam war riots, I never saw a Campus Cop, but now they are everywhere. I wonder what has happened. Has crime increased or are we becoming global helicopter parents. Sixty years ago you got a \$20 bill and a cardboard suitcase. You better have a job or find one, the campus did not give you one out the gate. Today? Kindly Campus Cops!



Labels: [Commentary](#)

[MORE ON CAR-T CELLS](#)

[We have been following the progress on CAR-T](#) cells over the past few years. The recent result reported in [Science Daily](#) is of special import. Namely:

In an early clinical trial, 33 out of 35 (94 percent) patients had clinical remission of multiple myeloma upon receiving a new type of immunotherapy -- chimeric antigen receptor (CAR) T cells targeting B-cell maturation protein or BCMA. Most patients had only mild side effects.

Namely, find a target on the desired cell and then create a "smart bomb" the CAR-T cell, and then set it loose. It seems to be working much more effectively now. It still has some "carpet bombing effects" but this may very well change the paradigm for cancer treatment.

Namely, find a surface target, then construct a patient specific attack element, then let the immune system loose. Very worth while to follow!



Labels: [CAR-T Cells](#)

FRIDAY, JUNE 2, 2017

[FAIR USE AND THE EU](#)

The EU/EC seems to be an ever expanding set of rules and regulations that at to control people's lives. Fundamentally it represents an entity which denies fundamental American values. The EUs stance as exemplified all too often by the German state, an entity which believes that its policies are all too often to dominate and control.

The most recent example is the intent to control free speech. We in the US have a mandated right to free speech. In the EU it is severely curtailed and controlled.

The [EFF](#) just recently notes:

This week, EFF joined Creative Commons, Wikimedia, Mozilla, EDRi, Open Rights Group, and sixty other organizations in signing an open letter [PDF] addressed to Members of the European Parliament expressing our concerns about two key proposals for a new European "Digital Single Market" Directive on copyright. These are the "value gap" proposal to require Internet platforms to put in place automatic filters to prevent copyright-infringing content from being uploaded by users (Article 13) and the equally misguided "link tax" proposal that would give news publishers a right to compensation when snippets of the text of news articles are used to link to the original source (Article 11).

Namely if one is analyzing a work which has been posted and one desires to refer to what was said and then in any way comment, that would be a breach of the proposed law. At best one could refer to the source and then let the reader go and try to find it. Frankly that defeats the ability to have free and open discourse and also makes a mockery of the very essence of the Internet.

The filter proposal also makes the Internet facilitators entities who must on their own filter and control. Pravda did that a while back and you know how that worked.

I suspect it is a mind set. We Americans do not understand Europeans and Europeans do not understand Americans. Both all too often look down on the other and I suspect the gap is widening. One could as if the Paris Accord was reflective of that?



Labels: [EU](#)

THURSDAY, JUNE 1, 2017

THE USPSTF

Over the last ten years we have commented upon what we feel is the generally inappropriate direction from the USPSTF. This is the collection of folks who thought that it was fine to do away with PSA testing.

Urotoday has a fantastic video describing the USPSTF and its failings. It is truly worth watching. The first slide shown below is what is truly terrifying.

USPSTF - ISSUES

- *Proceedings are not required to be made public*
- *Exempt from FACA review process*
- *Exempt from the Administrative Procedures Act (APA)*
- *Requires public disclosure and participation in activities*
- *Defines scope of judicial review*
- *Encompasses:*
- *The Freedom of Information Act (FOIA)*
- *The Privacy Act*

- *USPSTF is only Federal Agency which can set payment policy exempt from FAPA/APA*

Note that the ACA, known as Obamacare, allows this group of what in my opinion are less than truly qualified folks, to mandate what is proper care. The second slide shown below:

USPSTF - ISSUES

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shows that they do so without any accountability.

If one were to have followed the PSA debate, in the professional media or in my writings as

noted herein, one would see that the mortality from PCa has exploded since the USPSTF mandated no coverage of PSA testing and its sequellae.

These folks are in my opinion one of the many "Death Panels" established under the ACA. Yes, they denied coverage and people died.

Hopefully Congress will eliminate this, in my opinion, "mad dog" group as well as many others formed under the aegis of the ACA such as PCORI!



Labels: [Cancer](#), [Government](#), [Health Care](#)

WEDNESDAY, MAY 31, 2017

[WHAT IS A SPECIES?](#)

That question has been around for a while. Mayr had proposed a definition that essentially said a species was a collection of animals or plants which had the capacity of breeding among each other. As [Kevin de Queiroz](#) has stated:

Ernst Mayr played a central role in the establishment of the general concept of species as metapopulation lineages, and he is the author of one of the most popular of the numerous alternative definitions of the species category. Reconciliation of incompatible species definitions and the development of a unified species concept require rejecting the interpretation of various contingent properties of metapopulation lineages, including intrinsic reproductive isolation in Mayr's definition, as necessary properties of species. On the other hand, the general concept of species as metapopulation lineages advocated by Mayr forms the foundation of this reconciliation, which follows from a corollary of that concept also advocated by Mayr: the proposition that the species is a fundamental category of biological organization. Although the general metapopulation lineage species concept and Mayr's popular species definition are commonly confused under the name "the biological species concept," they are more or less clearly distinguished in Mayr's early writings on the subject. Virtually all modern concepts and definitions of the species category, not only those that require intrinsic reproductive isolation, are to be considered biological according to the criterion proposed by Mayr.

In the current [Nature](#) there is an ongoing debate as to the many conflicting definitions. The authors state:

The assumption that species are fixed entities underpins every international agreement on biodiversity conservation, all national environmental legislation and the efforts of many individuals and organizations to safeguard plants and animals. Yet for a discipline aiming to impose order on the natural world, taxonomy (the classification of complex organisms) is remarkably anarchic. There is reasonable agreement among taxonomists that a species should represent a distinct evolutionary lineage. But there is none about how a lineage should be defined. 'Species' are often created or dismissed arbitrarily, according to the individual taxonomist's adherence to one of at least 30 definitions. Crucially, there is no global oversight of taxonomic decisions — researchers can 'split or lump' species with no consideration of the

consequences.

The problem is that especially in plants we have a significant amount of inbreeding potential between what we call species. The plants have the same number of chromosomes of the same length with genes in the same positions, almost. Then why call them different species? All too frequently it is in the eye of the beholder.



Labels: [Genetics](#)

TEETH



One of the interesting things about Medical School is that every part of the body is open for examination and treatment, except the teeth. "No teeth!" Teeth are the exclusive purview of that clan of practitioners called Dentists. They have their own "school" and they stick together like taffy on teeth.

Now along come a piece by [Alan Alda](#) and his experience with this clan. I can sympathize with him greatly. Alda states:

I've come to see my exchange with the dentist that day as something that happens frequently in life — a brief encounter that threatens a relationship's delicate tissue; the tender frenum of friendship. I wasn't looking for friendship that day, but at least I wanted the feeling that I was actually being seen by him. Even though his gaze was intense, I realized that as far as he was concerned I wasn't really there — not as a person. If I was there at all, I was something on his checklist. He was speaking into the vague mist of interpersonal nothingness. That few minutes in his chair has become a symbol for me of really, really poor communication and of what causes it: not really seeing the other person. Since that day, I've spent a lot of time on two socially useful pursuits: figuring out how to be a little more engaged — and uncrooking my smile.

In my experience, one which has occupied the last year or so, began on a much more friendly manner. A nice dentist suddenly sends a letter telling us he is no longer practicing. OK, so find another dentist. Then get told you need 14 crowns, 4 of which are implants!. For those counting that amounts to three semesters at Harvard, room, board and tuition. Fortunately grandson number one is off to WVU to study Civil Engineering so that was not as expensive. But upon

asking the dentist, now one of several, I have a dental "team", what happened, I was told that it was the way they did dentistry 30-40 years ago. I then asked what if the same is true with what he does today? The answer was; "You won't live that long." So Alan had a smile problem, mine was, as I suspect would be his at this time, that any mistakes would go with me to the everlasting!

So what of dentists. We only spend a few tens of billion each year. Why s low you may ask for a total health care bill of \$3 trillion! Insurance. Most people have none and those that do can only get reimbursed for a tiny amount each year.

Teeth are important. A bad abscess can kill a person, a poorly inserted implant can lead to osteonecrosis and off goes the immune system. But dentists occupy a special place in our society. They treat us with at best lidocaine/procaine and in turn we sit there for hours with our mouth ajar while they are conversing as to what happened over the weekend and we can feel the drill, the extraction, or whatever, and I suspect the psychic damage can be significant.

Perhaps it is a result of my first dental visit. I believe it was 1949, a former Navy dentists who my father swore by, after all he was Navy all the way, and I sat there looking out his office onto Forest Avenue. Then he started the drill. I think a foot driven thing from some German camp. I instinctively let out a cry, then he slapped me across my cheek, and told me to sit still while he performed his torture. Somewhere there is an embedded limbic valence to this event! I think it is one of those things that get handed down genetically, some epigenetic modification, some methylation of a promoter somewhere in our DNA.

Thus if Alan has a smile problem, I have methylated DNA that turns on some abject terror reflex. I would rather have a 40 core prostate biopsy than a visit to the dentist. Yet as the good nuns told us, this is just another offering to make up for our sins. I wonder what dentists do to perform their penance? I dread to think! Thanks for the warning Alan, hope the smile thing works out!



Labels: [Dentists](#)

SUNDAY, MAY 28, 2017

[YA THINK?](#)

After a week of meeting with many world "leaders" the [Telegraph](#) reports:

Europe "must take its fate into its own hands" faced with a western alliance divided by Brexit and Donald Trump's presidency, German Chancellor Angela Merkel said on Sunday. "The times in which we could completely depend on others are on the way out. I've experienced that in the last few days," Merkel told a crowd at an election rally in Munich, southern Germany. "We Europeans truly have to take our fate into our own hands," she added. While Germany and Europe would strive to remain on good terms with America and Britain, "we have to fight for our own destiny", Merkel went on.

Frankly after seventy two years is it not time to grow up. Poland learned and look where it is going, well past Germany if all keeps on pace. Yes indeed Germany should finally take full

responsibility for itself. Relying on the US is not only morally wrong it is just plain dumb. If someone is paying for your defense and then you complain because you are now being asked to ante up what you said you would do is wrong, what logic is that based upon.

Germany and to some degree France have managed to build their economies. They did so with no burden of defense. But the question is; is the threat Russia or what we see as an entity already destroying its peoples.

As for the "destiny" of Germany, we have seen that several times, just ask the French.



Labels: [Political Analysis](#), [Politics](#)

FRIDAY, MAY 26, 2017

GLOBAL WARMING?



Over the past 25 years we have been monitoring the bloom dates of four Hemerocallis species. Namely *H. flava*, *minor*, *dumortieri*, *middendorffii*. We measure the date of bloom from the start date of the year. Thus a data of bloom of 125 is 125 days from January 1 of the year. Now the smaller the bloom date the earlier the bloom.

So what does it have to do with Global Warming. Well over a 25 year period the blooming data is a function of the integral of total input heat. Daylight hours, location, soil conditions etc have all been held constant. The more heat the earlier the bloom.

Now here are the four flowers:





We see in the data a minimal if any trend downwards, namely more heating. In fact if the CO2 lever were greater we would expect even faster blooming.

Thus this set of canaries in the mine have not been tweeting too much if at all. Just some facts from the front.



Labels: [Global Warming](#)

THURSDAY, MAY 25, 2017

[ANOTHER DAY ON PUBLIC TRANSPORTATION!](#)

I try, I really do! Take the train, don't use gas, keep the old CO2 down and all that stuff. Well today was another experience. Train to Hoboken, train to WTC. Now try and get home!

The run trains every three hours. This train made an old Aeroflot Tupolev look like a Rolls Royce!. Roof leaks, really water spraying into the car, windows sealed with duct tape, seats unstable etc. And here is the tale for those of you so anxious to get to New York!

1. From Hoboken to the towns on Mid Town Direct stations, the largest and most wealthiest in NJ, they run once ever 3 hours and are 6 cars long.
2. From Penn Station the same trains run once ever hour and are 12 cars long.
3. Amtrak, that grossly incompetent Government agency, remember the ACA and the VA folks, is closing Penn Station to the MD trains from July to September!
4. That means that somehow these 3 trains totaling 36 cars must get stuffed into one train of 6 cars! That means a 6:1 increase! What will this be, Bombay at holiday season? People grappling to the roof of decrepit cars!

5. Govs Cuomo and Chubby are clueless, really. It is one month away and there is NO Plan! Yep, not a single idea as to what to do! There should be some extensive communications to the citizens as to what will happen. Instead Amtrak and its morons are just closing Penn Station! Yep, just closing it. And frankly who says it will ever reopen! These are Government types, we should know them by now!

6. And where is the Fed Govt, the Senate's head's wife who allegedly is in charge of Transportation is probably off about God knows what, it is not anything about the millions trying to create an economy to pay this exclusive couples salaries and keep them in the style for which they have become accustomed!

Summary. We have an incompetent Government run railroad, with local Governors who appear to be clueless and a Federal agency who is out to lunch. Can the people take over and sub-contract to the Chinese. They seem to have no problems. Please, please China, we can pay you to fix this mess! We can even give you California as a bonus.



Labels: [Government](#)

WEDNESDAY, MAY 24, 2017

[REALITY IN HEALTHCARE](#)

Over the past ten years I have examined in some detail the various healthcare proposals and laws. The [CBO](#) announces a putative loss of coverage for some 20 million plus people. Why? Simple. The ACA covered people making up to 4 times the minimum wage and if perhaps you were a banjo player of "professional" graffiti artist making nothing at all, you were covered and paid a pittance.

See the following:

*Artists: **From the Wayback Machine only, scrubbed from HHS site!** Music is my life. I'm a lead guitarist and a singer with my sister Kim in the Breeders and other bands. But, in order to pursue my passion, I had to make sacrifices, and health insurance was one of them. Prior to the Affordable Care Act, as many artists know, health insurance on the individual market was hard to come by at an affordable price. For me, having a pre-existing thyroid condition, coupled with an uncertain paycheck from touring, recording and song writing meant I couldn't afford health insurance. And that was probably true for other artists as well. Thanks to the Affordable Care Act, I've been able to afford health insurance as a single, self-employed female for the first time in my life – and it feels really good. It's something that I can budget for. I feel empowered to be a participant in my health care. But this security is now in jeopardy for millions of Americans, like myself, and especially musicians, artists and others who rely on the Affordable Care Act. So as part of the #CoverageMatters campaign, we are designating today, January 12, as Artists Day of Action. So if you are a musician, writer, actor, painter, poet, sculptor, or artist of any stripe, share your story about why you support the law, what it's done for you and any personal Affordable Care Act story you or your families and friends may have on social media using #CoverageMatters.*

SideGig: I'm a creativepreneur. My goal is to encourage people to add creativity in their lives to reduce stress, express themselves and spend quality time with their family and friends. I call it spreading the gospel of glitter. And I've done it by sharing tutorials, business tips, videos and classes, as well as writing books and speaking across the country. My husband is an artist and musician, and together, we have crafted a life following our passion of making, selling and teaching art. But we couldn't run our business full time without the security of health insurance for our family. Before the Affordable Care Act, I had researched health insurance plans on the private market and could not find one we could afford. Thanks to the ACA and the Health Insurance Marketplace, I was able to leave my full-time job with health benefits in 2015 to start my own business. My side gig became my main gig, and my business has thrived. The Marketplace plan was perfect for our budget and lifestyle. The first year, I was even able to cover my then 23-year-old daughter because of the law's provision allowing adult children up to the age of 26 to stay on their parents' plan. My children are now employed at full-time jobs that offer coverage.

Farmer: I'm a fourth generation farmer, and farming is all I want to do. I raise corn, soybeans and Angus beef. It's been rough economic times for many farmers, and I'm no exception. I had health insurance when I was younger, but the premium kept going up 10 percent each year. It seemed like a waste of money, so I dropped it. It was also pretty difficult to get coverage at all because I had diabetes. Before the Affordable Care Act, insurers could refuse coverage to people like me with pre-existing conditions. I was pretty much on my own before the Affordable Care Act. Most people don't see what's going on out here. As farmers, we're all individuals. We don't have group insurance. I was hit with Hepatitis C in 2006 and had to get colon surgery in 2007. My medical costs for the two years amounted to about \$100,000. I had to refinance my 760-acre farm (I rent and farm another 440 acres as well) to pay my medical bills because I didn't have health insurance. There was no question about what I would do when the Health Insurance Marketplace opened in 2013. No one asked me about my pre-existing conditions, and I found an affordable plan for 2014 that would fit my needs for about \$400 a month after tax credits. My premium for 2015 was about \$364 a month and about \$390 a month for 2016.

So all of these folks are riding on the rest of us who work for a living. Musicians, SideGigs, Farmers, are having the rest of us carry them so they can follow their dreams! Yet the CBO says if we do not continue to pay for their healthcare as well as ours then we will not have music, gig stuff, or whatever this farmers is making. So what! Let them get a job just like those who are currently paying for them!

A note to the current Administration. You should keep these stories alive and at hand. It explains why we are in this mess!



Labels: [Health Care](#)

SATURDAY, MAY 20, 2017

MICROSOFT DOES IT AGAIN

In my opinion Microsoft is truly evil. Now that is my personal opinion. I have studied the meaning of evil and especially the work of Augustine and therein I believe I may have a valid opinion.

You see they update W10 again, 1703 "upgrade". Yes, a full complete, five hour upgrade. Dead in the water. Then they moved things around. You see, after 3/4ths of a century I know where things are on my desk. Pens in the right hand drawer, stapler to the top right, phone on top left. And so on. But what do these people do? Change everything as well as the location of everything. I guess they never had a mother who told them to put things back where they belong! The move things, not big moves, but evil little moves.

Then the upgrade kills off expensive software. Drivers do not work, files messed up, etc. One gets to spend a full day trying hopelessly to rearrange your desk! Yet every few months these people change your desk. For the better? Hardly.



Labels: [Microsoft](#)

SATURDAY, MAY 13, 2017

SECURE NETWORKS

The most recent flap on intrusion into large scale public networks has evoked responses by people who appear in my opinion and in my experience to have little in any understanding of what was and what is. For example the [NY Times](#) has apparently some Librarian commenting on the recent flap. The author states:

It is time to consider whether the current regulatory setup, which allows all software vendors to externalize the costs of all defects and problems to their customers with zero liability, needs re-examination. It is also past time for the very profitable software industry, the institutions that depend on their products and the government agencies entrusted with keeping their citizens secure and their infrastructure functioning, step up and act decisively.

But take a look back forty years, to the mid seventies. We worried about Soviet intrusion into networks and at the same time we were intruding into theirs. One of my best employees had been with the Brits and managed to [penetrate East German telephone lines. It was simple, just climb through the sewers, tap the copper pairs, and hope you do not get caught.

But in a similar fashion we had three key elements. First we had secure lines. They were not shared. They were encrypted. Finally we had secure Operating Systems, Kernelized OSs. What was a KOS? Simple it was an OS with a secure outer kernel that only allowed access to the OS functions such as DB access and I/O access in a fully secure manner. However, the MS/OS is an open system allowing third party software. It is a pure kluge. At least Apple has a somewhat better system. But MS systems ate a patch quilt of ports and access points that have evolved into

an uncontrollable mess. Anyone can get into them. Then add the Internet, an "open" network by design, and you have a recipe for disaster.

Thus what is the solution? Go back 40 years. Why is the NHS using the Internet! It is grossly insecure. Why do they use XP, it also is insecure. And finally, what do the people always open stuff they should not? What would one expect, just a disaster.



Labels: [Security](#)

TUESDAY, MAY 9, 2017

[MABS AND CAR-T](#)

Immunotherapy has become an explosive field. We have been focusing on Mabs, which have been around for quite a while, plus CAR-T cells which have been available for about five years. There is an interesting report by [Research and Markets](#) which sizes up the CAR=T cell market. They state:

As per report findings, the promise of CAR modified T cell therapy derives from its combined immunologic benefits and include the specificity of a targeted antibody, the ability to expand the T cell population and the potential for long term persistence to facilitate the ongoing tumor surveillance. The success in early phase trials, assess the feasibility of evaluating the treatment modality across the multiple centers and in larger patients. Currently, there are 99 CAR T Cell based therapies in clinical pipeline and most of them belong to Phase-I and Phase-I/II clinical trials.

We have examined this approach over the past few years and it does present potential. They also note the following players:

- 12.1 Autolus
- 12.2 Bellicum
- 12.3 Bluebird
- 12.4 Celgene
- 12.5 Collectis
- 12.6 Celyad
- 12.7 Eureka Therapeutics
- 12.8 Fortress Biotech
- 12.9 Immune Therapeutics
- 12.10 Juno Therapeutics
- 12.11 Kite Pharma
- 12.12 Novartis
- 12.13 Sorrento therapeutics
- 12.14 TILT Biotherapeutics
- 12.15 Ziopharm

It is well worth watching this landscape evolve.



Labels: [CAR-T Cells](#)

MONDAY, MAY 1, 2017

BRIDGE VS TUNNEL

Just a thought. What if they built a bridge to Penn Station in New York rather than a tunnel. Here is the result. First for a tunnel, I have used the average estimates from various sources:

| | Tunnel |
|---------------------|------------------|
| Amount | \$20,000,000,000 |
| Duration | 40 |
| Interest | 4.00% |
| Passengers per day | 600,000 |
| Passenger days | 156,000,000 |
| Fee per Trip | \$6.48 |
| Annual Bond Payment | \$1,010,469,786 |

Then for a bridge. I assume that one just duplicates the Tappan Zee Bridge.

| | Bridge |
|---------------------|-----------------|
| Amount | \$4,000,000,000 |
| Duration | 40 |
| Interest | 4.00% |
| Passengers per day | 600,000 |
| Passenger days | 156,000,000 |
| Fee per Trip | \$1.30 |
| Annual Bond Payment | \$202,093,957 |

Thus for a \$1.30 a trip we can get a bridge in about 3 years! So what is the problem?



Labels: [Government](#)

WEDNESDAY, APRIL 26, 2017

"RAMBLIN WRECK FROM GEORGIA TECH"

The old Georgia Tech song has significance in the ongoing collapse of transportation into and out of New York. Over 1 million people will be without a means of transportation. I guess there is a "wall" around New York keeping the aliens from without from getting within! It was also a free wall, just let the system collapse! Oh yes, Georgia Tech, that was where the CEO of Amtrak was trained. Economists from MIT and Train Managers from Georgia (getting paid almost \$10 million a year!)....the end of civilization as we know it is upon us.

As the [NY Times](#) reports:

After two derailments at Pennsylvania Station in New York, Amtrak officials are considering closing tracks at the station for an extended period to make long-term repairs — a drastic move that would cause huge disruptions for tens of thousands of commuters, according to officials who

were briefed on the plans. Officials at Amtrak, which owns and operates Penn Station, say the infrastructure at the terminal has become so brittle that it urgently needs an overhaul. The closings would probably prompt extensive delays and route changes for two of the nation's largest railroads, New Jersey Transit and the Long Island Rail Road, which rely on Penn Station. A decision to upend the lives of so many riders would follow years of failures to invest adequately in aging infrastructure even as ridership boomed in the busiest region of rail travel in the country, and it would be a break from Amtrak's traditional strategy of trying to minimize disruptions.

Yep, that's it folks, just close Penn Station and allow the in my opinion grossly incompetent Amtrak do its thing! Are these folks out of their minds? No, they apparently have no minds. The Times shows the CEO in a photo op wearing the compulsory green vest and hard hat. The CEO should be out of there, gone, get a new one, someone who has some competence!

And then there is the US DOT! Where is the Secretary of Transportation? Dinner in DC? Get a hard hat and joint the team.

It is insane to think you can close Penn Station. But not to the Government. The economic costs, direct and otherwise, will be monumental. The lost taxes. Gov. Christie started the process by cancelling the new tunnel. But he is gone soon. Yet not one of his replacements is commenting. Even the NY Governor should be concerned due to the potential loss in tax dollars from lost employment.

On and one more thing. NJ Transit has still not repaired Hoboken station which collapsed months ago when a train engineers apparently went to sleep on approach and crashed into the station and killed a woman. Imagine, half the capacity gone due to Amtrak and 30% of the remaining capacity gone due to NJ Transit. And you want Government Health Care!



Labels: [Government](#)

SATURDAY, APRIL 22, 2017

[COLLEGE FUND RAISING VIA POLITICS](#)

From the world of "You Can't Make This Stuff Up!" comes a rather strong request from the MIT Alumni Fund to send in money to defeat the current Administrations Plans! The person sending the request states, among other things:

*From the Internet to infant formula to the touchscreen technology that allows you to access all the information in the world from a device that fits in your pocket, public funds have lent support to some of our greatest scientific advancements—**but if the proposed federal budget comes to pass, that funding will be significantly cut.** Institutions like MIT will be forced to rely even more on the generosity of donors like you to provide the resources necessary for true innovation and progress that benefit the world at large. Please consider making a gift to MIT today, and together, we can keep marching both science and society forward.*

But what if I like the new Budget. I have no opinion but perhaps I could. Statistically perhaps 50% of Americans do. So what has this person done? Well she apparently told half the Alumni that they are wrong. Not a way to Fund raise. It is the old echo chamber effect. I and my friends think this way so everyone must! Ever look at a voting map?



THURSDAY, APRIL 20, 2017

[WORTH A READ](#)

The following in [PLOS](#) and in [Nature](#) is worth a read. Really. Namely:

In the first broad look at the behaviour of thousands of scientists on Twitter, researchers have found that women are better represented on the social-media site than on scientific papers. The team also noted that scientists tended to stick with researchers in their area of expertise while on the social-media site... “This is a really interesting finding,” ...says. Male scientists tend to have their papers cited more than female scientists, and there are more male full professors than female ones at US universities, she notes. So Twitter “may have more participation from women than we would expect”.

It may be interesting to follow. But just sit in any New York Restaurant and it is obvious.



Labels: [Academy](#)

[AMAZON AND AMZL](#)

How to really tick off your customers. Create a delivery service that always fails despite being told it is on its way. Amazon has AMZL which seems to consistently lose, misplace, or otherwise get deliveries lost. Yet they tell you that it is on its way. UPS, USPS, FedEx, and even the local independents get to deliver, but NOT Amazon. This is a sign of a serious malignancy! It has been happening for a couple of years and we are now going to other vendors. Even if it costs more reliability is essential. One can excuse a third party but when Amazon takes on full responsibility then the problem falls on their doorstep. We are batting 3:4 lost deliveries in the last two wee4ks on AMZL. The customer complaint blog is exploding. Perhaps a shorting of the stock may be in order! Just my opinion and my experience. Too bad, Amazon was once reliable.



Labels: [Amazon](#)

TUESDAY, APRIL 18, 2017

I HAVE GOOD NEWS AND I HAVE BAD NEWS



There is an old WW II joke about a German U Boat Captain who after a long under water journey to avoid the Americans announces to his now terrified crew:

"I have good news and bad news. The good news, we shall surface in ten minutes." A cheer erupts. "Now the bad news. It is either Buenos Aires or New York." The crew was silent.

Now for the latest version of that with our US Navy. Frankly my father would be ashamed of such an event. I report it from a Canadian newspaper, The [National Post](#) notes:

A spokesman for the Pacific Command linked the deployment directly to the "number one threat in the region," North Korea, and its "reckless, irresponsible and destabilizing program of missile tests and pursuit of a nuclear weapons capability." Defense Secretary James Mattis told reporters on April 11 that the Carl Vinson was "on her way up there." Asked about the deployment in an interview with Fox Business Network that aired April 12, President Trump said: "We are sending an armada, very powerful." The U.S. media went into overdrive and Fox reported on April 14 that the armada was "steaming" toward North Korea. But pictures posted by the U.S. Navy suggest that's not quite the case – or at least not yet. A photograph released by the Navy showed the aircraft carrier sailing through the calm waters of Sunda Strait between the Indonesian islands of Sumatra and Java on Saturday, April 15.



Yes, our very own Navy is sailing not where the bosses said it was but in the opposite direction. And we get this from the Canadians. At least they know who is where.

What Admiral is being demoted to Seaman Third Class for this one?

Now as for the Carrier Group Commander, I suspect a Rear Admiral, perhaps some Seaman Third Class could have seen on the Internet, you know Admiral, that thing they look at all time time when not responding to your commands, and have seen they were on their way to Korea, and that the Palm trees on the islands they were passing were not native to North Korea. There is no radio silence. Or perhaps a Skype call home could have gotten so Petty Officer Second Class to see he was not where he was supposed to be. One more billet for a Rear Admiral! Shame on you folks!



Labels: [Commentary](#), [Military](#)

[A WELL DONE PRESENTATION OF AN IMPORTANT MOVEMENT](#)

The book by Fenton, [Religious Liberties: Anti-Catholicism and Liberal Democracy in Nineteenth-Century U.S. Literature and Culture](#), is an interesting, valuable and well done work discussing the existence of and impact of the anti-Catholicism in the United States. It is the result of a doctoral thesis and as such reads somewhat like one but is readily accessible and to the point. The author argues that the anti-Catholicism was a major factor in shaping our democracy during this period.

She begins with a summary of the work and that section is well worth the read. Then she discusses the Canadian issue regarding French speaking Quebec and the rules that allowed them to practice Catholicism. On the one hand the "Founders" of the US had considered attracting all of Canada as well as the Colonies but the very presence of a potentially ever expanding Catholic only area was of significant concern. On p 31 the author introduces Thomas Paine and his considerations related thereto. Paine argued that the Inquisition, that Church State chimera, was a problem just because it was a fusing together of the Church and State. Thus because there was a dread among Protestants of the Inquisition, especially as exercised by Spain, then the issue was not the exercise of religion in a private sense, but the politicization of religion in any sense. His conclusion were two fold. First people should be able to practice whatever religion they wanted in private. Second, there must be no nexus between politics and religion, between the state and the church. The author's presentation is exceptionally lucid here and it exemplifies how many of the Enlightenment types were capable of excelling above their inborn prejudices.

The author then moves on to the Constitution and discussion of Madison. On p 43 is the discussion of republics, their size and their viability. Montesquieu is discussed as being the prime source. It can be argued by many, including Ullmann, that these ideas well preceded Montesquieu with 14th century writers such as Marsilius of Padua. Again on p. 55 Paine is quoted as stating that the American priest is as good a citizen as any.

The author continues discussing the well known 19th century anti-Catholics such as Mark

Twain, who seemed to be anti everything, and Nathaniel Hawthorne. Hawthorne's book, *The Marble Faun*, is a typical example of the aggressive anti-Catholicism of the New England "elite" which infested Boston and its environs.

Overall it is a well written and well argued piece and worth reading to better understand the 19th century and its connection to what the Founders managed to put in the Constitution and why. However it would have been of interest to see this stretched a bit to the 20th century. From the rejection of Al Smith to the election of Kennedy. Also it would have been interesting to examine the same strong anti Catholicism of academics such as Dewey and Hofstadter. There was a whole class of "Intellectuals" whose main focus was the expression and exercise of mass anti-Catholicism. The two aforementioned, both at Columbia, demonstrate the very institutional attitude of that University well through the 1960s. For example, while I got into MIT, I was denied admission to Columbia because I was educated at a Catholic secondary school. That was told me in a three page single spaced letter from the Dean. A far cry from what anyone would do today! Thus this work takes us far, but not all the way!



Labels: [Books](#), [Church](#), [Commentary](#)

[MARCH FOR SCIENCE](#)

Science funding is very akin to entrepreneurial financing. Really. It is competitive. It is driven by past results. It is assessed by impact. It has a political element. It depends on who you know. It often does not reflect the true value of what is being proposed. Remember that more than 90% of VC investments go nowhere. Oftentimes the same is true with scientific research. The latter is all too often a means to educate doctoral students. Post docs are a means to get lower cost lab help. It used to be a University had Lab techs, possibly with an MS but an employee. Now we have post docs, lower costs, no benefits, and you can fire them at will.

In reality then science funding is the same game, and the measure of success can be even more vague. There are no IPOs in science. Thus winners are far and few between. It is the process that often counts. There is no financial rate of return on pure science. A nexus with some start up may count but little study of this is done since science is done for science, not money, at least that is the mantra.

Now along comes this March for Science. [Nature](#) has been one of the promoters as has Science. Nature is the left wing Brits and Science is headed by a former Democratic Congressman with an agenda. In the Nature piece they give voice to some well chosen "science" representatives. They state:

Calls from US President Donald Trump to roll back environmental regulations and slash funding for health, environmental and research agencies have raised alarm in the scientific community. Earlier this year, a commenter on the social-media website Reddit made an off-hand remark about the need for scientists to march on Washington DC. That thread has since grown into an international movement. The March for Science now includes more than 500 events — including marches, rallies and teach-ins — planned for locations around the world.

What will this "March" result in? Some of the commenters noted it was being co-opted by the Left with Identity Politics being front and center. That can be a serious step backwards. Already any college website appears as an Identity Politics ad and as such has an impact on students and studies. Take foreign students. Many doctoral students are foreign students. Yes they may be very good but on the other-hand we the taxpayers are funding their studies. Is that fair? Should we not be incentivizing our US students first and then selecting the best. We are funding students in such areas as nuclear science and engineering from countries that vow to destroy us. Does that make sense? Did Admiral Yamamoto study Naval Architecture at MIT?

So take the comment by an Irish lecturer:

"I am going so I can stand up for evidence-based policies and the scientific method. I also support robust funding of science and transparent reporting of scientific results. The current wave of 'anti-science' rhetoric goes against everything that I am trying to do as a scientist and an educator. I keep telling my students that I'm going because science is worth protecting: for them, and for all of us."

Now just what does US research funding have to do with this person? There is no anti science rhetoric in Ireland as best as I can tell, I am an Irish citizen so I do have some first hand knowledge. So are we going to see a bunch of white coats and pink hats waving placards?

Science is often done for the sake of science. But science funding is done on that basis of a complex set of allocation schema; public and private. It is worthwhile every once and a while to reassess that scheme.



Labels: [Academy](#), [Politics](#)

SUNDAY, APRIL 16, 2017

[POLITICAL SCIENCE IN THE 14TH CENTURY](#)

Dante and his Divine Comedy have been read and studied for centuries. However to understand its context and complexities one must have a reasonable understanding of the temporal context of the world Dante wrote in. One key element was the battle between the Franciscans and the Papacy regarding the issue of poverty. The book by Havelly, [Dante and the Franciscans: Poverty and the Papacy in the 'Commedia'](#), is an excellent introduction to this essential dimension.

The Franciscans in the early 14th century were divided into two camps; the Spirituals and the Conventionals. The Spirituals had a view of poverty which was in the extreme. That is no Franciscan could "own" anything or it was a breach of their vow of poverty. Even to the extent of their tunics, which were communal and limited in number to what they wore and a possible clean spare. The Conventionals on the other hand limited poverty to actual ownership, such as a horse or even a book. Their horses and books were communal and the ownership was in the name of the Pope and not the order per se.

By the late 13th century and early 14th several trends tended to collide, with poverty being a focal point. The major tendency was that of the increasing opulence of the Papacy and its alignment

with France and its ultimate move to Avignon from Rome. Too many, and Dante included this was a breach of duty of the Pope and the excesses of these erstwhile Popes were a denial of their prime duty as Bishops of Rome. Pope after Pope were handing out favors for money, and some of these favors were forgiveness of sins. Popes were appointing massive numbers of family members to key positions in the Church, so that what had been a fundamental religious position was not a secular organization taking money for the issuance of religious gifts.

Add to this the city states in Italy, such as Florence from whence Dante came and was expelled, and Bologna, Milan, Venice, Ravenna. Across Italy there were Guelphs and Gibberlines, supporters of the Holy Roman Emperor or Pope.

In a sense these three waves of conflict, poverty and its Christ and Apostle like adherence, the Pope and his legitimacy as Bishop of Rome, and the conflict between Church and State as to secular rule. The contrasts led to massive conflicts in society.

The author then takes the reader through Dante's Divine Comedy laying out how the three parts of it reflect his view of these conflicts. In the Inferno, home to evil Popes and public figures who have betrayed the trust that people put in them are shown to suffer the pains of Hell.

Chapter 1 is a superb discussion of Franciscan poverty. It is essential to understand some of the elements since Dante came from Florence and Santa Croce in Florence was a Franciscan school which Dante may very well have attended. It was also a hot bed of many of the Spirituals of the time.

Chapter 2 is the core chapter on Inferno. As Virgil takes Dante around the Inferno, he stumbles, literally as well as figuratively, upon Popes whose presence is there as a result of avarice. Pure abject greed and use of the office for personal gain and aggrandizement, which is what Dante relates over and over. The second theme is authority after avarice. This is a key combination. For when Dante ages thinkers like Marsilius of Padua has begun promoting his ideas of leadership and political science. Marsilius sees the Pope as a religious leader, separate from the world, and further see the secular leaders as serving those to whom they lead, and furthermore selected by those very people. Marsilius introduces into the political thought the construct of the individual, the individual as a separate and autonomous agent and not as a subject of any king or Pope. William of Ockham was soon to take this further in his battles with John XXII. One can see many of these ideas starting to come forth in Dante and his Inferno.

Chapter 3 is Purgatorio is driven by the theme of poverty in spirit. Chapter 4 is Paradiso and its theme is poverty and authority. Chapter 4, Epilogue, is a superb summary of all the issues the author considers.

To understand Dante, in my opinion it is essential to understand his time and the issues which drove him. Estranged from Florence, he spends time throughout the city states of northern Italy, writing in his Divine Comedy about the issues of his time, but they are also issues which rise above what he sees. The issue of poverty and the Franciscan Spirituals is truly an issue of authority. It is also an issue of what responsibilities those who rule have, not just what powers

they can exert. What one sees in the Inferno are not just evil people being punished, but evil deeds which must be corrected.

This book is an essential reference for anyone studying Dante. Dante can be read as a student in the context of a compulsory exercise or as an educated adult as insight to the cruelties of abused power. Dante, in focusing on the Franciscan issue of poverty, sets a sounding board for the developing change in governance, spiritual as well as temporal. This book is a brilliant light on those issues and is essential not only for understanding Dante but also in understanding the early development of political change. The centuries before Montesquieu, Locke, Mill, were started by the arguments of poverty, and then authority and its source.



Labels: [Books](#), [Politics](#)

SATURDAY, APRIL 15, 2017

[THE OTHER LEFT](#)

The [NY Times](#) has some author bemoaning the lack of precision in the use of the English language. The author states:

Americans can't agree on much these days. They've obviously fallen out over politics. They can't even agree on the facts. Now they're fighting over words. For years, we mild-mannered lexicographers have been posting online about the most common lookup of the moment on our website. So when, in January, the White House press secretary, Sean Spicer, told reporters he wasn't going to define the word "betrayal," and lookups spiked, we saw it as our duty to post a definition. But all of a sudden, people were furious, usually because of something related to Donald Trump: "facts," after the presidential adviser Kellyanne Conway created alternative ones, and "Svengali," when this paper's editorial board wrote that Stephen Bannon, the White House strategist, was "positioning himself not merely as a Svengali but as the de facto president."

I am reminded of a friend of my wife, let us call her "Gracie" who had this habit, before GPS was common, of giving directions like, "Turn left" and then shout out "the other left". For those of you who missed the point she meant right.

Then there are those who keep saying I was born in Staten Island. In 1969 I found out I was born "on" Staten Island. Otherwise perhaps I was a worm of chipmunk.

Having picked up five other languages in my lifetime, mostly to speak to cab drivers and hotel staff, although my French is not that bad, one learns a great deal about English. Namely, no one uses a dictionary, and we all are flexible enough to get the point across.

Now words mean something. Take laws that are written. Take contracts. In each case there is often a section on definitions. Not the ones in a dictionary. Rarely is one used, especially since there are many dictionaries and they may conflict. Thus a law or a contract defines say a specific term which is then somehow restricted in the body of the law or contract.

Does that solve the problem? Ever been to court? Most trials are about definitions. What was really meant.

Now take wiretapping. I have seen some in my life. It was on a pair of copper lines, indicated by a "red block" and carefully segregated. It was old fashioned telephony, analog calls on copper. Now we have all digital calls on IP and they are just as easily intercepted and wiretapped. Not the same technique but the same outcome.

Having been around the world several time what I also found is that English is the most flexible language out there. A cab driver can survive with say 100 words, prosper with 1,000. The syntax may be rudimentary but we somehow manage to "get the idea".

So I would ask, when was the last time any one used a dictionary? Like libraries they are artifacts of the past. The keepers of the definitions like the author the the piece mentioned above want us to believe they are the holders of truth. In fact, truth is what we meant to say, not necessarily how it may have come out. After a couple of years I understood "Gracie". Somehow we all can do that, humans are rather interesting non AI machines! Let's see the Silicon Valley guys replace that one! Good for "Gracie"!



Labels: [Commentary](#)

TUESDAY, APRIL 11, 2017

[THE USPSTF IS AT IT AGAIN!](#)

The USPSTF has been at it again and again especially in suggesting that prostate cancer screening be denied.

First let us examine just [who these folks are](#):

Task Force members come from the fields of preventive medicine and primary care, including internal medicine, family medicine, pediatrics, behavioral health, obstetrics and gynecology, and nursing. Their recommendations are based on a rigorous review of existing peer-reviewed evidence and are intended to help primary care clinicians and patients decide together whether a preventive service is right for a patient's needs.

Namely they generally are NOT specialists in the area upon which they are opining. Frequently they are administrators or academics.

Second, [they have now modified their PSA recommendation](#) from a D to a C. D means useless and C means a toss up. As [Healio](#) notes:

5 years after the U.S. Preventive Services Task Force issued a recommendation against PSA screening for prostate cancer in all men — the task force amended its stance in a draft statement, determining that the decision about whether to be screened should be an individual one. The new recommendation — which changed the grade for PSA screening from D to C — states

the potential benefits and harms of PSA-based screening are closely balanced in men aged 55 to 69 years. As a result, the U.S. Preventive Services Task Force (USPSTF) recommends clinicians talk to these men about the potential benefits and harms of screening. For men aged 70 years and older, the USPSTF maintained the D recommendation, based on the position that the potential benefits of PSA-based screening do not outweigh the harms, and these men should not be screened for prostate cancer.

What changed the recommendation? Dead bodies one could presume. Dead male bodies. But under the ACA that was irrelevant.

The data upon which they based their analysis is in my opinion flawed. They state that of 1,000 men screened, 240 received a positive result and 100 were found to have PCa. If screening had been done then 2 lives would be saved. First the screening was done several years apart! That is non-sense. PSA testing demands annual tests with velocity being measured. The analysis grossly misrepresents the facts in my opinion. No genetic analysis is performed. It is well known that about 5-10% of PCa is aggressive, the remaining is non life threatening. Thus one would expect a small percent death but finding that small but critical segment is not done by random and intermittent testing.

At some point those who deal with this every day on both the clinical and research level should become part of the panel, and a key part. We are in my opinion poorly served by this organization.

Finally, the USPSTF again disregards anyone over 70! That is just another way to "let the old folks die!" of the ACA.



Labels: [Cancer](#)

[IF ALL ELSE FAILS LISTEN TO THE CUSTOMER!](#)

United Airlines has in my opinion and in my experience been one of the worst carriers in the world. And I used Aeroflot! Flew at 4,000 ft from Moscow to Prague one day, hopping over corn stalks.

But the recent United handling of a customer goes beyond the pale. [The Guardian](#) notes:

In one video clip guards aggressively grab then drag the passenger down the aisle of the plane as other passengers shout: "Oh my God" and "Look what you did to him". On Tuesday chief executive Oscar Munoz attracted criticism after calling the passenger "disruptive and belligerent" and saying that the airline's employees "followed established procedures". The passenger is overheard in one video claiming he was being profiled for being Chinese, and the video has caused outrage in China and calls for a boycott. Ahead of the market's open, United shares had been down by as much as 6% in premarket trading.

Perhaps they should place a sign akin to Dante's Inferno, "Abandon all hope ye who enter" above any United facility. The CEO clearly seems in my opinion to be clueless and heartless (see bio).

Perhaps a 50% or 60% stock drop would be useful. Add TSA and then add Chicago, and well, the KGB was kind, really it was!



Labels: [Commentary](#)

MONDAY, APRIL 10, 2017

[SNATCHING DEFEAT FROM THE JAWS OF VICTORY](#)

Like so many people I am a significant user of Amazon. However one of the things they must learn to do is to deliver on their promises. I have been seeing significant breaks recently. Namely with Amazon's own delivery services. They have in my experiences a significant failure rate. Amazon conditions customers to accept a certain level of service but then tries to expand well beyond their competence. The result in my experience is failure. If I were running the company, or at least that part, I would be exceedingly careful not to drop the ball. However it appears that whoever is in that position seems in my opinion to be clueless.

The result. You create a customer looking for an alternative. Not really a good idea. But unfortunately there is no way to let the folks at Amazon know this, or perhaps arrogance leads to just not caring?



Labels: [Amazon](#)

SUNDAY, APRIL 9, 2017

[AMATEUR?](#)

What is an amateur? On the one hand it is someone skilled in a certain area but not compensated for what they do. Thus an amateur botanist may be someone who on their own funding performed certain botanical science works, such as hybridizing plants and analyzing plant genetics. Likewise an amateur is used as a dilettante, one who feigns to be a botanist, one who has the use of words but never got their hands dirty. Thus an amateur ranges from a competent person not compensated by some entity, thus having no reliance on a third party, to someone pretending to be competent but not.

So what definition do we use. Take the [NY Times](#). In a recent article they state:

....a 1997 work by two amateur historians....

So what definition do they use? It is after all the Times so it must be the most derogatory! What is a historian? Does a historian have to be compensated by some entity? Such as a Harvard? Not really. An historian is one who uses original sources to present what happened in some specific period. It is after all still an interpretation but referenced to the original source. Is Edmund Wilson an historian in his work, *To the Finland Station*? No, he was a Communist sympathizer telling a tale to promote his personal views. Was Gibbon an historian? He used some original sources but he interposed his own personal view so strongly and ignored other historical facts that one seriously questions his presentation no less than his integrity.

So what does the term really mean. The only way is to examine who they are commenting on and about. Thus in this case we are again in the middle of news which is colored by the political opinions of the medium through which it is presented. Amateurs after all are both free and unbiased by their sponsors.



Labels: [Academy](#), [Commentary](#)

MONDAY, APRIL 3, 2017

[FUNDING, PATENTS, AND MONETIZATION](#)

There is a new [MIT study](#) which alleges:

To conduct the study, the scholars examined 365,380 NIH grants funded between 1980 and 2007 — nearly every NIH grant awarded for decades. Exactly 30,829 were the direct basis for patents; 17,093 of those were so-called “Bayh-Dole” patents issued to universities and hospitals, something federal legislation made possible starting in 1980. Of the NIH grants, 112,408 were additionally cited in a total of 81,462 private-sector patents. And as the authors put it in the new paper, even these NIH-backed research projects that are indirectly cited in later patents “demonstrate the additional reach that publicly funded science can have by building a foundation for private-sector R&D.” Azoulay, an economist who studies the production and dissemination of scientific knowledge, says the bottom-line figures in the study — the 31 percent and 8 percent of NIH grants that contribute to and more directly generate patents — strike him as being significantly large because of the broad scope of research the NIH supports.

Now let us examine this a bit.

First, under the Dole Law the beneficial ownership of patents resulting from Government work go to the sponsoring institution. Some interest accrues to the Principal Investigator and Patent filer.

Second, patents are not always filed and not always issued. CRISPR is a real counter example. Universities file for patents if the IP Office believes it is worth the effort. That determination varies widely from institution to institution.

Third, patents are not businesses. Patents are often over turned or contested and thus are no assurance of anything. Patents are also an invitation for litigation, lots of expensive litigation.

Fourth, patent portfolios really do not generate that much money, on average. Sometimes one patent can be great but most of the time they are not money generators.

Fifth, dealing with a university IP Office can be near impossible because they are trying to maximize their return with no understanding of the risk in monetizing the patent.

Sixth, many patents are used solely to block others. Namely a patent may be licensed just to stop

a competitor. That means that the patent is shelved and is dormant.

[The Scientist](#) notes:

They also found that basic research was nearly as likely to contribute to a patent as applied projects. The authors separated grants awarded through a request for applications (RFA)—indicating a focus on addressing a particular disease—from those that were unsolicited—likely representing more basic science—and discovered a similar citation rate in associated patents.

Given what was noted above, one must wonder to what use the patent was licensed for. The study, supposedly to be released, may or may not contain any details. One is left wondering.

[EurekaAlert](#) notes:

A 2015 working paper released by Azoulay, Li, Sampat, and Joshua Graff Zivin, a professor at the University of California at San Diego, estimated that every \$1 of public NIH funding yielded between \$1.5 and \$2 in private-sector pharmaceutical drug sales. That study is still undergoing peer review.

This above connection seems quite difficult to ascertain. First the result is drug sales. That is the gross output for the pharma industry. The input alleged is NIH funding. Just consider the following:

1. A single patent is but one part of a new drug.
2. A new drug has about a 1:100 chance of ever getting FDA approval.
3. A successful FDA drug may also be problematic in total market acceptance.

Thus the claim as noted above seems highly unlikely. It may also lead to negative criticism of NIH. That often is the problem with academics.



Labels: [Academy](#), [Health Care](#)

SUNDAY, APRIL 2, 2017

[WHERE IS THE ARMADA?](#)

Spain is willing to support a separate Scotland and it wants Gibraltar back. So says the [Guardian](#). It states:

Spain has said it would not veto an attempt by an independent Scotland to join the EU, in a boost to Nicola Sturgeon's campaign for a second independence referendum and the clearest sign yet that Brexit has softened Madrid's longstanding opposition. Alfonso Dastis, the Spanish foreign minister, made it clear that the government would not block an independent Scotland's EU hopes, although he stressed that Madrid would not welcome the disintegration of the UK.

As for Gibraltar, again the [Guardian](#),

Theresa May would be prepared to go to war to protect Gibraltar as Margaret Thatcher once did for the Falklands, former Conservative leader Michael Howard has suggested, in comments that were immediately criticised as inflammatory. Lord Howard's suggestion that the prime minister would be ready to follow in the footsteps of her predecessor 35 years ago came alongside a government pledge to protect the sovereignty of Britain's overseas territory.

First, Scotland by itself really is not much. A golf course and sheep, lots of sheep. If Northern Ireland also leaves, it has three options. First, go alone. Like that would work. Go with Scotland. Now frankly all the Protestants were sent from there by Cromwell so if you think the Troubles were bad just wait. Go with Irish Republic, and live with Catholics. The latter may ironically be the safest.

Now as for Spain, remember Elizabeth I. But now Britain has a wimpy Navy. But Spain has nothing! Spain most likely could not raise ferry fare to get to Gibraltar.



Labels: [Commentary](#)

FRIDAY, MARCH 31, 2017

ZIMMERMAN TELEGRAM

The following was sent by Germany to Mexico 100 years ago.

We intend to begin on the first of February unrestricted submarine warfare. We shall endeavor in spite of this to keep the United States of America neutral. In the event of this not succeeding, we make Mexico a proposal of alliance on the following basis: make war together, make peace together, generous financial support and an understanding on our part that Mexico is to reconquer the lost territory in Texas, New Mexico, and Arizona. The settlement in detail is left to you. You will inform the President of the above most secretly as soon as the outbreak of war with the United States of America is certain and add the suggestion that he should, on his own initiative, invite Japan to immediate adherence and at the same time mediate between Japan and ourselves. Please call the President's attention to the fact that the ruthless employment of our submarines now offers the prospect of compelling England in a few months to make peace.
Signed, ZIMMERMANN

Just a thought. I guess they did not want California back even then.



Labels: [Politics](#)

THURSDAY, MARCH 30, 2017

EVERYTHING ON A SMART PHONE?

The [Guardian](#) is showing British Drivers Licenses on smart phone next year. Today we can go to the bank, get a car, get on a plan, etc all on a smart phone. Two questions:

1. What is I do not want to spend \$600-\$1,000 for a smart phone. Must I now have one? To do everything? Don't I have a right to live without one? Where does it say in the Constitution that I must have one? I must pay some foreign company for the right to exist?
2. Given the gross lack of security in any such device, is this single point of contact not making each of us ever so much more vulnerable? A single point of contact is great for the Government. They can see where we were, who we were with (really, by pinging who is around us), what we eat, what we watch, etc. And with the new Internet Lack of Security law just passed by Congress it is all readily and commercially available!

So perhaps we should just slow down a bit and ask what these folks in Silicon Valley really have in mind. You see Government officials are generally rather slow on the uptake and the Lobbyists can convince them of anything for a price.

Perhaps Brandeis was right, we should have a right to be left alone. But we don't. Pity.



Labels: [Commentary](#), [Privacy](#)

WEDNESDAY, MARCH 29, 2017

FREEDOM OF SPEECH?

The Constitution protects Freedom of Speech. Especially political speech. I thought. Now along comes a [California legislator with a bill](#) which states:

SEC. 2.

Section 18320.5 is added to the Elections Code, to read:

18320.5.

It is unlawful for a person to knowingly and willingly make, publish or circulate on an Internet Web site, or cause to be made, published, or circulated in any writing posted on an Internet Web site, a false or deceptive statement designed to influence the vote on either of the following:

- (a) Any issue submitted to voters at an election.*
- (b) Any candidate for election to public office.*

Well I guess if one says, "Your mother wears combat boots!" off to Lompoc you go in California. You see California is a strange place. Before the TSA started taking control of our lives at airports the California law required that you have and show upon demand by a police officer a form of personal identification satisfactory to them. If you refused or did not have it they could arrest you as a vagrant.

The [EFF](#) makes a strong point against this proposed law. They state:

This bill will fuel a chaotic free-for-all of mudslinging with candidates and others being accused of crimes at the slightest hint of hyperbole, exaggeration, poetic license, or common error. While those accusations may not ultimately hold up, politically motivated prosecutions—or the threat of such—may harm democracy more than if the issue had just been left alone. Furthermore, A.B. 1104 makes no exception for satire and parody, leaving The Onion and Saturday Night Live open to accusations of illegal content. Nor does it exempt news organizations who quote deceptive statements made by politicians in their online reporting—even if their reporting is meant to debunk those claims. And what of everyday citizens who are duped by misleading materials: if 1,000 Californians retweet an incorrect statement by a presidential candidate, have they all broken the law?

It is truly amazing how some Parties are dealing so loosely with the rights which remain. Perhaps California should BRExit as they so desire. Better yet, the Treasury could swap California with the PRC in lieu of all payments due, plus a bit more. We could dramatically reduce the debt. Most likely the deficit as well.

This is truly one of the most poorly crafted, offensive, and unconstitutional laws yet!

Perhaps, this is just a supposition and not "fake news", this law may make it illegal for the NY Times to operate in the State of California? Just a thought.



Labels: [Constitution](#)

[PLATELETS, CHECK POINTS AND CANCER](#)

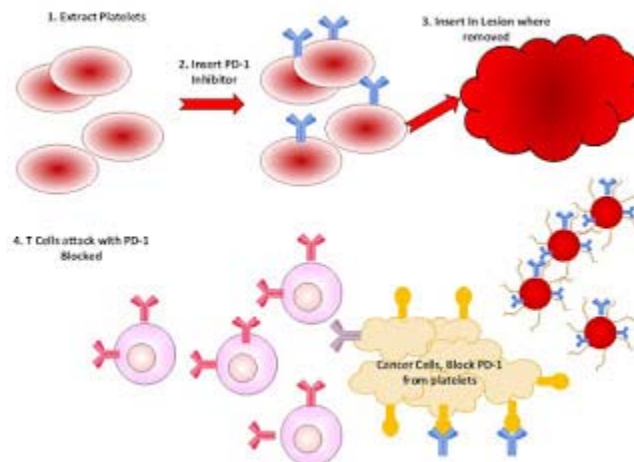
Introduction

Various elements of the immune system have been used to attack cancers. T cells, Dendritic cells, antibodies, NK cells, and now the humble platelet or thrombocyte. The platelet is a remnant of the megakaryocyte which can eject thousands of these small nucleus free cells, albeit with many mitochondria. Now when these cells see a break in the blood stream, say a cut or some other way they are exposed to activating cells not the walls of the blood system, they begin aggregating and forming a clot by sticking to these non-normal, for them, cells. They have the ability to see what is not supposed to be there, attach themselves and then produce a plug.

When surgical excision of a tumor occurs, there is frequently a few cells left behind, even in a wide margin excision. The idea is to now treat that area with immune therapy but in a local manner, not systemically. This means attacking the tumor cells with a PD-1 blocker. The vehicle for that is a modified platelet delivery system. Now the idea is to modify platelets so that when they are activated they release anti PD-1 or similar checkpoint inhibitors so that T cells can then attack and kill remaining cells.

From Nature we have the following Figure^{7[1]}:

^{7[1]} <http://www.nature.com/articles/s41551-017-0031>



As Nature notes^{8[2]}:

Platelets are modified by covalent attachment of anti-PD-L1 to surface proteins through a bifunctional linker. The engineered platelets are deployed to the surgical wound site, become activated, and produce both inflammatory mediators and platelet-derived microparticles (PMPs) with anti-PD-L1 on their surfaces. The release of PMPs and inflammatory mediators results in the activation of CD8+ T cells and hence antitumor activity mediated by the interaction between T-cell receptors (TCR) and the major histocompatibility complex (MHC).

From the recent paper by Wang et al the authors state:

Cancer recurrence after surgical resection remains a significant challenge in cancer therapy. Platelets, which accumulate in wound sites and interact with circulating tumour cells (CTCs), can however trigger inflammation and repair processes in the remaining tumour microenvironment. Inspired by this intrinsic ability of platelets and the clinical success of immune checkpoint inhibitors, here we show that conjugating anti-PDL1 (engineered monoclonal antibodies against programmed-death ligand 1) to the surface of platelets can reduce post-surgical tumour recurrence and metastasis.

Using mice bearing partially removed primary melanomas or triple-negative breast carcinomas (4T1), we found that anti-PDL1 was effectively released on platelet activation by platelet-derived microparticles, and that the administration of platelet-bound anti-PDL1 significantly prolonged overall mouse survival after surgery by reducing the risk of cancer regrowth and metastatic spread. Our findings suggest that engineered platelets can facilitate the delivery of the immunotherapeutic anti-PDL1 to the surgical bed and target CTCs in the bloodstream, thereby potentially improving the objective response rate.

[Check Point Inhibitors](#)

^{8[2]} <http://www.nature.com/articles/s41551-017-0031/figures/2>

There are a multiplicity of ligands and receptors which can enhance the process or inhibit the process. The inhibitory one are checkpoints and therapy addressing these inhibitory functions are termed checkpoint blockade. We briefly depict some of the current and somewhat well-known ones. A warning should be noted. It seems to be common place amongst immune therapies that as one barrier is climbed others soon appear. Thus, this may very well be merely a first step in an ever continuing understanding of the complexities of the immune systems.

[CTLA-4](#)

CTLA-4 is a checkpoint inhibitor. It has the potential to inhibit the actions of the immune cells to the cell expression this. As Topalian et al state:

The conventional wisdom underlying our vision of how CTLA-4 blockade mediates tumor regression is that it systemically activates T cells that are encountering antigens.

CTLA-4 represents the paradigm for regulatory feedback inhibition. Its engagement down-modulates the amplitude of T cell responses, largely by inhibiting co-stimulation by CD28, with which it shares the ligands CD80 and CD86. As a “master T cell co-stimulator,” CD28 engagement amplifies TCR signaling when the T cell receptor (TCR) is also engaged by cognate peptide-major histocompatibility complex (MHC).

However, CTLA-4 has a much higher affinity for both CD80 and CD86 compared with CD28, so its expression on activated T cells dampens CD28 co-stimulation by out-competing CD28 binding and, possibly, also via depletion of CD80 and CD86 via “trans-endocytosis”. Because CD80 and CD86 are expressed on antigen-presenting cells (APCs; e.g., dendritic cells and monocytes) but not on non-hematologic tumor cells, CTLA-4’s suppression of anti-tumor immunity has been viewed to reside primarily in secondary lymphoid organs where T cell activation occurs rather than within the tumor microenvironment (TME).

Furthermore, CTLA-4 is predominantly expressed on CD4+ “helper” and not CD8+ “killer” T cells. Therefore, heightened CD8 responses in anti-CTLA-4-treated patients likely occur indirectly through increased activation of CD4+ cells. Of note, a few studies suggest that CTLA-4 can act as a direct inhibitory receptor of CD8 T cells, although this role in down-modulating anti-tumor CD8 T cell responses remains to be directly demonstrated. The specific signaling pathways by which CTLA-4 inhibits T cell activation are still under investigation, although activation of the phosphatases SHP2 and PP2A appears to be important in counteracting both tyrosine and serine/threonine kinase signals induced by TCR and CD28.

CTLA-4 engagement also interferes with the “TCR stop signal,” which maintains the immunological synapse long enough for extended or serial interactions between TCR and its peptide-MHC ligand. Naive and resting memory T cells express CD28, but not CTLA-4, on the cell surface, allowing costimulation to dominate upon antigen recognition.

[PD-1](#)

In a similar manner to CTLA-4, PD-1 is also an inhibitor. As Topalian et al state:

The PD-1 system of immune modulation bears similarities to CTLA-4 as well as key distinctions. Similar to CTLA-4, PD-1 is absent on resting naive and memory T cells and is expressed upon TCR engagement. However, in contrast to CTLA-4, PD-1 expression on the surface of activated T cells requires transcriptional activation and is therefore delayed.

Also in contrast to CTLA-4, PD-1 contains a conventional immunoreceptor tyrosine inhibitory motif (ITIM) as well as an immunoreceptor tyrosine switch motif (ITSM). PD-1's ITIM and ITSM bind the inhibitory phosphatase SHP-2. PD-1 engagement can also activate the inhibitory phosphatase PP2A. PD-1 engagement directly inhibits TCR-mediated effector functions and increases T cell migration within tissues, thereby limiting the time that a T cell has to survey the surface of interacting cells for the presence of cognate peptide-MHC complexes.

Therefore, T cells may "pass over" target cells expressing lower levels of peptide-MHC complexes. In contrast to CTLA-4, PD-1 blockade is viewed to work predominantly within the TME, where its ligands are commonly overexpressed by tumor cells as well as infiltrating leukocytes. This mechanism is thought to reflect its important physiologic role in restraining collateral tissue damage during T cell responses to infection. In addition, tumor-infiltrating lymphocytes (TILs) commonly express heightened levels of PD-1 and are thought to be "exhausted" because of chronic stimulation by tumor antigens, analogous to the exhausted phenotype seen in murine models of chronic viral infection, which is partially reversible by PD-1 pathway blockade.

Importantly, the phenotypes of murine knockouts of PD-1 and its two known ligands are very mild, consisting of late-onset organ-specific inflammation, particularly when crossed to autoimmune-prone mouse strains. This contrasts sharply with the Ctla-4 knockout phenotype and highlights the importance of the PD-1 pathway in restricting peripheral tissue inflammation. Furthermore, it is consistent with clinical observations that autoimmune side effects of anti-PD-1 drugs are generally milder and less frequent than with anti-CTLA-4. Despite the conventional wisdom that CTLA-4 acts early in T cell activation in secondary lymphoid tissues whereas PD-1 inhibits execution of effector T cell responses in tissue and tumors, this distinction is not absolute.

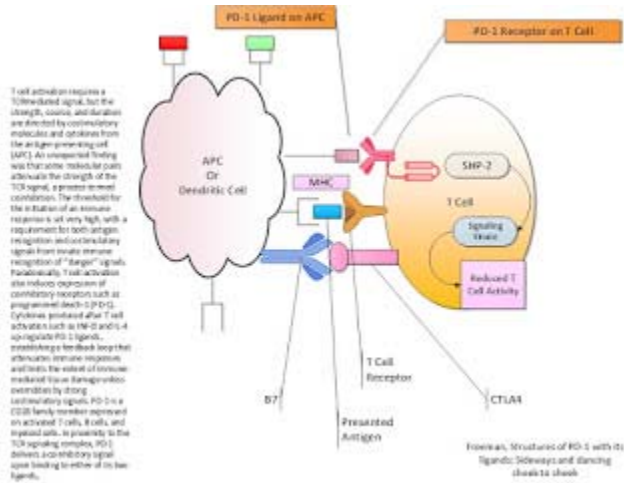
Beyond its role in dampening activation of effector T cells, CTLA-4 plays a major role in driving the suppressive function of T regulatory (Treg) cells. Tregs, which broadly inhibit effector T cell responses, are typically concentrated in tumor tissues and are thought to locally inhibit anti-tumor immunity.

Therefore, CTLA-4 blockade may affect intratumoral immune responses by inactivating tumor-infiltrating Treg cells. Recent evidence has demonstrated anti-tumor effects from CTLA-4 blockade even when S1P inhibitors block lymphocyte egress from lymph nodes, indicating that this checkpoint exerts at least some effects directly in the TME as opposed to secondary lymphoid tissues.

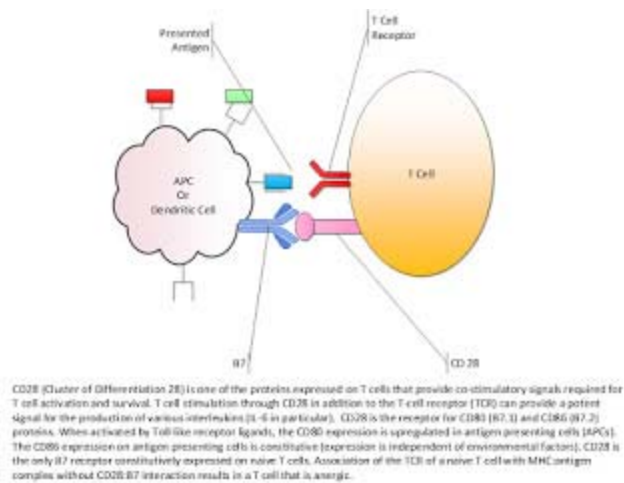
Conversely, PD-1 has been shown to play a role in early fate decisions of T cells recognizing antigens presented in the lymph node. In particular, PD-1 engagement limits the initial "burst

size'' of T cells upon antigen exposure and can partially convert T cell tolerance induction to effector differentiation.

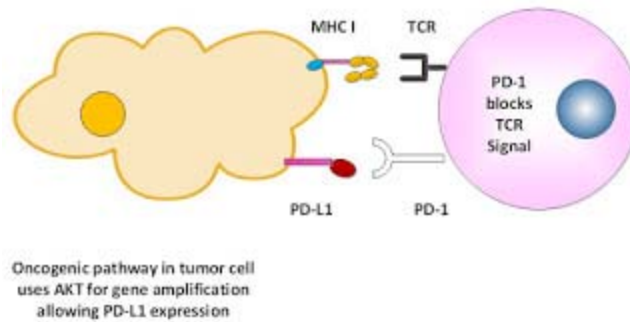
The authors present a graphic regarding how this blocking or checkpoint functions. We depict this below. Let us briefly review the issue of checkpoint inhibitors.



The process can be simplified as below:



The authors present a graphic regarding how this blocking or checkpoint functions. We depict this below.



As Freeman states:

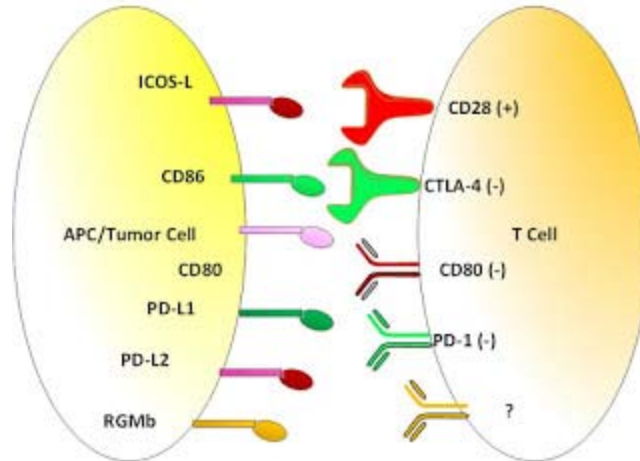
T cell activation requires a TCR mediated signal, but the strength, course, and duration are directed by costimulatory molecules and cytokines from the antigen-presenting cell (APC). An unexpected finding was that some molecular pairs attenuate the strength of the TCR signal, a process termed coinhibition. The threshold for the initiation of an immune response is set very high, with a requirement for both antigen recognition and costimulatory signals from innate immune recognition of “danger” signals.

Paradoxically, T cell activation also induces expression of coinhibitory receptors such as programmed death-1 (PD-1). Cytokines produced after T cell activation such as INF- and IL-4 up-regulate PD-1 ligands, establishing a feedback loop that attenuates immune responses and limits the extent of immune-mediated tissue damage unless overridden by strong costimulatory signals. PD-1 is a CD28 family member expressed on activated T cells, B cells, and myeloid cells. In proximity to the TCR signaling complex, PD-1 delivers a coinhibitory signal upon binding to either of its two ligands, PD-L1 or PD-L2.

Engagement of ligand results in tyrosine phosphorylation of the PD-1 cytoplasmic domain and recruitment of phosphatases, particularly SHP2. This results in dephosphorylation of TCR proximal signaling molecules including ZAP70, PKC, and CD3, leading to attenuation of the TCR/CD28 signal.

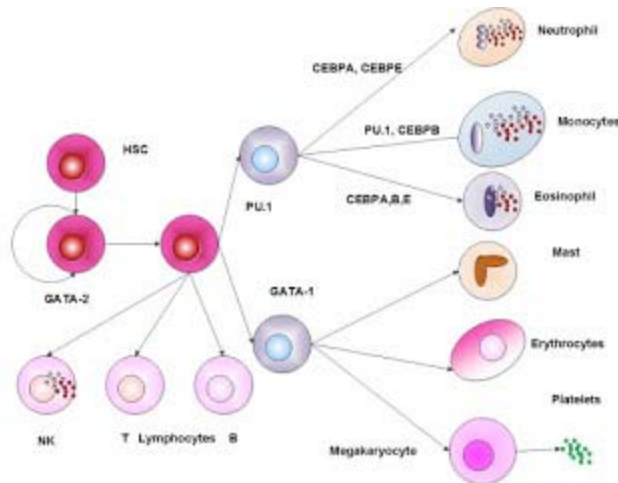
The role of the PD-1 pathway in peripheral T cell tolerance and its role in immune evasion by tumors and chronic infections make the PD-1 pathway a promising therapeutic target.

There are potentially many such check points. Some of them are graphically shown below.

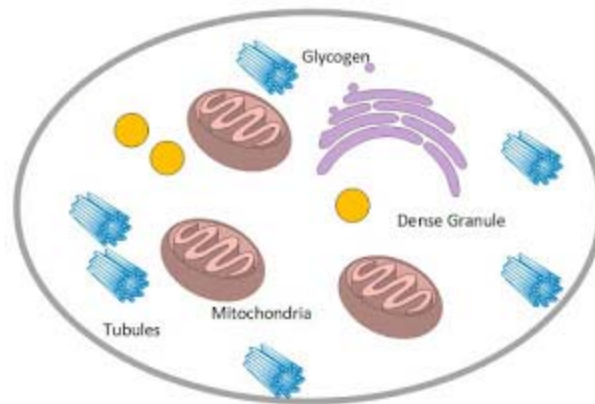


Platelets

Now we briefly review the issue of platelets. The diagram below is the now classic description of the blood stem cell development. Platelets derive from Megakaryocytes. Their primary function is to provide barriers to the blood stream when there is some form of compromise such as a cut. Normally platelets just flow in the blood stream and do nothing, unless there is some aberrant factor where a clot may result as may happen in a clot in a stroke or heart attack.



The platelet is a small cell like structure with multiple mitochondria along with several other elements all of which allow the platelet to perform its function.



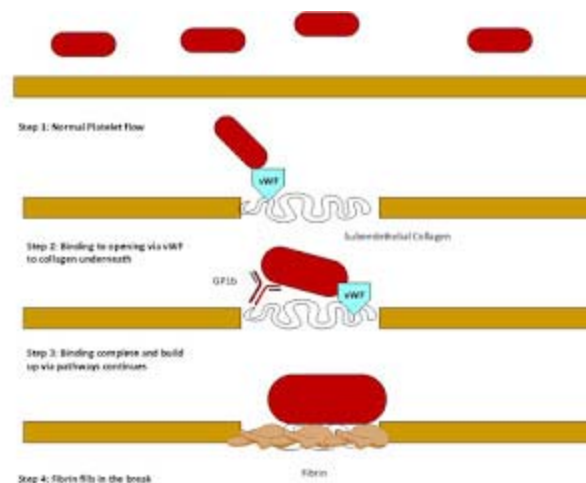
Now we can describe how the platelet is activated to do what it is supposed to do. Below we show the basic processes which occur. Normal blood flow allows the platelets to just move through the blood stream.

Then if a break or cut occurs and the platelets are exposed to the subendothelial collagen they get activated and adhere via a von Willenbrand Factor connection.

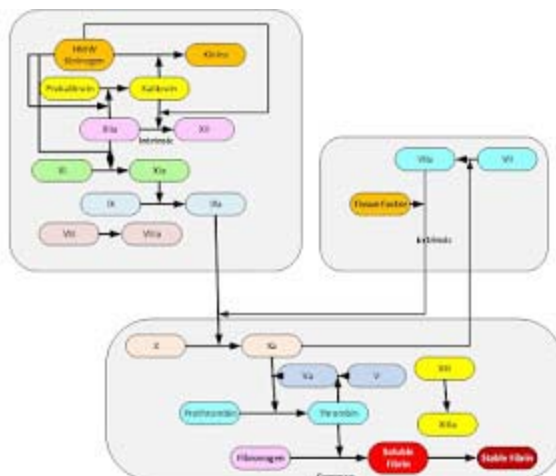
Once this attachment occurs several other steps make the various attachments and allow the platelet to expand.

Finally via the process of the pathways the process produces a clot that seals the open lesion.

Fundamentally all of this involves the adhesion of the platelets to the surfaces outside the blood stream.



Now the formation of the clot is a result of the interaction of a set of proteins in the blood stream. The flow of these proteins and their different activations result in a fibrin clot. We show below the three pathways that effect; extrinsic, intrinsic and common.



As noted in Hoffman et al:

If vascular injury occurs, a measured response is triggered in that the extent of damage regulates platelet and fibrin deposition.

Activated platelets provide the membrane surfaces upon which coagulation enzymes can be anchored, assembled, and expressed. Therefore, the activated platelet membrane, provides both an initiating and limiting component to the extent of a coagulation reaction.

More vascular damage produces more anchored activated platelets, and more membrane allows the assembly of more coagulation enzymes, which ultimately results in increased fibrin formation. When the vascular system is perturbed, the initial stages of the hemostatic response are triggered.

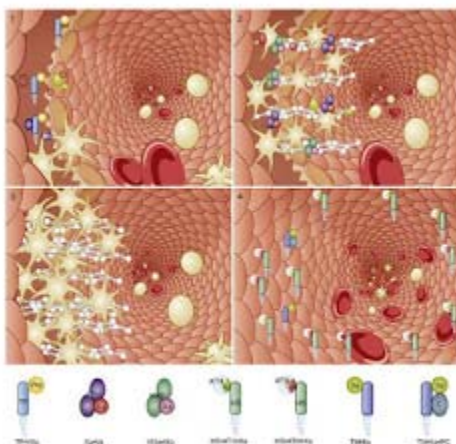
The initial principal player is the extrinsic tenase complex (tissue factor; factor VIIa), which is composed of a cell membrane; tissue factor exposed by vascular damage or cytokine stimulation; Ca^{2+} ; and the serine protease plasma factor Vila, which is already present in its active form at 1% to 2% of the factor VII zymogen concentration.

Before binding to tissue factor, the plasma serine protease factor Vila is essentially inert from the catalytic perspective and thus impervious to the abundant protease inhibitors in plasma.²⁸⁹ Factor VII also competes with factor Vila for tissue factor binding, thus serving as a negative regulator that buffers the overall reaction.

Factor VII activating protease (FSAP) has also been shown to activate factor VII in the absence of tissue factor. The physiologic function of FSAP still is unclear but most recently has been suggested to be involved in inflammation.

The extrinsic tenase complex (tissue factor-factor Vila) activates low levels of the zymogens factor X and factor IX to their respective serine protease enzymes factor Xa (~10 pM) and factor IXa (=1 pM).^{296,297} Factor X is the more efficient and abundant substrate.

A simplistic view from Hoffman et al is shown below:



As Mahmoudi and Farokhzad note:

Platelet activation has been shown to result in the release of an estimated 300 proteins and biomolecules, among which are key pro-inflammatory molecules including CD154 (also known as CD40 ligand), which is a potent molecule involved in lymphocyte activation¹¹. Capitalizing on the functions of platelets both in haemostasis and inflammation, Gu and colleagues show that the engineered anti-PD-L1 immunoplatelet conjugates accumulate and activate at the site of surgery, inducing T-cell activation through the synergistic action of PMP-bound anti-PD-L1 and a myriad of released pro-inflammatory mediators. The authors also demonstrate the value of their technology over conventional anti-PD-L1 therapy.

Now Hoffman et al discuss how these propagate:

When a sufficient stimulus is provided to overcome the antagonist-inhibitor threshold, the accumulating mass of activated platelets will support increasing intrinsic tenase and prothrombinase complex formation on their surfaces through specific platelet receptors, and the local inhibitor concentrations are overwhelmed.

These platelet-bound catalysts execute the propagation phase of the reaction, during which massive amounts of thrombin are produced." This phase of thrombin generation continues, independent of the initially presented tissue factor, as long as there is a continuous supply of blood to deliver new plasma procoagulant reactants, platelets, and fibrinogen to the site of perforation in the vascular endothelium.

Important to the formation of the prothrombinase complex is the generation of factor Xa. Factor Xa is a unique regulatory enzyme in that it is formed through both the intrinsic tenase and the extrinsic tenase complexes. Under normal conditions, the concentration of factor Xa is the rate-limiting component of the prothrombinase complex.

The other components of the complex, platelets (membrane surface binding sites), and the cofactor (factor Va) are activated rapidly to produce a surplus that is ready for action.¹ The coagulation mechanism can become sensitive to factor V or platelets when confronted with

congenital deficiencies, thrombocytopenia, platelet pathology, or pharmacologic interventions. The initial factor Xa is generated via the tissue factor-factor Vila complex during the initiation phase. Additional factor Xa is then generated by the intrinsic tenase complex (factor IXa-factor VIIIa-membrane-Ca²⁺). Initially, the concentration of the factor Vila -tissue factor complex is higher than the concentration of the factor Villa-factor IXa complex, which requires activation and assembly.

As time progresses, the contribution of the intrinsic tenase complex to factor Xa generation exceeds that of the extrinsic tenase. " The intrinsic tenase complex is kinetically more efficient and activates factor X at a 50- to 100-fold higher rate than the extrinsic tenase complex. The burst of factor Xa that is generated overcomes the levels of factor Xa inhibitors, such as TFPI, and achieves maximal prothrombinase activity and propagation of the procoagulant response.

The bulk of thrombin (.95%) is formed during the propagation phase after fibrin clot formation. Without the intrinsic tenase complex being formed, as occurs in hemophilia A or B, factor Xa is not generated in levels sufficient to produce the propagation phase of thrombin generation.

Observations

The principle of checkpoint blockade has become an essential paradigm in the treatment of cancers via immunotherapy. Namely, these checkpoint molecules can prevent the immune system from attacking the cancer cell. However if one were to systemically introduce blockers to these checkpoints, using say a monoclonal anti-body, Mab, then one could allow the immune system to do what it is supposed to do. This is a systemic approach however, since it blocks all PD-1 or similar check points. In this example use if made of platelets, which can be used to seek out specific spots, namely where surgery on a tumor may have been performed, and use that approach to block the checkpoints using locally provided Mabs. It is an intriguing application that deserves some examination.

As Mahmoudi and Farokhzad state:

Striking a balance between T-cell activation and inhibition is crucial for the proper functioning of the immune system. Among the expanding list of molecules referred to as immune checkpoints and involved in the inhibition of T-cell function, the two most validated to date are the cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), expressed on activated T cells, and the programmed cell death protein-1 (PD-1), which binds to its ligands (the PD-L1 and PD-L2 proteins expressed on many cell types) and interrupts signalling mediated by the T-cell antigen receptor.

The ability to modulate the activity of these checkpoints has given rise to the field of immune-checkpoint therapy, now considered a pillar of cancer therapy. On the basis of the most validated immune checkpoints identified to date (CTLA-4, PD-1 and PD-L1), four antibodies have been approved for clinical use: ipilimumab, nivolumab, pembrolizumab and atezolizumab. Durable patient responses have been documented, and in the case of ipilimumab, which has the longest clinical history, survival of 10 years or more has been reported in a subset of patients with melanoma.

As they note, currently there are a limited number of Mabs which have been approved but their existence and use has become a substantial paradigm shift. Yet one of the major concerns is still the systematic impact. Some patients can respond reasonably while other have adverse responses. Perhaps it is the systematic application

Although the clinical success of these drugs has transformed immune checkpoint inhibitors into a powerful class of therapeutics (for example, global sales of nivolumab are projected to reach ~US\$3 billion in 2020)⁵, the exaggerated T-cell activation that they trigger leads to a broad range of adverse effects.

The latter remark is often the most compelling. Mabs, albeit somewhat straightforwardly designed and produced still have to bear the substantial clinical costs associated with safety and efficacy.

The above authors also note:

Gu (see Wang et al) and colleagues' conjugation strategy for the targeted delivery of immune checkpoint inhibitors to the surgical wound may pave the way for safer and more effective checkpoint therapy in an adjuvant setting while ameliorating some of the adverse effects of systemic administration. Although the system is complex and the scalability, regulatory and manufacturing hurdles are considerable, it is tantalizing to imagine that the efficacy of the authors' approach may be further improved by attachment of anti-CTLA-4, which has a mechanism of action distinct from, but synergistic with, that of PD-L1. In fact, clinical experience to date has shown that combination therapy with anti-CTLA-4 and anti-PD-1 confers additional clinical benefits. But the application of such therapy is limited by a higher incidence of toxicities and their broader spectrum. Gu and co-authors' approach could thus facilitate such combination therapy and mitigate its adverse effects.

This again addresses the focusing of the Wang/Gu approach to specific locations. However as we know the concerns that some of these address have a significant potential for rapid metastasis. That presents a challenge if we see only local application.

Additionally, the authors' conjugate approach could be combined with recently developed nanotechnologies that make use of platelet biology, such as nanoparticle-coating platelet membranes isolated from human blood that enhance the nanoparticles' circulation time and their ability to target injured vasculature.

The combination of both methods might eventually lead to the in situ synthesis of anti-PD-L1-conjugated platelet-membrane-coated nanoparticles that can simultaneously carry other agonists to augment T-cell responses. To accelerate the clinical translation of such strategies, proper regulatory standards must be established to overcome any issues associated with the development of biologically modified platelets and to ensure robust and reproducible conjugation chemistry in combination with analytical methods to support the manufacturing of the final biologic product.

As Wang et al note:

Cell-based systems have recently emerged as biological drug carriers; examples include erythrocytes, bacterial ghosts, and genetically engineered stem and immune cells. Among them, platelets are anucleated cellular fragments released from megakaryocytes and are best known for their function in hemostasis. The average life span of circulating platelets is 8 to 9 days, which could greatly improve the pharmacokinetics of intravenously injected therapeutics.

Moreover, transfused platelets could migrate to the site of surgical wounds³³, where residual tumours may survive after surgery. Emerging evidence has shown that platelets also have the capability to recognize and interact with CTCs, which are shed from the primary tumour into the bloodstream and can lead to metastases. Along with their intrinsic tendencies to accumulate at wounds and to interact with CTCs, platelets are also considered immune 'cells' that initiate and enhance many inflammatory conditions. Platelet-derived chemokines recruit and awaken T cells as well as other immune cells.

As the major source of soluble CD40L (sCD40L), platelets can boost the T-cell immune response and are necessary for inducing dendritic cell maturation and B-cell isotype switching for production of immunoglobulin G (IgG). It has also been reported that PDL1 and PDL2 are upregulated in response to inflammation, which results in PDL1-positive tumours, making the tumour more sensitive to anti-PD therapy and potentially improving the objective response rate. In this work, inspired by the intrinsic properties of platelets, we conjugated anti-PDL1 (antibodies against PDL1; hereafter, aPDL1) to the surface of platelets for use as a preventative treatment for post-surgical tumour recurrence.

With the help of platelets, aPDL1 can be targeted to the cancer cells after surgery, while reducing off-target effects.

It is the above observation which has substantial merit. Many of the Mab check point inhibitors systematically engage all cells in the body, often with substantial effects.

We found that the binding of aPDL1 to non-activated platelets was highly stable, while release of aPDL1 could be significantly promoted on the activation of platelets. We reasoned that the aPDL1 release may result from the platelet-derived microparticles (PMPs), which are generated from the plasma membrane of activated platelets⁴³. Such structural alterations can facilitate aPDL1 binding to tumour cells and APCs.

By intravenous injection of aPDL1-conjugated platelets (P-aPDL1) into mice with B16 melanomas and triplenegative mammary carcinomas that had been previously resected (~1% remaining), we showed that platelets can facilitate aPDL1 transport to residual microtumours at the surgical site, and to CTCs in the blood.

The issue of micro-tumors has always been of significant interest. Melanomas are notorious for escaping un-noticed. Often with lymph node resection, small clusters of melanoma cells can be seen, even where they are least expected.

A T-cell-inflamed tumour microenvironment was created by the platelets on activation, leading to increased PDL1 expression at the tumour site. aPDL1 was effectively released after platelet activation, thereby blocking PDL1 on tumour and APCs. Our results show that platelets have promise as a means of targeted, controlled delivery of aPDL1 for the prevention of cancer recurrence post-surgery.

The post-surgical results are especially favorable and this is for a quasi-system approach. Notwithstanding this approach could be used in a balanced multiprotocol effort as well as a post-surgical adjuvant approach.

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Labels: [Cancer](#)

MONDAY, MARCH 27, 2017

SNOWFLAKES?

I think I am understanding this snowflake explosion. namely folks who believe the world is collapsing about them and the world is dominated by evil people and that they must be protected. Thus the idea that science is being suppressed and that resistance is essential to their survival. Now we are not in Stalinist USSR nor in Hitlerian Germany. Yet the response of these folks seems to be on such a level.

I will be the first to admit that Washington is a mess. It was ever since George gave the country the swamp land along the Potomac. It was a malaria ridden piece of useless land, not good for farming and on the wrong side of the Potomac for George. Now George like Mount Vernon, up on a hill side, good farmable land, and safely in Virginia. So why not look good and give the new country that Maryland side which no one wanted anyhow. Even the Brits had DC as a hardship post for its diplomats in the 19th century. Malaria and even yellow fever at times. It was a swamp! Nothing really has changed, metaphorically that is.

Now along comes the snowflakes in [NEJM](#):

In the face of suppression of science, should scientists resist, or quietly proceed with their work? Resistance seems essential. That the CDC postponement prompted a coalition to form and organize an alternative meeting, reminds us that resistance is as much about ensuring effective dissemination of findings as about continuing to conduct science. But it's critical to recognize that suppressing science does not cause disbelief; rather, disbelief, particularly of science pertaining to highly politicized topics such as climate change, creates a cultural environment in which suppression of science is tolerated. So the real question is how do we resist effectively? How do we convince a skeptical public to believe in science?

Just what suppression is occurring? Government changes and focus changes. Ever think of striking out on your own! Like entrepreneurs, independent of Government, get a great deal done on less. Government should not and must not be the sole supporter of science. No one is silencing any scientist, even if a Government changes hands. Go elsewhere, young person, and strike out on your own! As for resistance, the ultimate form is the same, going out on your own! You will not melt.

This fear that "mommy" Government may not "give" them what the "need", or "demand", is neither suppression nor should it warrant resistance. Cancer cure is a challenge. Cancer inflicts its pain on everyone, sooner or later. So go out and get funding from everyone. Frankly Government funding has its own serious drawbacks. Government bureaucrats determine what direction is best, demand large "team" efforts, and can just as quickly and arbitrarily change course.

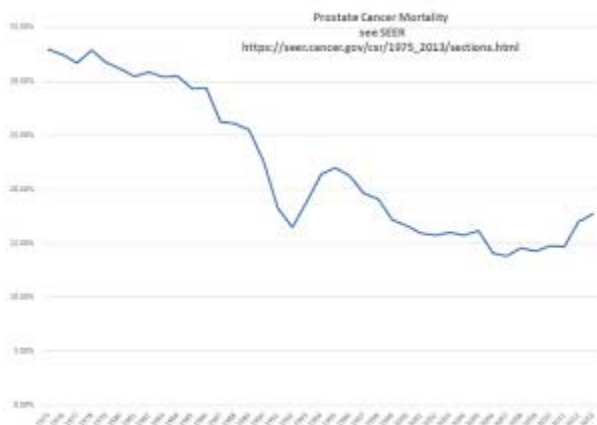
So stop crying, stop resisting, and do something productive!



Labels: [Health Care](#)

SUNDAY, MARCH 26, 2017

[TO TEST OR NOT TO TEST?](#)



Prostate cancer mortality had dropped more than 50% with the introduction of PSA testing as shown above. The along came the previous Administration and its Medical advisors and they recommended the elimination of PSA testing. The result appears above, albeit the SEER data stopped reporting because of alleged massive irregularities in the data gathered. I guess if the facts don't measure up to the "theory" one then changes the facts. Welcome to Washington.

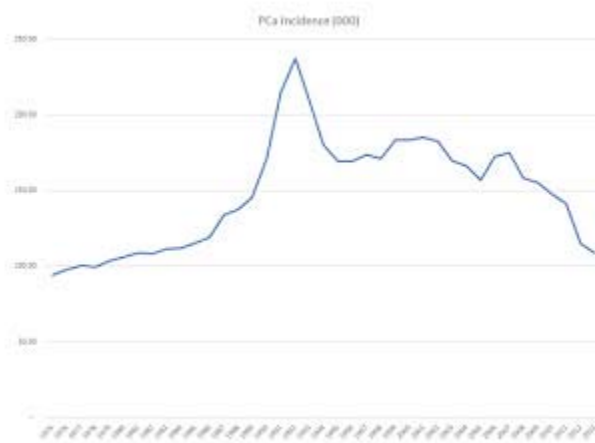
As just reported in [UroToday](#):

In the last update of the ERSPC with follow-up truncated at 13 years, a significant 21% relative reduction in prostate cancer was demonstrated in intention to screen analyses, and 27% in men who actually attended screening. The absolute risk reduction of death from prostate cancer at 13 years was 1.28 fewer prostate cancer deaths per 1,000 men randomized. A total of 781 men needed to be invited to screening and 27 to be diagnosed with prostate cancer to avert one death from the disease. These numbers are predicted to go lower in the next update of the study incorporating 16 years of follow-up. The main disadvantage of screening is the increased risk of over-diagnosis of prostate cancer due to screening, meaning detection of non-significant low risk cancers. Despite showing a clear prostate cancer mortality reduction, the findings were not sufficient to justify population-based screening. The harms of screening will need to be further assessed and strategies to overcome over-diagnosis and overtreatment will need to be implemented. In the interim, well-informed men suitable for screening should be able to undergo PSA testing if they wish, after careful consideration of the pros and cons. Dr. Hugosson emphasized on the incidence of prostate cancer after termination of screening which has doubled. He also noted that there is a difference in the intensity of screening in different European countries. This translates into differences in mortality reduction. Additionally, the number of PSA tests is also correlated to mortality. Results show that the better patients are screened and the more PSA blood test are done, less death occurs.

Even the above has problems:

1. Fundamentally and simplistically, PCa falls into two distinct types; indolent (Type I) and aggressive (Type II). Frankly we really do not know which is which other than Type II can go from nothing to death in four to five years. Type I just seems to go no where fast. Many genetic studies have examined those with less than sterling results. We have estimated that 10% are Type II and 90% are Type I.
2. Thus measuring for PCa with PSA annually really only affects Type II, in general. Thus is the incidence if say 100,000 pa and there are 10,000 Type II, and we do not test them then they will all die. In fact. the PCa is so aggressive that no matter what they will almost surely die.
3. In addition is there are some of the Type I who will die, a small percent, say 5%.
4. Then the total mortality is say 15%. This is just a back of the envelope calculation to make the point.
5. Now we also have a strange set of data. Namely the incidence of PCa is dropping. Namely the denominator is dropping for reasons we do not seem to fully understand. The results below are

difficult to reason with since there is a massive peak and then a precipitous drop. The real world does not work this way unless we understand why. Bad data, however, does.



6. Now what does this all say? Well simply that PSA seems to help, and perhaps even helps in reducing the incidence, if we believe that data. The other problem of course is the diagnosis of HGPIN initially as carcinoma in situ. This may or may not be swept into the total. Since HGPIN may disappear then how does one readjust the data? There does not seem to be an answer to this.

7. Now a second result from UroToday on the use of MRI is also telling.

8. The use of [Multi Parametric MRI](#) has been suggested as essential. They state:

...utilizing multiparametric MRI (mpMRI) for all patients when clinically indicated for prostate cancer. He highlighted that mpMRI truly encompasses three different entities: prostate (i) anatomy (T2-weighted imaging (T2W)), (ii) biology (diffusion-weighted imaging (DWI)), and (iii) vascularity (dynamic contrast enhancement (DCE)). T2W imaging allows for an excellent assessment of the transitional and peripheral zones of the prostate, as well as the neurovascular bundles. DCE..

We have argued that based upon some tests that MRI often picks up previous biopsy scar tissues which may get vasculated as suspect then actually requiring a subsequent biopsy.

9. A [second study indicating that MRIs](#) can be performed in a simpler environment (ie mpMRI) where they state:

that mpMRI has improved biopsy decision making and the yield of clinically significant prostate cancer, albeit with the caveat of significant cost and time. On the other hand, bMRI (T2W and diffusion-weighted imaging (DWI)) can give a "quick, 15 minute, no frills MRI of the prostate" described how when he started in the prostate imaging arena nearly 20 years ago, he wanted "everything" that an MRI had to offer, namely T2, DWI, diffusion contrast enhancement (DCE), and spectroscopy. Over time it became evident to... that MR-spectroscopy was costly and added very little to the clinical picture. Since then he has also advocated for only utilization of DCE (ie mpMRI) for challenging cases.

The same argument as above also applies. MRIs are expensive and the use of gadolinium has significant adverse effects in some, especially the use of cumulative gadolinium.

10. Overall we still see significant uncertainties with PCa and the fact that a Government entity removes from the toolbox the only tool we may have to save money under the guise of preventing "harms", namely discomfort after an exam, pales in contrast to the horrible death from this disease.

Thus despite the Government's clawing hold on health care, perhaps a walk down a cancer ward, if any still exist, could enlighten some of the folks i Washington! Yet I doubt it.



Labels: [Cancer](#), [Health Care](#)

WEDNESDAY, MARCH 22, 2017

[INCIDENTAL](#)

What is the meaning of words. Take "incidental". In medicine it oftentimes has an ominous meaning. Say we do a physical. The patient looks fine. The patient is a marathon runner, no heart problems, no other issues. Great lipids, low blood sugars, great blood pressure, EKG perfect. The on a CBC we see an incidental finding. The thrombocytes look a bit off, well, quite a bit off.

This incidental finding then leads to a bone marrow test. Ooops. Myelodysplastic Syndrome, MDS. This patient may be 6 months away from AML and another six months away from death! The patient hears incidental, the physician hears terminal.

Beware of the downplaying of incidental. Especially in espionage. You see, good intelligence, against them or us, just ask MI6 about their blunders, all those Communist Spies from Cambridge, that the incidental can expose a foreign entity as well as a domestic.

Beware of "incidental". It can be deadly!



Labels: [Commentary](#)

[I GUESS YOU CAN CORRELATE ANYTHING!](#)

We know that Type 2 Diabetes is caused in almost all cases by obesity. The causative path has been well defined via the inflammatory results of obesity. Now along comes a bunch of authors who find that the change in local temperature, also known as Global Warming, is the putative cause of this obesity. Namely that fat people live in warm States.

The [authors state](#):

Our findings indicate that the diabetes incidence rate in the USA and prevalence of glucose

intolerance worldwide increase with higher outdoor temperature.

This is a correlation at best and NOT a causation. The problem is that one must look at the socioeconomic status. Just look at West Virginia. I know it well. Low economic status, poor diets, less exercise, and many folks on Government type meals, aka high carbs. It is not the temperature.

If one were to look worldwide, hot climates do not engender high BMI and in turn high rates of Type 2 Diabetes. It is just the opposite. The Congo is not filled with obese people and has low Type 2 Diabetes.

Besides all the authors are from the Netherlands. Perhaps a trip through West Virginia would help. Can they even find it on a map!



Labels: [Academy](#), [Health Care](#)

SATURDAY, MARCH 18, 2017

THE TRIVIUM

Current Academics have been promulgating the use of what at best is "sloppy English". Namely that we should not penalize or even comment on poor Grammar. But the [NY Times](#) presents an interesting case where Grammar applies. Namely:

The debate over commas is often a pretty inconsequential one, but it was anything but for the truck drivers. Note the lack of Oxford comma — also known as the serial comma — in the following state law, which says overtime rules do not apply to:

The canning, processing, preserving, freezing, drying, marketing, storing, packing for shipment or distribution of:

- (1) Agricultural produce;*
- (2) Meat and fish products; and*
- (3) Perishable foods.*

Does the law intend to exempt the distribution of the three categories that follow, or does it mean to exempt packing for the shipping or distribution of them? Delivery drivers distribute perishable foods, but they don't pack the boxes themselves. Whether the drivers were subject to a law that had denied them thousands of dollars a year depended entirely on how the sentence was read. If there were a comma after "shipment," it might have been clear that the law exempted the distribution of perishable foods. But the appeals court on Monday sided with the drivers, saying the absence of a comma produced enough uncertainty to rule in their favor. It reversed a lower court decision.

Thus words and punctuation have consequences. There is a trend in schools that we should accept common usage of English because it is a fluid language and if some child makes up some phrase then we should not tell them otherwise. It would be threatening to them. Tell that to the folks who lost \$10 million. Perhaps their attorneys should return to the Fifth Grade at Blessed Sacrament Grammar School. Sister Rosita drilled this into us then.

Words have meanings and words have consequences. Everywhere! God Bless Sister Rosita!

Also remember that the Trivium was the required study of Grammar, Logic, and Rhetoric, in that order, during the High Middle Ages. First, words mean something. Then, second, words that mean something alone can only mean something when assembled in the proper manner. Third, explaining your conclusion must be done in a rational and reasoned and articulate manner. Once you have mastered this you can get a College degree. Don't master these in the 14th Century and you shovel dung for a few decades at best!



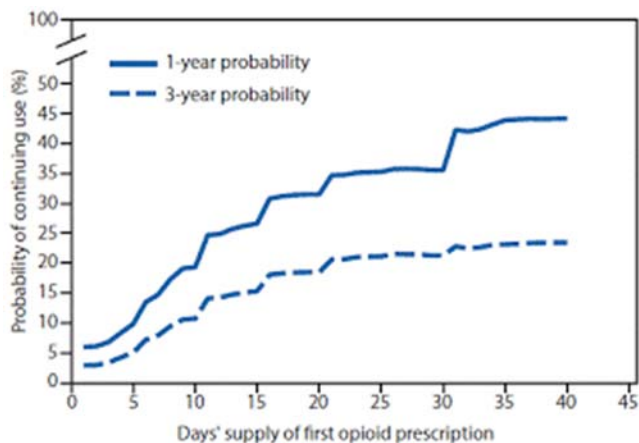
Labels: [Academy](#)

OPIOID ABUSE

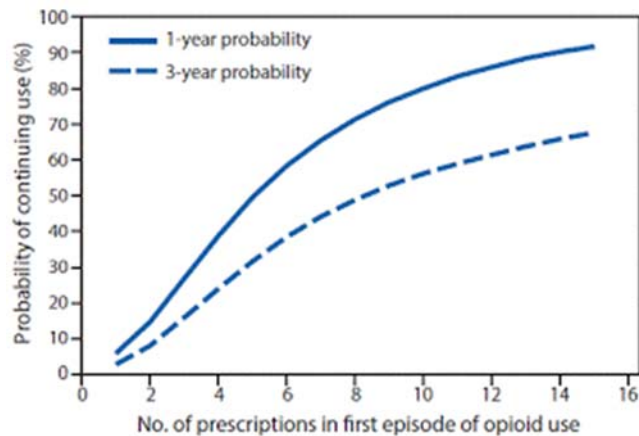
The CDC in this weeks [MMWR](#) notes:

The probability of long-term opioid use increases most sharply in the first days of therapy, particularly after 5 days or 1 month of opioids have been prescribed, and levels off after approximately 12 weeks of therapy. The rate of long-term use was relatively low (6.0% on opioids 1 year later) for persons with at least 1 day of opioid therapy, but increased to 13.5% for persons whose first episode of use was for ≥ 8 days and to 29.9% when the first episode of use was for ≥ 31 days. Although ≥ 31 days of initial opioid prescriptions are not common, approximately 7% do exceed a 1-month supply. Discussions with patients about the long-term use of opioids to manage pain should occur early in the opioid prescribing process, perhaps as early as the first refill, because approximately 1 in 7 persons who received a refill or had a second opioid prescription authorized were on opioids 1 year later. As expected, patients initiated on long-acting opioids had the highest probabilities of long-term use. However, the finding that patients initiated with tramadol had the next highest probability of long-term use was unexpected; because of tramadol's minimal affinity for the μ -opioid receptor, it is deemed a relatively safe opioid agonist with lower abuse potential than other opioids

The results are below:



and also:



They conclude:

Transitions from acute to long-term therapy can begin to occur quickly: the chances of chronic use begin to increase after the third day supplied and rise rapidly thereafter. Consistent with CDC guidelines, treatment of acute pain with opioids should be for the shortest durations possible. Prescribing 1 week of opioids or when authorizing a refill or a second opioid prescription because these actions approximately double the chances of use 1 year later. In addition, prescribers should discuss the long-term plan for pain management with patients for whom they are prescribing either Schedule II long-acting opioids or tramadol.

This is a significant and important result. All physicians for license renewal must take a course and be tested on dealing with opioid abuse. Hydrocodone and Oxycodone have been distributed somewhat freely in the past and their impact not fully understood. Today with the above results as a start much more careful handling is essential.



Labels: [Health Care](#)

THURSDAY, MARCH 16, 2017

[POVERTY, CHASTITY AND DISOBEDIENCE](#)

In the 13th and 14th centuries various religious orders took vows. Sometimes it worked at others it led to a mess. Just look at the battle between William of Ockham and the non resident Bishop of Rome in Avignon, John XXII. That was over the definition of poverty.

Along comes the [MIT Media Lab](#) where they will issue a Disobedience Award. Perhaps an award for the other two vows, reversed of course, as well. Just think, a greed award (Wall Street), an award for licentiousness (Hollywood) and disobedience (MIT or the Academy at large). Pity that MIT used to be an academic bastion but it now seems to become land of snowflakes.

The Tech states:

The topic of civil disobedience has sparked conversation in pockets around MIT, and was recently brought into the spotlight by last week's launch of the Media Lab's Disobedience Award. The \$250,000 award will go to an individual or group, anywhere in the world, that is engaging in "extraordinary disobedience for the benefit of society," according to the Media Lab. Joi Ito, the director of the Media Lab who helped conceive the award, sees it as a way to support and encourage those furthering society even when laws get in the way. Launching the award from the Media Lab, however, raises the issue of what disobedience has to do with the Media Lab and the broader MIT community. In Ito's view, MIT is a place ripe for thoughtful disagreement, where creativity and controversial ideas are welcomed.

In the above there is a difference between disagreement and disobedience. Scientific progress is often driven by disagreements. Try disobedience in a cancer lab. "Why can't I eat my PBJ sandwich at my lab bench! Johnny does it?"

There are rules, agreed many may be foolish, but there are some which can save your life. Like; don't light that Bunsen burner over that open ether can!

But enough is enough. The real question is; whose quarter million is being spent on this? What is the role of the Media Lab? Does MIT Administration support and approve the use of the Institutes name for this effort? Ultimately one should ask; how does this affect alumni funding? There is well over \$10 billion at stake.



Labels: [Academy](#)

UESDAY, MARCH 14, 2017

[THE DISTINCT DISADVANTAGE OF EXPERIENCE](#)



In my experience and in my opinion, Academic lawyers generally have never done anything real, especially with regard to the operations and technology of a broadband fiber system. Like walk a town and do a pole count. Like try and get a pole attachment agreement. Like scheduling fiber

pulls across front laws and then dealing with the blow-back from home owners. Like trying to sell fiber to the home. Like managing a fiber data network. Like trying to raise funding for what "you" want to do.

Unfortunately and fortunately I have been in all of those spots. So I have a basis upon which to opine. In contrast the academic attorneys most likely would not in my opinion be accepted as an expert witness. The Daubert rule most likely would knock them out. Hearsay does not an expert make.

Now in [Backchannel](#) one of these folks states:

We do need fiber, everywhere. But we're talking about basic infrastructure when we talk about fiber. And it is not in any private company's short-term interest to make that basic fiber infrastructure—which amounts to a substantial upgrade to the last-century copper and cable lines with which Americans are now stuck—available to everyone at a reasonable price. Google's retreat is all about the bottom line. It wanted an unrealistic rate of return on basic infrastructure. It wanted to see rapid cost declines per subscriber, like the Moore's Law changes in productivity that have taken place when digital technologists squeeze costs from other legacy businesses.

Now in my opinion and in my experience there a mass of less than correct statements in the above. First we do NOT need fiber everywhere. I have argued elsewhere that wireless, especially 5G, will very effectively compete with fiber. Secondly fiber is very very expensive. Been there done that. Why the costs? Duh! Politics. Pole attachments, rights of way, franchises, local boards, and on and on. If one has ever tried this then one can see what happens.

So when I see articles of this type I am amazed that they continue. That at no point do they ever ask; what really happened. Google was in my opinion wrong from the start. I think I know what may have happened, but all too often it is egos and too much money.



Labels: [Broadband](#)

SATURDAY, MARCH 11, 2017

[ECONOMISTS: DO THEY MAKE SENSE?](#)

Perhaps it is because I am writing a long work centered in the 14th century amidst the academics studying grammar and logic, among a few other things, I have become concerned by the use of words and the application of logic. Let's leave aside the induction/deduction issue and consider a [NY Times piece by one of those Harvard folks](#).

The piece states:

The question is whether Mr. Trump can alter these disturbing trends. Few economists point to flawed trade agreements as the main source of the problem, as the president often does. More important is what economists call skill-biased technological change. When entrepreneurs

introduce new technologies — think robots, for instance — those advances are likely to replace unskilled workers. At the same time, skilled workers are needed to implement and maintain the new technologies. As the demand for unskilled workers falls and the demand for skilled workers rises, the wage gap grows larger. The solution is to increase the skills of the labor force through better education and training. Yet this is easier said than done.

Yes it is easier said than done. The assumption in the above, and it may be correct, is that as technology advances, technology developed by engineers using scientific advancements, no T&M parts here, I include Math folks in science, it is after all the Queen of all of them, and frankly I have no idea what Technology means. Then we have these smart productive people building better machines and improved medicines and treatments, and real smart people using them, where do all the other people go? Namely the people who failed to be productive in High School or majored in graphic arts, History, or political science. We can afford just so many lawyers and I suspect that they too will become somewhat obsolete.

What is a skilled worker? Clearly an economist most likely is not a skilled worker. What can they make? Charts, projections, like the Roper curve, which often do not turn out even nearly close. Can they install a light bulb, a faucet, a bookcase? The solution is not to increase the capabilities of the labor force. We cannot do that. People must make a choice to defer some gratification and work hard and be productive learning the skills. You cannot "teach" them. Frankly I have never been able to "teach" someone, especially some one who would rather be drinking beer or watching some football game.

What motivates someone to do this? Generally the reality of the alternative. More so the reality of the economic choice they are making. If we want these types of people then we can spend money on them. Namely we give student aid to those in productive fields and no others. No loans for economics, history, political science. Full room board and tuition for engineering and science. Oh yes, throw medicine in that pool as well. That way at a very early age we can send real economic messages to students. Get a good job and at no cost. They win, the economy wins. The criteria for these sets of funding are merely performance. Do well in Grammar School, you get a good secondary, then do the same and a good college, and so forth. I believe that is economics without economists.



Labels: [Academy](#), [Economics](#)

[SHOUTING FROM THE ROOFTOPS](#)

Reading the Press these days leaves one with a wonder of the long term stability of anything. Riding the E train in New York is just the same as it always has been but with one observation. I can no longer find a reader of a newspaper! I wonder where they get their information? I guess it is all that fake news stuff.

Now seventy years ago in the same subway there must have easily been a dozen different newspapers, and those were just the English language ones. Back then you could see a Telegraph, Journal American, Post, News, and so forth. Even a NY Times would possibly appear. Each paper had its own slant on the news and thus perhaps a fake news also.

Now we come to the seemingly terror drive calls from erstwhile "scientists" who fear attacks on science. I see this in [Science](#), [Nature](#), and even NEJM. The question one may pose is: doth they protest too much.

Take a recent [NEJM](#) screech:

Now, a U.S. administration that has demonstrated dogged disregard for truth has raised concern not only that the clash between science and belief will intensify, but also that science might be frankly suppressed. President Donald Trump has called climate change a "hoax," voiced skepticism about vaccines, and appointed as head of the Environmental Protection Agency a man who has fought against its mission. ... The Centers for Disease Control and Prevention (CDC) recently postponed a planned Climate and Health Summit, though that move may have been cautionary, meant to assuage an administration on which the agency relies for its funding. In the face of suppression of science, should scientists resist, or quietly proceed with their work? Resistance seems essential. That the CDC postponement prompted a coalition to form and organize an alternative meeting reminds us that resistance is as much about ensuring effective dissemination of findings as about continuing to conduct science. But it's critical to recognize that suppressing science does not cause disbelief; rather, disbelief, particularly of science pertaining to highly politicized topics such as climate change, creates a cultural environment in which suppression of science is tolerated. So the real question is how do we resist effectively? How do we convince a skeptical public to believe in science? First, we need to stop assuming that disbelief necessarily reflects a knowledge deficit and can thus be remedied by facts. When doubt is wrapped up in one's cultural identity or powerful emotions, facts often not only fail to persuade, but may further entrench skepticism. This phenomenon, often referred to as "biased assimilation," has been demonstrated across a range of issues, Moreover, the propensity to dismiss evidence that threatens our identity or beliefs is nonpartisan: liberals, for instance, are far more likely than conservatives to dismiss science suggesting that genetically modified foods are safe. ... Second, in this highly polarized moment, we have to be careful not to inadvertently politicize science that has not already been pegged to a particular worldview. Dan Kahan, an expert on the way emotion and identity affect our interpretation of scientific facts, recently coauthored a study assessing how "culturally antagonistic memes" affected people's ability to process information about an ostensibly neutral scientific issue: ... This risk of adding an identity-laden valence to otherwise neutral scientific matters makes resisting science denialism in the Trump era particularly tricky...

I think this writer is a bit over the top. DNA is still DNA and gravity still exists. As for global warming am I to believe the shouters or my lying eyes. Yes for thirty years I have seen a clear trend in earlier and earlier bloom times on sentinel plants. That is not weather it is climate. Do I know the cause? Not really, not my area of expertise. Is the problem bad? Not for me, I like the flowers, but then again my descendants may inherit ocean front property. We are 300 ft above sea level, now. So is it worth doing something about? Most likely, and best was is rational engagement. Now the premise of the above is that somehow the current administration is taking simple scientific ideas and politicizing them. Yeah! Its politics. Even been to Washington! The politicize everything.

Now is the current administration a bunch of Luddites? So far they seem to just want to get rid of massive Government control of everything. Does that mean the baby goes out with the bath water? All science comes to an end? Use your eyes!

As a [former Democrat politician turned controller of a major science magazine](#) states:

Based on a long career in science, with a substantial interlude in elected office, I say that these are excuses for inaction. Taking action is the best course when science is threatened or when science can illuminate public issues. Scientists should not fool themselves with the misconception that politics is dirty compared to the scientific enterprise, and they should therefore avoid the fight. Nor should scientists think that by standing back and letting the facts speak for themselves, they allow reason to prevail and proponents of flawed policies to wilt.

I also wonder why NEJM and others have become so politically sensitive. Perhaps they should focus on cancer, Zika, TB. Right now those are real problems that can be handled. Is politics dirty, you bet! For the past eight years as hundreds of million have clawed their way out of the economic disaster due to Washington, look at what has happened to DC. It has prospered beyond all belief. So is it a swamp. Yes. Always bring some garlic around your neck insides the Beltway!



Labels: [Political Analysis](#), [Political Correctness](#), [Politics](#)

FRIDAY, MARCH 10, 2017

[TYPE 2 DIABETES AND SMART PHONES](#)

Over the past decade we have argued based on a multiplicity of clinical evidence that Type 2 Diabetes is dominated by weight issues. HbA1c is directly proportional to BMI. Plain and simple, almost always. Thus drop BMI, namely loose weight and HbA1c goes down.

Now along comes a new start up [which apparently claims](#):

Blending this expertise with technology and artificial intelligence, Virta has developed a platform for continuous, remote care and personalization for each patient to use online with physicians and health coaches in effort to lower their blood sugar. In a clinical trial run conducted in partnership with Indiana University, researchers looked at 262 people with type 2 diabetes over a 10-week period to assess the impact of the Virta platform. At the end of the study, which was published in the Journal of Medical Internet Research, 56 percent of patients were able to lower their blood glucose to non-diabetic ranges (meaning A1c falls below 6.5 percent) and 87 percent were able to reduce or completely eliminate their dependence on insulin. Seventy-one percent of them also saw a weight loss of 5 percent, which is considered a clinically significant threshold.

What is strange here are two factors:

1. Getting obese folks to lose weight is difficult. My statistics is we see a 2-5% success rate. Even with gastro surgical intervention obesity all too often returns.

2. HbA1c is red blood cell dependent. Red blood cells last 60-90 days. Thus to see a result in 10 weeks or 70 days is at best pushing the envelope. One physically needs a full 90 cycle AFTER BMI reduction below 25. HbA1c must be below 5.6 to get normalized and even that is pushing the envelope.

Thus one may suspect this is an option with limited long term effects even though there is a claim on 100 million people! Most of those obese will not stop eating. Try and stop them...



Labels: [Diabetes](#)

THURSDAY, MARCH 9, 2017

[MARSILIUS OF PADUA](#)

In Defensor Pacis in 1328 Marsilius noted:

The fruits of peace or tranquillity, then, are the greatest goods, as we have said, while those of its opposite, strife, are unbearable evils. Hence we ought to wish for peace, to seek it if we do not already have it, to conserve it once it is attained, and to repel with all our strength the strife which is opposed to it. To this end individual brethren, and in even greater degree groups and communities, are obliged to help one another, both from the feeling of heavenly love and from the bond or law of human society. This admonition Plato also gives us, as Tully attests in the first book of his treatise On Duties, when he said: "We were not born for ourselves alone; to part of us our native land lays claim, and to part, our friends." To this sentence Tully adds: "And so, as the Stoics were wont to say, the things that grow in the earth are all created for the use of men; but men are born for the sake of men. In this we ought to follow the lead of nature, and to bring forth common utilities for all." 11 But it would be no small common utility, indeed it is rather a necessity, to unmask the sophism of this singular cause of wars which threatens no small harm to all states and communities. Hence, whoever is willing and able to discern the common utility is obliged to give this matter his vigilant care and diligent efforts. For while this sophism remains concealed, this pestilence can in no way be avoided, nor its pernicious effect be completely uprooted from states or cities.

Peace is not just with respect to external threats but just as well to internal. Marsilius is credited with the articulation of the principle of the individual, as the fundamental element of the state, not as a subject of the state. For Marsilius the individual was every human, all with equal rights and all having a say for the selection of those who lead, once selected, then agreed to. Internal threats were also key to Marsilius since he was observant of the wars within the Italian city states, the internal savagery of families and groups destroying the fundamental essence of individual freedom.

Just a thought for a few.



Labels: [Political Analysis](#)

MONDAY, MARCH 6, 2017

[HERE WE GO AGAIN](#)

The [Old](#) and the [New](#). Now we can start all over again!



Labels: [Health Care](#)

THURSDAY, MARCH 2, 2017

[A HEALTH CARE PLAN](#)

Perhaps thinking about a Health Plan is too hard. Let's try something easy. Ask if there are insurance plans that almost everyone has that seem to work. The answer is yes; it is automobile insurance. So let's start with that idea, there are no mass rallies on unfair auto insurance, at least none on the media, so we make the following suggestion.

1. A Health Plan must be mandatory for all. Too bad, you got to have one.
2. The Health Plan is on an individual basis, no employer nonsense. That means we are all on a level playing field.
3. The minimum coverage is like an auto plan. You have to have say a \$1 million catastrophic coverage plan. Want more? Then go pay for it but it is not mandated. Want towing, broken windows, oil changes, go but it and pay for it.
4. There should be no age penalty. If you have to have coverage then you have it all your life. That means the actuaries must factor in a life time coverage cost. Too bad for the kids, but they too will get old.
5. No pre-existing condition coverage concerns. You sign up, no questions asked. However that it only for catastrophic coverage.
6. Drugs? Now drugs are part of treatment, and catastrophic often being the most costly. So they get covered. However need an antibiotic or birth control are whatever, you can buy a plan or pay. You choose.
7. Now for the hard part. Insurance must be country wide and you must be able to deal directly with an insurer. No brokers, no state limitations. Can rates be different by region? Good question? Don't have a good answer for that one.
8. Support? If someone cannot work, due to say a disability, then they get covered. If someone wants to explore their dreams, tough, get a job or pay a penalty, a big one. That was a big problem with the ACA. The arrogant characters in HHS lauded the fact that some thirty year old

could get full coverage for say \$10 a month while pursuing their dream of being a Tibetan flute player while folks on Medicare were paying tens of thousands on top of what they already contributed for over 50 years! The HHS snowflakes just rubbed it into the eyes of the poor schlubs paying their salaries.

9. Otherwise you can do this in just a few pages. Keep Medicare out of the fray for now. Just solve the other problem first.

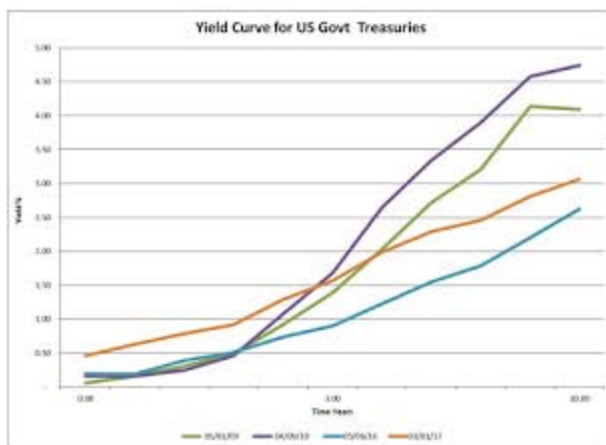
10. Now I said this eight years ago but Politicians being Politicians just approved what some third parties wrote for them.

11. Finally, keep the evil academics out of this! Really. One academic, one economist, and well, see you on the ninth circle of Hell!

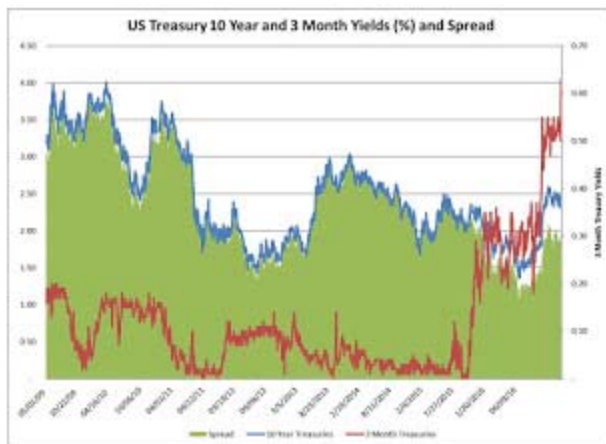


Labels: [Health Care](#)

TREASURY SPREADS MARCH 2017



The above is the yield curve for Treasuries. There is significant flattening, namely short term higher and long term lower.



The above is the summary for the last ten years. Note the "explosion" of short term. Also the tightening of the spread. The FED still has a massive Balance Sheet problem loaded with truly junk mortgage notes. Wait till they unload that stuff. Perhaps they will also load it up with Student Debt!



Labels: [Economy](#)

SUNDAY, FEBRUARY 19, 2017

[WHY DID DANTE DIE IN RAVENNA?](#)

Florence in the thirteenth through the sixteenth centuries was fraught with battles between factions. Primarily the Guelphs and Ghibellines. The Guelphs support the Pope, who himself went from Rome to Avignon and eventually back again, and the Ghibellines who supported the Imperial forces from the Holy Roman Empire. Family killed off family. It led to even more internecine war between Black Guelphs and White Guelphs.

Expelled from Florence were the likes of Dante and Petrarch. Ending with the Medici and their own form of butchery, including if one likes the famous St Bartholomew's Day Massacre of Huguenots in Paris, under the influence of the Medici French Queen mother. One can best understand this Massacre by reading Dumas, his brilliant work on this event.

Thus, Civil Wars are not as simple as our own between North and South. It can occur between the first floor and the second floor. It can start over what Pope is best or whether one likes Germans or French, Pope or Emperor.

Perhaps a deep breath and a focus on Springtime may help.



Labels: [Commentary](#)

[SNOWFLAKES IN YEMEN](#)

Yemen has gone through a rather long rough patch, to say the least. Around the time of the Prophet the port city of Aden change control from Ethiopians, Jews, Persians, Arabs, and before that Romans. So one would assume Yemeni folk would have some sense of this ongoing turbulence.

But we now have what seems to be the "snowflake" syndrome. Namely, despite millennia of conflict the current generation abhors any sense of unease. The most recent is the use of [Science](#), as well as Nature, as vehicles of complaining. Perhaps on the Nature side we have the left in England, and on the Science side we have a former Democrat politician at its head.

It may be useful to get politicians out of everything. Otherwise we may find ourselves in a blizzard of snowflakes.



Labels: [Commentary](#)

DARWIN AND CONCORD AND CAMBRIDGE

In the recent book by Fuller, [The Book That Changed America: How Darwin's Theory of Evolution Ignited a Nation](#), the author claims to present how the introduction of Darwin's work transformed the United States. I would beg to differ. Perhaps a better title would have been, "The Book that Changed Concord and Cambridge" because it clearly focused on the group from Concord along with a smattering from Cambridge.

The author starts out with the recognition of Boast as the "Hub" at this period as compared to New York, albeit bigger, yet a more raucous version of an American city. Boston reached back to European intellectual elitism whereas New York was starting to become an eclectic American melting pot. Boston sought comfort in lineage, whereas New York had quickly abandoned its Dutch heritage, predating the Pilgrims, and was decade by decade introducing one culture after another, with the conflicts, but working towards an amalgam.

Concord was at this time literally a train ride, at that time, from Boston, Cambridge a collection of people, high and lower class, factories and Harvard. Harvard was founded as many Bostonian may recall as a place to send the graduates from Boston Latin School, the educational establishment for the local "well-off". Back in Concord were fields for modest farms as well as a small collection of educated folks who founded such places as Concord Academy, aside the Concord River and just on the outskirts of then the center of Concord. Along the adjoin streets were gracious homes of those who constituted the general Concord society.

Along comes Darwin into this Transcendental soup of Thoreau, Alcott, Emerson and others and in a strange way the fact based scientific observations of Darwin and his line of reasoning leading to evolution gets absorbed by this group who have to then eschewed this very approach to understanding. Thus sayeth the author.

At first the author introduces Gray and Agassiz. Gray the botanist, and Agassiz the broadly based naturalist. Gray comes across as the mild manner scientists who sees in Darwin a way to explain many of the observations concerning nature he has made in plants. Gray is subdued, and academic. Then there is Agassiz, the Swiss naturalist, with an ebullient personality, who sees in Darwin the conflicts with his fundamental religious beliefs. Gray sees the facts and is willing to follow them, Agassiz sees the conflicts and fights them. Thus is the theme of the first part of the book.

The second part moves to Concord and the collection of Transcendentalists. This virtually self-contained community of mid-nineteenth century thinkers see Darwin as a window onto their world. What would have been seen as a putative conflict is seen for example in Thoreau's eyes as an explanation for the natural harmony of his world of nature. It explains why a small pine tree has managed to survive and prosper far from its source, and how the squirrels take part in the dissemination of species who survive and the fact that one sees robins and not parakeets in the Spring and pine trees and not palm trees in the forests. At least that is what we are led to understand.

Somehow we get John Brown and his assault on Harper's Ferry in the mix. One nexus is that Brown's two daughters end up at the Alcott's and attend Concord Academy. This perhaps is the mixing of the abolitionist with the evolutionist. One can see these individuals seeing in evolution, man from a common ancestor, being the key element in their strong abolitionist views. Namely the issue that all humans are from the same stock and thus have the same rights. Not quite an acceptance of fundamental individualism, the belief that all individuals have individual rights equally, but a step in that direction.

Now as to some specific observations:

p. 74 the comment on Thoreau adopting methods of science without a scientific theory is an excellent observation. Thoreau was an excellent observer of facts, but his core beliefs were more Transcendental than scientific.

p 85 is an excellent introduction to Agassiz and his grandiosity. One can even today on Oxford Street see this collection of the naturalist age. This museum was to Agassiz what the American Museum of Natural History and stuffed mammals was to Teddy Roosevelt. Namely an expression of what they felt Nature was.

p 88 is a concise description of the view of Agassiz and his dispute with the monogenesis view of a single human ancestor. Agassiz was of the view that the "races" came from differing ancestors and as such were different species.

pp. 108-109 This is a good discussion of Gray and his negation of the Transcendental view. What is especially insightful is understanding that induction was a key element of science. One collected facts and then using a scientific method, Baconian in nature, assembled the facts and from them induced a conclusion. That in essence was the heart of Darwin.

p. 111 This is a set of comments from Agassiz. Here he states there can be no connection between an arctic whale and a tropical tiger. This is done without basis. Had Agassiz understood DNA, a Century in the coming, then the evidence would be there. This is a classic example of those who prognosticate conclusions without the slightest evidence in facts. Induction is always subject to some missteps, but ex cathedra statements are often subject to near immediate disproof.

p. 141 This is an attempt to connect Darwin and Thoreau in his Walden. It is not clear how accurate this may be. Thoreau as a believer in nature qua nature had to see Nature as a temporal dynamic combative process. Some elements of this may be culled from Walden but I suspect it may require a deeper digging to fully justify.

p. 151 Here he states that Alcott invented Darwin's evolutionary ideas. But this theory had creatures descending from man rather than man from species. Perhaps this may have been stated differently.

p.247. The author states Thoreau died from influenza gotten from Alcott. It appears that the generally accepted cause was TB from which Thoreau had suffered for almost a decade. Perhaps a fact checking would work here.

In summary, other than the title and some comments above, the book is well written and well-structured for its purpose. It is not a discussion of Darwin. Somehow one should come to the book with a good understanding of Darwin circa 1860. That is missing. It is not a discussion of Darwin in America, at best as noted just in Concord and Cambridge. Transcendentalism was not a universally accepted view of the world at the time, in fact it was viewed by many as idiosyncratic to that small portion of the Commonwealth.



Labels: [Books](#)

THURSDAY, FEBRUARY 16, 2017

[GOOGLE FIBER](#)

We thought Google Fiber was a dumb idea from the outset. Why? Well we tried it before they did. What was the problem. Costs. What costs. Three types. 1. Delay. It takes forever to get permits etc. The Incumbent can throw tons of stiff at you. 2. Franchise. You need one for every town. 3. Pole Attachments: Again the Incumbent. Fundamentally fiber can be real cheap. It costs about \$20,000 per mile if nothing else is counted. Then if you consider the number of homes per mile at 50% penetration you can get the fiber down to \$500 per customer! Drops are \$200 and electronics per sub is about \$300. Overall about \$1,000. Then add the above and it goes to well over \$3,000 and drop penetration to 25% and it doubles to \$6,000! Now it is no longer a business. I recall speaking to some Google folks a decade or so ago. Back of the envelope stuff. It took them a decade and hundreds of millions to learn! That's Silicon Valley!

Now [Wired](#) states:

Eventually Google Fiber could offer even more radical wireless technologies. For example, Webpass has tested technology from Artemis Networks, a startup building a new type of wireless service that can “follow” users from place to place and guarantee a certain amount of bandwidth. Developing those sorts of technologies is a radical departure from building a network that provides actual fiber to homes, and requires a different type of workforce. In a letter to employees about the transition, Alphabet CEO Larry Page said the leaner Access will largely work in the field, not from the company’s headquarters in Mountain View. A more wireless future for Fiber still comes with risks. More traditional telcos are also eyeing high-speed wireless internet as a way to bypass more expensive traditional broadband. In the meantime, Alphabet is still trying to figure out how to be a company that provides internet at all.

All you had to do was read what I wrote a decade or more ago. But that is West Coast vs East Coast. Wireless is the future, if one can get out of their own way. Now come Verizon. Buy Yahoo. Yeah, right. Look at Verizon stock, down almost 20% while the market is up 20%. Is the Board asleep? They are sitting on a gold mine in wireless licenses and they go after AoL and Yahoo. They could be the next Google in doing dumb things!



Labels: [Google](#)

WEDNESDAY, FEBRUARY 15, 2017

TIME FOR DANTE - NEED I SAY MORE

THROUGH ME THE WAY TO THE CITY OF WOE,
THROUGH ME THE WAY TO EVERLASTING PAIN,
THROUGH ME THE WAY AMONG THE LOST.
JUSTICE MOVED MY MAKER ON HIGH.
DIVINE POWER MADE ME,
WISDOM SUPREME, AND PRIMAL LOVE.
BEFORE ME NOTHING WAS BUT THINGS ETERNAL,
AND ETERNAL I ENDURE.
ABANDON ALL HOPE, YOU WHO ENTER HERE.

These words, dark in hue, I saw inscribed
over an archway. And then I said:
'Master, for me their meaning is hard.'
And he, as one who understood:
'Here you must banish all distrust,
here must all cowardice be slain.
'We have come to where I said
you would see the miserable sinners
who have lost the good of the intellect.'
And after he had put his hand on mine
with a reassuring look that gave me comfort,
he led me toward things unknown to man.....

I drew closer to my leader.
And he to me: 'Turn back! What are you doing?
Look, there Farinata stands erect --
you can see all of him from the waist up.'
Already I had fixed my gaze on his.
And he was rising, lifting chest and brow
as though he held all Hell in utter scorn.

At which my leader: 'Choose your words with care,'
and his hands, ready, encouraging,
thrust me toward him among the tombs.
When I stood at the foot of his tomb
he looked at me a moment. Then he asked,
almost in disdain: 'Who were your ancestors?'
And I, eager to obey, held nothing back,
but told him who they were,
at which he barely raised his eyebrows
and said: 'They were most bitter enemies
to me, my forebears, and my party --

not once, but twice, I had to drive them out.'

'If they were banished,' I responded, 'they returned from every quarter both the first time and the second, a skill that Yours have failed to learn as well.' Then, beside him, in the open tomb, up came a shade, visible to the chin: I think he had raised himself upon his knees. He looked around me as though he wished to see if someone else were with me, and when his hesitant hopes were crushed, weeping, he said: 'If you pass through this dark prison by virtue of your lofty genius, where is my son and why is he not with you?' And I to him: 'I come not on my own: he who stands there waiting leads me through, perhaps to one Your Guido held in scorn.'

His words and the manner of his punishment already had revealed his name to me, and thus was my reply so to the point.

Suddenly erect, he cried: 'What? Did you say "he held"? Lives he not still? Does not the sweet light strike upon his eyes?' When he perceived that I made some delay before I answered, he fell backward and showed himself no more. But the other, that great soul at whose wish I had stopped, did not change countenance, nor bend his neck, nor move his chest.

And he, continuing from where he'd paused: 'That they have badly learned this skill torments me more than does this bed. 'But the face of the lady reigning here will be rekindled not fifty times before you too shall know how difficult a skill that is to learn. 'And, so may you return to the sweet world, tell me, why are your people, in every edict, so pitiless against my kin?'

Then I to him: 'The havoc and great slaughter that dyed the Arbia red caused them to raise such prayers in our temple.' He sighed and shook his head, then spoke:

'I was not alone, nor surely without cause
would I have acted with the rest.
'But it was I alone, when all agreed
to make an end of Florence, I alone
who dared speak out in her defense.'
'So may Your seed sometime find peace,
pray untie for me this knot,' I begged him,
'which has entangled and confused my judgment.
'From what I hear, it seems
you see beforehand that which time will bring,
but cannot know what happens in the present.'
'We see, like those with faulty vision,
things at a distance,' he replied. 'That much,
for us, the mighty Ruler's light still shines.

'When things draw near or happen now,
our minds are useless. Without the words of others
we can know nothing of your human state.
'Thus it follows that all our knowledge
will perish at the very moment
the portals of the future close.'
Then, remorseful for my fault, I said:
'Will You tell him who fell back down
his son is still among the living?
'And let him know, if I was slow to answer,
it was because I was preoccupied
with doubts You have resolved for me.'

And now my master summoned me,
so that I begged the spirit to reveal,
at once, who else was down there with him.
His answer was: 'More than a thousand lie
here with me: both the second Frederick
and the Cardinal. Of the rest I do not speak.'



Labels: [Political Analysis](#)

MONDAY, FEBRUARY 13, 2017

ECONOMISTS TAKE ON MEDICINE!

[Several Tax and Spend Republicans](#) have taken on Excess Carbon Emissions by taxing it. Well imagine what they can do for Medicine and Health Care in general.

Let's say you have Leukemia. You are dying. Yep, near death. These bright folks have the solution. A thousand years ago they would have bled you, but now, they tax you! Yep. They tax you say \$50,000, but, if you get well, well they give you a tax credit! Yep a good old Republican

tax credit. That means if you live and get back out there in the fields cutting the sugar cane for 16 hours a day, you will not have to pay taxes for at least 50 years. If you die, then they get to put a lien on your estate, on top of the death tax, and the estate tax, and....

Don't we all love these Tax and Spend Republicans. Imagine what they can do replacing the ACA. Bad to worse? No way, think of all those tax credits you get if you somehow heal thyself!

Oh, and better yet, that \$1.5 trillion in Health Care costs, they just disappear! Imagine that. Gone!

After all, if it works for one kind of carbon why not another? Harvard can just shut down the Med School, and triple the Economics Department. And don't forget those folks at MIT who brought you the ACA in the first place! And they thought you were just dumb!



Labels: [Academy](#)

THURSDAY, FEBRUARY 9, 2017

[SOME THOUGHTS ON PROSTATE CANCER IMMUNOTHERAPY](#)

Prostate cancer, PCa, is a significant cancer especially in older men. It is more than likely a highly heterogeneous cancer and thus unlike many of the others we have examined there may not be a single strategy. There has been a significant amount of effort to try and determine if immunotherapy can be applied to PCa. This is especially true in that it does metastasize to the bone and many hematological cancers have been addressed by immunotherapy. We have examined many details of PCa elsewhere and refer the reader to that^{9[1]}.

As Drake, has indicated:

Prostate cancer is not traditionally considered an immunologically responsive malignancy like melanoma or renal cell carcinoma, yet the prostate glands of men with cancer are frequently diffusely infiltrated with both CD4 and CD8 T cells, and several factors suggest that adenocarcinoma of the prostate might prove an attractive target for immunotherapy.

First among these is the slow-growing nature of the disease, allowing time for immunological intervention to overcome immunosuppressive factors in the tumor microenvironment and to mount a clinically meaningful response.

Second, serum PSA level, while not a true surrogate marker, is routinely utilized in clinical decision making, and can serve to guide the development of immunotherapy approaches.

^{9[1]} See

<http://www.telmarc.com/Documents/Books/Prostate%20Cancer%20Systems%20Approach%2003.pdf>

Third, both proteomic and microarray analyses of prostate cancer progression have delineated a number of relatively tissue-specific proteins that may serve as tumor/tissue antigens.

Finally, abundant preclinical data suggest that an antitumor immune response can be elicited, particularly when active immunotherapy is combined with maneuvers to mitigate tolerance such as immune checkpoint blockade, androgen ablation, or radiotherapy.

At least five phase III immunotherapy trials have been initiated in the context of metastatic, castrate-resistant prostate cancer, but none have yet met their predetermined end points

PCa has had a limited success with immunotherapy but not as successful as other cancers. We will argue that a main reason is the complex genetic makeup of PCa. However, the current genetic/immunological tool box available may offer some new options.

The Prostate

The prostate is a glandular organ which appears upon microscopic examination as a multiplicity of glands with muscle, nerve, blood, and other stromal and parenchymal tissues. It has a high incidence of cancer as men age and the cancers for the most part are indolent, namely have low chance of metastasis, yet a fraction show highly aggressive behavior. Also an alleged precursor of PCa, prostate cancer, is High Grade Prostate Intraepithelial Neoplasia, an inflammatory disorder wherein the existing glandular regions generally composed of basal and luminal cells, demonstrate significant growth within the gland itself. It has been argued that this is a natural precursor to PCa but we have demonstrated that the conclusion has significant exceptions. Yet we know that inflammation is a driver to cancers and there thus is a putative correlation but not a causation. (See Nunzio et al):

Evidence in the peer-reviewed literature suggested that chronic prostatic inflammation may be involved in the development and progression of chronic prostatic disease, such as BPH and PCa, although there is still no evidence of a causal relation. Inflammation should be considered a new domain in basic and clinical research in patients with BPH and PCa.

PCa is quite complex on a genetic basis. Berger et al have discussed this at length. They state:

Prostate cancer is the second most common cause of male cancer deaths in the United States. Here we present the complete sequence of seven primary prostate cancers and their paired normal counterparts. Several tumors contained complex chains of balanced rearrangements that occurred within or adjacent to known cancer genes.

Rearrangement breakpoints were enriched near open chromatin, androgen receptor and ERG DNA binding sites in the setting of the ETS gene fusion TMPRSS2-ERG, but inversely correlated with these regions in tumors lacking ETS fusions. This observation suggests a link between chromatin or transcriptional regulation and the genesis of genomic aberrations. Three tumors contained rearrangements that disrupted CADM2, and four harbored events disrupting either PTEN (unbalanced events), a prostate tumor suppressor, or MAGI2 (balanced events), a PTEN

interacting protein not previously implicated in prostate tumorigenesis. Thus, genomic rearrangements may arise from transcriptional or chromatin aberrancies to engage prostate tumorigenic mechanisms.

We have further examined this in detail in McGarty, Prostate Cancer (2012). Now in 2009 Drake stated:

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First among these is the slow-growing nature of the disease, allowing time for immunological intervention to overcome immunosuppressive factors in the tumor microenvironment and to mount a clinically meaningful response.

Second, serum PSA level, while not a true surrogate marker, is routinely utilized in clinical decision making, and can serve to guide the development of immunotherapy approaches.

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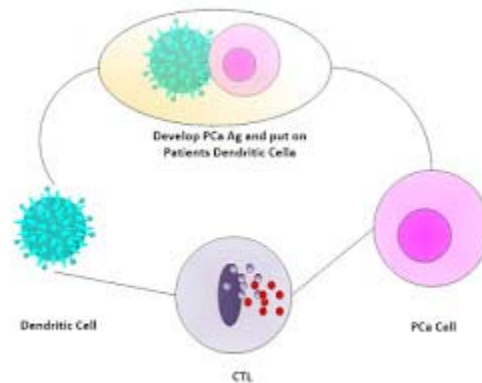
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Drake was noting the potential for immunotherapeutic approaches for this solid tumor. It is well known that the prostate is subject to various inflammatory factors and that these factors have been linked to cancer changes. The counter would be to examine using the immune responses to address the changes. As we noted in melanoma, when observed, a melanoma often has an accumulation of T cells, CTLs, indicating the natural defense mechanism.

On the other hand, it is intriguing to note the significant impact that inflammation has on PCa and that immune response are present but not yet active.

Current Techniques; Dendritic

One of the earliest treatments of PCa using an immunotherapeutic approach is to use the patient's dendritic cells and prime them. Recall that the dendritic cells are out in the body searching for intruders. When they find one they then bring it back to the immune system for presenting and for activating the immune system. Thus, rather than modifying a T cell or an NK cell directly, the approach seeks to "prime" the dendritic cells which will then start the immune response. This is an example of examining the many entry points into using the immune system.



As Westdorp et al note:

Prostate cancer (PCa) is the most common cancer in men and the second most common cause of cancer-related death in men. In recent years, novel therapeutic options for PCa have been developed and studied extensively in clinical trials. Sipuleucel-T is the first cell-based immunotherapeutic vaccine for treatment of cancer. This vaccine consists of autologous mononuclear cells stimulated and loaded with an immunostimulatory fusion protein containing the prostate tumor antigen prostate acid phosphatase.

The choice of antigen might be key for the efficiency of cell-based immunotherapy. Depending on the treatment strategy, target antigens should be immunogenic, abundantly expressed by tumor cells, and preferably functionally important for the tumor to prevent loss of antigen expression. Autoimmune responses have been reported against several antigens expressed in the prostate, indicating that PCa is a suitable target for immunotherapy.

In this review, we will discuss PCa antigens that exhibit immunogenic features and/or have been targeted in immunotherapeutic settings with promising results, and we highlight the hurdles and opportunities for cancer immunotherapy.

The authors above then consider a collection of putative prostate antigens useful for applications of multiple approaches.

| <i>Antigen</i> | <i>Function</i> | <i>Action</i> |
|-----------------|---|---|
| PSA | PSA Serine protease which cleaves high molecular weight proteins into smaller peptides, resulting in the necessary liquification for spermatozoa to swim freely | Stimulates CTL Produces cytokines |
| PAP | PAP Protein tyrosine phosphatase which enhances the mobility of sperm | Stimulates CTL |
| PSMA | Folate hydrolase activity | Presented on cell surface. Elevated in PCa and HGPIN |
| PSCA | Unknown, overexpressed by most PCas | T-cell activation and proliferation |
| MUC-1 | Limiting the activation of inflammatory response. | T-cell proliferation |
| NY-ESO-1 | Unknown, expressed in a variety of tumors | CTLs and antibody-mediated responses |
| MAGE-A | Down-regulates p53 function through histone deacetylase recruitment | Stimulates CTLs in vivo |
| AKAP-4 | Binding protein involved in cytoskeletal regulation and organization by affecting cyclic AMP-dependent protein kinase-A | Stimulated CTLs in vitro |

Now for the dendritic cell targets they employ PAP as above as well as GM-CSF. The dendritic cells mature in a solution with a fusion protein (PA2024). The result is returned to the patient.

As Drake noted in 2009:

One of the few immunotherapy agents in late-stage development for prostate cancer is Sipuleucel-T. In this approach, patients undergo plasmapheresis, and a personalized immunotherapy product is produced by culturing a patient's peripheral blood monocytes with a proprietary protein that couples granulocyte macrophage colony-stimulating factor with a target antigen (PAP).

Phase I and phase III trials of Sipuleucel-T have been reported, with encouraging results. Clinical development of this agent is pivotal on a large (500 patients) randomized placebo-controlled phase III trial (ImPACT; Immunotherapy Prostate Adenocarcinoma Treatment) which completed accrual in October 2007, and for which additional survival data are expected sometime this year (see Note Added in Proof).

In addition, considerable clinical development has focused on a viral vector approach in which PSA itself is targeted using sequential injections with recombinant vaccinia and fowlpox constructs. Here, both constructs have been engineered to include a number of costimulatory molecules in an effort to augment an immune response.

As Jahnisch et al note:

Dendritic cells (DCs) are professional antigen-presenting cells (APCs), which display a unique capacity to induce, sustain, and regulate T-cell responses. In tumor setting, DCs circulate through the blood and migrate to tumor tissues, where they interact with malignant cells. Immature DCs are particularly efficient in the uptake of tumor-derived material. DC maturation is induced by tumor-derived molecules such as heat shock proteins and high mobility-group box 1 protein as well as proinflammatory cytokines produced by various tumor-infiltrating immune cells.

During maturation DCs migrate from tumor tissues to T-cell-rich areas of secondary lymphoid organs, where they activate tumor-reactive CD8⁺ cytotoxic T lymphocytes (CTLs) and CD4⁺ T cells. CD8⁺ CTLs efficiently recognize and destroy tumor cells, which expose peptides derived from tumor-associated antigens (TAAs) in the complex with human leukocyte antigen (HLA) class I molecules.

Clinical studies focusing on the adoptive transfer of cytotoxic effector cells revealed tumor regression in cancer patients. CD4⁺ T cells recognizing peptides in the context of HLA class II molecules also play an important role in antitumor immunity. CD4⁺ T cells improve the capacity of DCs to induce CTLs by the interaction between CD40 on DCs and CD40 ligand on activated CD4⁺ T cells.

In addition, CD4⁺ T cells provide help for the maintenance and expansion of CTLs by secreting cytokines such as interleukin (IL)-2 and can eradicate tumor cells directly. Besides their extraordinary capacity to induce and stimulate T-cell responses, DCs efficiently improve the immunomodulatory and cytotoxic potential of natural killer cells, which essentially contribute to the elimination of tumor cells.

Furthermore, DCs can also directly mediate tumor-directed cytotoxicity. Owing to their various antitumor effects, DCs evolved as promising candidates for vaccination protocols in cancer therapy

Now as Mellman et al note:

While Provenge is clearly a cell-based therapy, there may be other mechanisms involved. Although the majority (66%) of survivors showed an antibody response to the fusion protein, the fraction of patients producing antibodies that recognized endogenous PAP was much lower (28.5%).

Moreover, T-cell responses to either the fusion protein or PAP were not associated with survival. These discrepancies might reflect a limitation of monitoring antitumor immune responses in the peripheral blood compared with the tumour microenvironment. However, they also raise the possibility that other undefined factors in the cellular product may have an important role. Further studies are required to understand the therapeutic mechanism of Provenge, and to define the impact of the different cell-processing procedures on the placebo product. The lack of tumour shrinkage, the criterion typically used to gauge the efficacy of cancer treatments, in the face of a survival benefit is surprising, but perhaps not unexpected for immunotherapy. As seen

pre-clinically, an effect on pre-existing tumour due to immune manipulations can be delayed while an immune response develops.

Furthermore, biopsies of metastases after vaccination in some clinical trials revealed the presence of immune infiltrates that mediate tumour destruction in association with extensive edema, which may be followed by fibrosis⁴⁶.

These histopathological findings suggest that monitoring tumour size alone may be inadequate for assessing the overall therapeutic effects of vaccination. As discussed later, these considerations apply to the evaluation of CTLA-4 antibody blockade, highlighting the need to modify tumour response criteria in light of new insights into the biology of immunotherapy.

Now Mellman et al make several key points as to the dendritic approach. First, RESIST approaches measure tumor size and in classic chemotherapy cases it does shrink. Yet as has been seen again and again in the more sophisticated and targeted approaches the shrinking takes time as the tumor, albeit present, it being attacked and killed off, albeit still visible on say a CAT Scan. Second, there is the putative supposition that there are other factors afoot. The latter we shall explore with the checkpoint examination.

Checkpoint Targets

Checkpoints are simply receptor-ligand pairs which when activated can inhibit the actions of T cells and other immune pathway actions. As Topalian et al note:

The rapid-fire clinical successes from blocking CTLA-4 and PD-1, the first checkpoint receptors to be discovered, have opened prospects for extending the potential of cancer immunotherapy by inhibiting more recently discovered checkpoint ligands and receptors. It is clear that, despite some commonalities, CTLA-4 and PD-1 have distinct patterns of expression, signaling pathways, and mechanisms of action. Although discovered over 20 years ago, there are still many unanswered questions about their biology, particularly in the context of cancer.

The authors continue:

The immune system recognizes and is poised to eliminate cancer but is held in check by inhibitory receptors and ligands. These immune checkpoint pathways, which normally maintain self-tolerance and limit collateral tissue damage during anti-microbial immune responses, can be co-opted by cancer to evade immune destruction. Drugs interrupting immune checkpoints, such as anti-CTLA-4, anti-PD-1, anti-PD-L1, and others in early development, can unleash anti-tumor immunity and mediate durable cancer regressions. The complex biology of immune checkpoint pathways still contains many mysteries, and the full activity spectrum of checkpoint-blocking drugs, used alone or in combination, is currently the subject of intense study.

Thus, the issue would be; what other check points are there and how can they be addressed? From Kono we have the following Table which presents some putative targets:

| Target | Biological function | Antibody (fusion protein) | Phase | Cancer type |
|--------------|---------------------|--------------------------------------|---------------------------------------|--|
| CTLA4 | Inhibitory receptor | Ipilimumab | FDA approved Phase II and III | melanoma, multiple cancers |
| PD1 | Inhibitory receptor | MDX-1106 MK3475 CT-011 AMP-224 | Phase I/II Phase I Phase I Phase I | melanoma, renal, lung multiple cancers multiple cancers multiple cancers |
| PDL1 | Ligand for PD1 | MDX-1105 | Phase I | multiple cancers |
| LAG3 | Inhibitory receptor | IMP321 | Phase II | breast cancer |
| B7-H3 | Inhibitory ligand | MGA271 | Phase I | multiple cancers |
| B7-H4 | Inhibitory ligand | | | Preclinical |
| TIM3 | Inhibitory receptor | | | Preclinical |

From the recent work of Beer et al:

Ipilimumab is a fully human monoclonal immunoglobulin G1 antibody that increases antitumor T-cell responses by binding to cytotoxic T-lymphocyte antigen 4.17-19 Blocking by ipilimumab of the T-cell negative regulator cytotoxic T-lymphocyte antigen 4 allows CD28 and B7 interactions, which result in T-cell activation; proliferation; tumor infiltration; and ultimately, cancer cell death. Treatment with ipilimumab, as a single agent or in combination with dacarbazine, provided significant survival benefit in two phase III trials of advanced melanoma. Of note, approximately 20% of ipilimumab-treated patients with melanoma experienced longterm survival

We have seen this in detail when examining the melanoma therapeutic approaches. Now the application of this to PCa is interesting and challenging. Melanoma is an aggressive and rapidly growing cancer and it is well known that it often evokes an immune response when examined on biopsy. In contrast PCa is quite different. Melanoma is derived from melanocytes which have developed from the neural crest. PCa is exocrine glandular. The results of the Beer trial were not conclusive.

More recently Schweizer and Drake (2014) noted:

Since the approval of sipuleucel-T for men with metastatic castrate resistant prostate cancer in 2010, great strides in the development of anti-cancer immunotherapies have been made. Current drug development in this area has focused primarily on antigen specific [i.e. cancer vaccines and antibody based therapies] or checkpoint inhibitor therapies, with the checkpoint inhibitors perhaps gaining the most attention as of late.

Indeed, drugs blocking the inhibitory signal generated by the engagement of cytotoxic T-lymphocyte antigen-4 (CTLA-4) and programmed cell death-1 (PD-1) found on T-cells has emerged as potent means to combat the immunosuppressive milieu. The anti-CTLA-4 monoclonal antibody ipilimumab has already been approved in advanced melanoma and two

phase III trials evaluating ipilimumab in men with metastatic castrate-resistant prostate cancer are underway.

A phase III trial evaluating ProstVac- VF, a poxvirus-based therapeutic prostate cancer vaccine, is also underway. While there has been reason for encouragement over the past few years, many questions regarding the use of immunotherapies remain.

Namely it is unclear what stage of disease is most likely to benefit from these approaches, how best to incorporate said treatments with each other and into our current treatment regimens and which therapy is most appropriate for which disease. Herein we review some of the recent advances in immunotherapy as related to the treatment of prostate cancer and outline some of the challenges that lie ahead.

More recently Martin et al noted:

Primary prostate cancers are infiltrated with PD-1 expressing CD8+ T cells. However, in early clinical trials, men with mCRPC did not respond to PD-1 blockade as a monotherapy. One explanation for this unresponsiveness could be that prostate tumors generally do not express PD-L1, the primary ligand for PD-1.

However, lack of PD-L1 expression in prostate cancer would be surprising, given that PTEN loss is relatively common in prostate cancer and several studies have shown that PTEN loss correlates with PD-L1 up-regulation - constituting a mechanism of innate immune resistance. This study tested whether prostate cancer cells were capable of expressing PD-L1, and whether the rare PD-L1 expression that occurs in human specimen's correlates with PTEN loss...These studies show that some prostate cancer cell lines are capable of expressing PD-L1.

However, in human prostate cancer, PTEN loss is not associated with PD-L1 expression, arguing against innate immune resistance as a mechanism that mitigates anti-tumor immune responses in this disease.

Unfortunately, the results are less than positive. They seem to agree with the prior results.

Options

There are many options available for dealing with PCa but the efficacy of these known options is at best problematic. Yoo et al have summarized the recent (2016) immunotherapeutic options for PCa. They note the following:

Despite advances in treatment of prostate cancer, curative therapy is not yet available for CRPC. Novel therapeutic options have thus been sought, and vaccines, immunotherapy, and gene based therapy are considered to be attractive candidates in this respect.

Up to now, sipuleucel-T is the only such treatment approved by the Food and Drug Administration.

...the authors will briefly introduce investigational vaccines, immunotherapy, and gene-based therapy for CRPC.

5.1. Vaccine

GX301 is a dual-adjuvant telomerase vaccine. GX301 is reported to be safe and highly immunogenic in patients with prostate cancer. A Phase II randomized trial is underway.

Prostvac is a vector based therapeutic cancer vaccine. A Phase II study reported that prostvac was well tolerated and it improved overall survival compared with control vectors (25.1 months vs. 16.6 months) in patients with minimally symptomatic CRPC. However, another Phase II study, which evaluated the effect of the combination of docetaxel and prostvac, failed to show improvements in overall survival; this lack of positive results may be due to limited accrual of patients. Investigation on the relative efficacy of simultaneous versus sequential docetaxel p prostvac is currently ongoing.

DCVAC is an autologous dendritic cell-based vaccine. In a Phase I and II trial, combination chemoimmunotherapy with DCVAC and docetaxel resulted in longer than expected survival (19 months vs. 11.8 months) without significant complications. A Phase III study, evaluating the merits of DCVAC when added to standard chemotherapy, is due to commence.

Vaccines have been examined by many over the past few years. As noted, perhaps multi-therapeutic methods may also prove beneficial.

5.2. Immunotherapy

Ipilimumab^{10[2]} is a monoclonal antibody that blocks the activity of CTLA-4 (cytotoxic T-lymphocyte-associated protein 4) and was approved by the Food and Drug Administration for the treatment of melanoma in 2011. As preclinical and clinical studies suggested that radiotherapy might activate the immune system in patients with prostate cancer, a Phase III trial of ipilimumab in addition to radiotherapy for metastatic CRPC patients was initiated. However, this Phase III study did not show any improvement in overall survival after radiotherapy followed by ipilimumab, compared with radiotherapy followed by placebo.

Currently, combination trials with abiraterone, ADT, sipuleucel-T, and prostvac are underway. 177Lu-J591, a humanized monoclonal antibody, was primarily developed in a radiolabeled form for PET, binding to the extracellular domain of prostate-specific membrane antigen (PSMA). After binding to PSMA, the 177Lu-J591ePSMA complex undergoes endocytosis and is accumulated in prostate cancer cells.

In this regard, 177Lu-J591J591 is considered to be a potential carrier for cytotoxic drug conjugates to maximize therapeutic effectiveness and a promising agent for radioimmunotherapy. Currently, a Phase 2 clinical trial is in the process of patient recruitment.

^{10[2]} Also, known as Yervoy.

Immunotherapy via check point inhibitors has become quite popular after the success in melanoma therapy. It has not, however, seen as significant in PCa.

5.3. Gene-based therapy

Olaparib, recently approved for treating ovarian cancer with BRCA1/2 mutations, is a poly-ADT-ribose polymerase inhibitor. Poly-ADT-ribose polymerase is involved in the DNA repair process, and genomic aberrations observed in CRPC are thought to confer sensitivity to poly-ADT-ribose polymerase inhibitors. In recent studies, olaparib showed a considerable response rate of 33% in post-docetaxel prostate cancer patients with defects in DNA repair genes, and a Phase II trial has commenced.

Thus, the only accepted approach is the dendritic approach that have been approved. The checkpoint approach has not yield any significant positive result although trial continue.

Let us review the options.

| Dendritic | CTL | NK | Mab |
|--|--|--|---|
| <ul style="list-style-type: none"> This is the current working approach. It is costly and requires ex vivo processing | <ul style="list-style-type: none"> Check point inhibitors work if they are the operative block to CTL attack. Uncertain | <ul style="list-style-type: none"> The NK approach does not rely upon an MHC contact but doe look for | <ul style="list-style-type: none"> Mabs can be developed as they have been for Check Point elements. Can they be expanded elsewhere? |

| CRISPR | CAR T | Gene Drive | CIK |
|--|--|---|---|
| <ul style="list-style-type: none"> We know that CRISPRS can insert and/or alter genes and we know some cells can be altered to express Ag which can be addressed. | <ul style="list-style-type: none"> The CAR T cell approach works well for some hematological cancers. CD 19 is a typical marker. The question is; is there a similar PCa marker or can we insert such a marker? | <ul style="list-style-type: none"> The Gene Drive approach would attempt to insert a new genetic structure in CTLs and force them forward. | <ul style="list-style-type: none"> CIK has been found useful in some hematological cancers and we ask if this may work here as well. |

Let us examine these in some further detail in the following Table. In this Table, we lay out some options for consideration.

| <i>Approach</i> | <i>Mode of Operation</i> | <i>Issues/Opportunities</i> |
|-------------------|--|--|
| Dendritic | The dendritic cells are antigen presenting cells. They manage to move throughout the body and identify various potential pathogens. | This seems to be the first of the putatively efficacious approaches in dealing with PCa. |
| CTL | Cytotoxic T Lymphocytes, Killer T cells, are the T cells which are an integral part of the adaptive immune system. | CTL need targeting via Ab specific paths. |
| NK | NK cells are part of the innate immune system, albeit being a lymphocyte lineage. They function by a balancing act between activators and inhibitors. | NK cells are effective innate killers of intruders. However, they can also release their killing cytokines which in turn may do harm to cells. |
| Mab | Monoclonal antibodies, Mab, are fundamentally Ab designed to recognize certain antigens, or epitopes, and attach to them and bring out the adaptive immune system response. | Mabs require the identification of targets. These targets must have some uniqueness. |
| CRISPR | CRISPRs allow for the editing of genes for the inclusion or excision of segments of DNA. | CRISPRs are somewhat independent of targets per se. They may have the ability to find alternative means for attacking the PCa cells. |
| CAR T | CAR T cells are T cells which have been genetically modified to attack specific targets which would normally be suppressed by MHC surface molecules identifying the cell as self. | CAR T cells like Mabs need targets. This is another example of identifying unique PCa cell targets. |
| Gene Drive | Gene Drives have been used in trying to "drive" a specific gene into some species. They generally drive at the embryo level, the fundamental stem cell level is you will, into a species. However, one could consider this also being used to "drive" into T cells or NK cells the ability to attack specific PCa cells. | Gene Drives can potentially drive into the stem cells of the immune system. Instead of changing the total species they can introduce self-replicating cells to attack the PCa. |

| <i>Approach</i> | <i>Mode of Operation</i> | <i>Issues/Opportunities</i> |
|-----------------|--|---|
| CIK | Cytokine-induced killer (CIK) cells are polyclonal T effector cells generated when cultured under cytokine stimulation. CIK cells exhibit potent, non-MHC-restricted cytolytic activities against susceptible tumor cells of both autologous and allogeneic origins ^{11[3]} . | CIK cells have shown to be effective is properly targeted. They have not been so for PCa but perhaps their broader spectrum capability for genetic markers may be useful. |

Observations

Based upon some of the recent results there are several observations worth examining. The most significant issue is the complexity of the PCa genome. Thus, the main problem we believe in PCa is the complex nature of the genetic makeup. As Gundem et al noted in 2015:

Cancers emerge from an ongoing Darwinian evolutionary process, often leading to multiple competing sub-clones within a single primary tumour. This evolutionary process culminates in the formation of metastases, which is the cause of 90% of cancer-related deaths. However, despite its clinical importance, little is known about the principles governing the dissemination of cancer cells to distant organs. Although the hypothesis that each metastasis originates from a single tumour cell is generally supported, recent studies using mouse models of cancer demonstrated the existence of polyclonal seeding from and inter-clonal cooperation between multiple sub-clones.

Here we sought definitive evidence for the existence of polyclonal seeding in human malignancy and to establish the clonal relationship among different metastases in the context of androgen deprived metastatic prostate cancer. Using whole-genome sequencing, we characterized multiple metastases arising from prostate tumour in ten patients. Integrated analyses of sub-clonal architecture revealed the patterns of metastatic spread in unprecedented detail. Metastasis-to-metastasis spread was found to be common, either through de novo monoclonal seeding of daughter metastases or, in five cases, through the transfer of multiple tumour clones between metastatic sites.

Lesions affecting tumour suppressor genes usually occur as single events, whereas mutations in genes involved in androgen receptor signalling commonly involve multiple, convergent events in different metastases. Our results elucidate in detail the complex patterns of metastatic spread and further our understanding of the development of resistance to androgen-deprivation therapy in prostate cancer.

^{11[3]} See Linn and Hui.

Namely many genetic changes are occurring continuously as PCa progresses. Thus, seeking a single marker may be fruitless. Yet, the immune approach can be designed to address the significant genetic complexity of PCa. Namely by addressing a broad spectrum of possible cells as would be the case with a CIK approach one could envision a treatment akin to a chronic disorder.

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Labels: [Cancer](#)

THURSDAY, FEBRUARY 9, 2017

[TAX AND SPEND REPUBLICANS](#)

They are at it again. The Luddites who believe that the only way to attack an issue is to tax it. The [NY Times](#) presents another article by the group of tax and spend Republicans. The authors state:

First, the federal government would impose a gradually increasing tax on carbon dioxide emissions. It might begin at \$40 per ton and increase steadily. This tax would send a powerful signal to businesses and consumers to reduce their carbon footprints. Second, the proceeds would be returned to the American people on an equal basis via quarterly dividend checks. With a carbon tax of \$40 per ton, a family of four would receive about \$2,000 in the first year. As the tax rate rose over time to further reduce emissions, so would the dividend payments. Third, American companies exporting to countries without comparable carbon pricing would receive rebates on the carbon taxes they've paid on those products, while imports from such countries would face fees on the carbon content of their products. This would protect American competitiveness and punish free-riding by other nations, encouraging them to adopt their own carbon pricing. Finally, regulations made unnecessary by the carbon tax would be eliminated, including an outright repeal of the Clean Power Plan.

Has anyone ever heard of the Government "returning" money! Are they living in some alternate universe. Also, again, unlike Harvard Professors, what of the poor person living pay check to pay check. Tax the hell out of everything and then a year later perhaps send them a check. That may have starved to death by then!

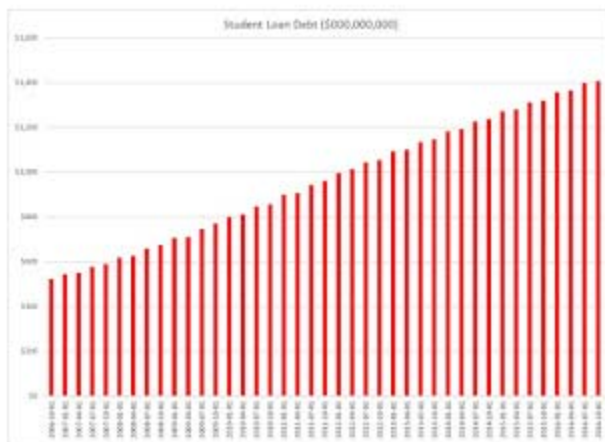
Why not solve the problem. Like engineers do! Perhaps that is why Harvard has no Engineering school, it would harm the economists!



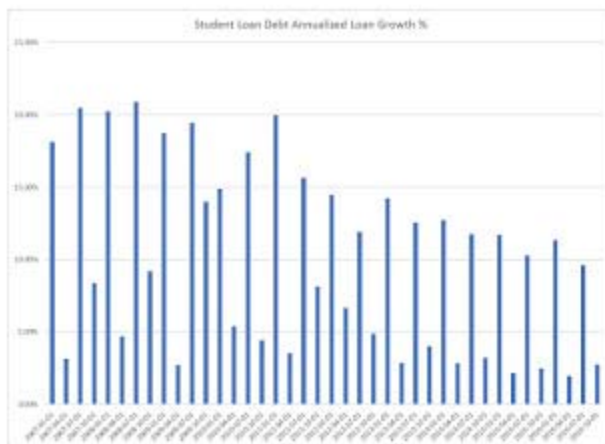
Labels: [Academy](#), [Economics](#), [Global Warming](#)

TUESDAY, FEBRUARY 7, 2017

SOME THOUGHTS ON STUDENT DEBT



Student debt continues to rise. What value is it? Clearly it continues to explode and laves us with what? Unemployed millennials? Is it the education that is failing? It was a pity to see students at MIT in the main lobby with finger paints making posters as if they were in Kindergarten. The failure is leadership. We have an overburden of in my opinion useless and dysfunctional administrators. More Deans than students. Everyone gets a title, an office, and massive benefits.



The above is the plot of annualized growth by quarter. A reduction from before 2008 but not a great deal. Somehow this burden will boomerang back on those who built what we had, and those who created this mess will prosper even more.

I suspect each snowflake will seek to blame everyone but themselves. Pity.



Labels: [Academy](#)

SUNDAY, FEBRUARY 5, 2017

SET POINTS VS CHECK POINTS

There has been a multiplicity of applications of such therapeutics as monoclonal antibodies which are used as "checkpoint inhibitors" to treat a variety of cancers. These therapeutics are proteins which can block the action of inhibitors on T cells which if activated and prevent the T cell from attacking the cancer cell. We have seen the proliferation of these therapeutic approaches in melanoma, lung cancer and even prostate cancer. In a recent White Paper we examine the concept of "[Check Points](#)" and "[Set Points](#)".^{12[1]}

The main driver for this analysis is the recent work of Chen and Mellman. In a recent paper these two authors state:

Immunotherapy is proving to be an effective therapeutic approach in a variety of cancers. But despite the clinical success of antibodies against the immune regulators CTLA4 and PD-L1/PD-1, only a subset of people exhibit durable responses, suggesting that a broader view of cancer immunity is required. Immunity is influenced by a complex set of tumour, host and environmental factors that govern the strength and timing of the anticancer response. Clinical studies are beginning to define these factors as immune profiles that can predict responses to immunotherapy. In the context of the cancer immunity cycle, such factors combine to represent the inherent immunological status — or 'cancer-immune set point' — of an individual.

The concept of a "set point" is in our opinion rather poorly used. The construct, if properly understood, means that there is some point at which T cell activators and inhibitors either permit activation and effective T cell immunotherapeutic action or inhibit that. Namely there is some set of activations less inhibitions which all T cells to perform and under that "set point" they no longer function.

If such a concept has physical meaning, then the authors state:

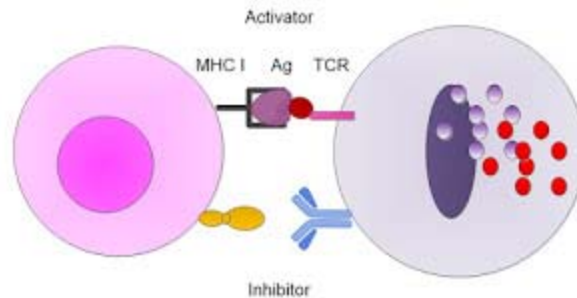
Although largely conceptual, the idea of a set point provides a framework to help organize the torrent of clinical and biomarker data that will emerge over the coming months and years. The number of targets that could prove effective for cancer immunotherapy is great; the number of potential combinations of therapeutic agents that are directed against these targets (or combinations of such agents with conventional standard-of-care agents) is even greater. The development of some cancer therapies may be largely empirical, but it can be guided by considering, even in general terms, the elements that comprise cancer immunity

Thus, our objective in this paper is to examine this set point concept and explore its dimensions. Specifically, we examine how it may be used for therapeutic uses.

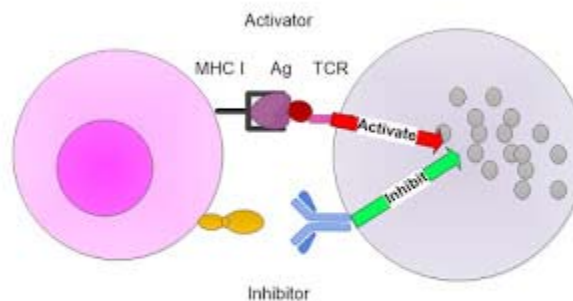
To best understand some of the principles we examine some simplistic model.

^{12[1]} See: <http://www.telmarc.com/Documents/White%20Papers/142SetPoint.pdf>

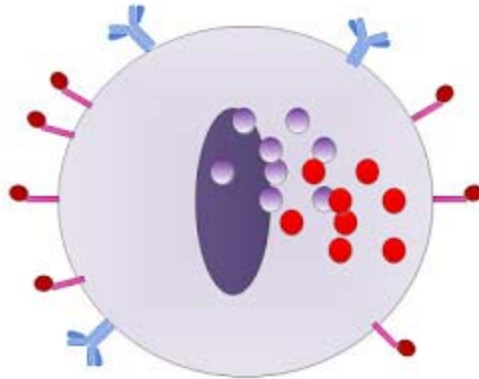
Let us begin with a simplistic but representative set of examples. We know that a CD8 T cell has a receptor, the TCR, T cell receptor, and it examines an antigen presenting cell, APV, which presents an antigen on its MHC I protein. This process is essentially an activator process. If that were all which was needed, then the T cell would be activated and sent out its cytokines and destroy the cell. However, there are also inhibitor ligands which activate inhibition in the T cell. Now if the T cell is activated and the inhibition is not then we get the T cell sending out cytokines and killing the offending cell.



However, if the T cell has an inhibitor also connected then the inhibitor sends out an internal T cell signal which stops the release. The presenting cell survives.



Now in reality the T cells do not have just one receptor. It may have a multiplicity over the surface. Thus, there are a multiplicity of activators and inhibitors. It is a multiplicity amongst the same type as well a multiplicity of types. In fact, the T cell may be just covered with receptors searching out antigens.



Thus, the first layer of complexity of the immune response is not a simple activator/inhibitor complex but a mass of receptors and ligands interacting in a complex manner. The question then is; at what point does the T cell go from active to inactive and back again? In fact, we may ask if there is some hysteresis effect. If so can we therapeutically take advantage of it.

Ligands and receptors are basically two separate chemical elements. The binding of them is also essentially a chemical process whereby the ligand finds the correct location on the receptor to bind. It is in many ways like any chemical reaction. As such there is a reaction rate whereby the ligand and receptor combine, but equally there is the reverse reaction, the breaking apart of a bond.

In the work by Stone et al the authors note:

The interaction between the T-cell receptor (TCR) and its peptide–major histocompatibility complex (pMHC) ligand plays a critical role in determining the activity and specificity of the T cell. The binding properties associated with these interactions have now been studied in many systems, providing a framework for a mechanistic understanding of the initial events that govern T-cell function. There have been various other reviews that have described the structural and biochemical features of TCR: pMHC interactions. Here we provide an overview of four areas that directly impact our understanding of T-cell function, as viewed from the perspective of the TCR: pMHC interaction: (1) relationships between T-cell activity and TCR: pMHC binding parameters, (2) TCR affinity, avidity and clustering, (3) influence of coreceptors on pMHC binding by TCRs and T-cell activity, and (4) impact of TCR binding affinity on antigenic peptide specificity.

Now they conclude:

The binding properties of TCRs for their pMHC ligands are critically important in the function of T cells, leading to outcomes that can involve T-cell selection in the thymus or full peripheral T-cell responsiveness or homeostatic T-cell proliferation in the periphery. The processes are even more complicated because the same TCR could interact with multiple pMHC ligands on the same antigen-presenting cell, each with heterogeneous binding properties. These reactions

would result in a complex integration of signals that ultimately determine the nature of the T-cell response. While there have been numerous studies to elucidate the precise binding parameters that correlate with different T-cell activities, various questions remain unanswered (in part because of the technical difficulties associated with performing binding experiments on low-affinity reactions). Further understanding of the TCR binding properties that generate defined signals is important, not only from a basic science perspective but also toward developing optimal strategies that improve T-cell responses to foreign antigens and tumour antigens.

Thus, one must be careful in developing an immune set point theory to be cautious about the affinity issues as discussed above.

We have examined the complex process fundamentally as a build. Specifically:

1. Activation: When an antibody binds with the TCR we expect a response.
2. Inhibitor: When there is an inhibitor, however, it may be possible to block the pathway leading to the activation.
3. Notwithstanding the above, the cell actually has a multiplicity of the previous two and thus there may be some race with a finish line defined by what has been called a "set point", or simply some collection of activators and inhibitors seeing which one dominates.
4. There are not just one possible activator and inhibitor. For a T cell, we have the TCR but we may have well more than a PD-1. New inhibitors are arising each day.
5. The internal machinations of the cellular pathways may also effect the net result. Thus, genetic changes can affect what happens.
6. The kinetics of the binding can and often do play a significant role. Binding is not a one-way street, and the result may be loss of tumor control.
7. Exogeneous Factors: The human biome is often a driving factor to the efficacy of immunotherapy.

As Chen and Mellman note:

Factors that are extrinsic to the tumour or host genomes may also affect the immune profile of tumors. Chief among these is the gut microbiome, which has an important role not only in influencing the initiation of some cancers, but also in the response to chemotherapy and immunotherapy...mice bearing subcutaneous syngeneic tumors do not respond to chemotherapy if sterilized by prior treatment with antibiotics or when raised in germ-free conditions. The effect was attributed to the ability of commensal bacteria to activate the innate immune system of the host following chemotherapy, possibly by causing symbiosis and penetration of commensal bacteria into the gut lamina propria. Subsequent work established an even clearer link between T-cell responses and an intact microbiota. Fecal transfer or co-housing experiments in mice demonstrated that defined species of gut bacteria enabled antitumor responses after treatment

with anti-PD-L1/PD-1 or anti-CTLA4 therapies. Furthermore, the gut microbiota even influenced spontaneous antitumor responses, which correlated with the degree of T-cell infiltration into tumors before any therapy had been administered.

Each of these elements can be considered as a therapeutic target for immunotherapy. We summarize some of these below.

| Activator | Inhibitor | Multiplicity | Checkpoints |
|---|---|--|--|
| <ul style="list-style-type: none"> • Activators start the process of making the immune system attack the putative pathogen | <ul style="list-style-type: none"> • Inhibitors are often a "self" determinant yet are used by cancer cells to neutralize the immune system. | <ul style="list-style-type: none"> • The receptors are spread all across the surface of a cell. Also there is a multiplicity of different receptors. Thus, multiplicity has two meanings: <ul style="list-style-type: none"> • (i) multiplicity of a single type on a single cell, and • (ii) a multiplicity of different types on a single cell. • This is both a complexity and an opportunity for immunotherapeutic targets. | <ul style="list-style-type: none"> • Checkpoints are an extension of inhibitors and has become a key factor in current immunotherapy. |

| Pathways | Enzymatic Reactions | Exogenous Factors |
|---|--|--|
| <ul style="list-style-type: none"> • Pathways in normal cells allow both activation and inhibition to function. However genetic alterations which block those factors result in loss of function of the immune response. | <ul style="list-style-type: none"> • Activation and Inhibition are fundamentally enzymatic reactions. Understanding the dynamics of these reactions as well as the ability to manipulate them is an added factor in the immunotherapeutic tool box. | <ul style="list-style-type: none"> • The human biome is but a single example of these types of factors. |

Thus, understanding the specifics may be a useful approach in guiding therapeutic development using the immune system.

The previous brief summary lays out some of the issues inherent in the Chen and Mellman paper. To better understand let us now return to the ideas of Chen and Mellman. Specifically, their definition of a "set point". They state:

The cancer-immune set point is the threshold that must be overcome to generate effective cancer immunity. The set point can be understood as a balance between the stimulatory factors (F_{stim}) minus the inhibitory factors (F_{inhib}), which together must be equal to or greater than 1, over the

summation of all T-cell antigen receptor (TCR) signals for tumour antigens. The cancer-immune set point is shown here:

$$\int (F_{stim}) - \int (F_{inhib}) \geq 1 / \sum_{n=1}^y (TCR_{affinity} \times frequency)$$

The set point is defined by the summation of the frequency of peptide-MHC-TCR interactions and TCR signalling in all anticancer CD8+ T-cell clones (mainly, the TCR affinity for the antigen-MHC class I complex) against antigens present in the cancer cells, including neoantigens and cancer-associated antigens, and the endogenous balance of the positive and negative immune regulators that are inherent to each host or patient.

Now just what this means is somewhat open for debate because it is written by a biologist not a physical scientist and definitely not an engineer. Permit me to attempt an interpretation. First let us try to be specific about a definition. Namely some definition of a variable which is measurable.

Let us try to first understand the F terms.

Fstim: This is a stimulatory factor. What is it? One could guess it is some cell with an MHC I presenting some antigen Ag to a T cell receptor TCR. Should we examine cell by cell? Should we look at every possible T cell, namely ones that say are CD 8 T cells, or how about other immune cells. Why not include NK cells as well? Should we look at stem cells only, do we know what they are? Do we then count these for every T cell, for a mass of T cells, for what?

Finhib: We know some of these we believe. There is PD-1 and CTLA-4. They can block the T cell from attacking. We also suspect that there are many others we have yet to find. So, let us simplistically assume we can model with the two mentioned. But what are we measuring? Are we measuring a single cell, a collection of cells, the totality of all cells? Are we measuring all stimulatory factors or just a few? Are we measuring all inhibitory factors or just the ones we know? Are we weighting some differently than others or the same?

This if we have two single cells and it has say 50 T cell receptors and 45 PD-1 receptors, then we can have activated say 35 of the TCR and have activate say 22 of the PD-1. Now what happens? Is activation by each TCR the same and can a TCR being activated be inhibited by an activated PD-1 on a one to one basis?

$$\int_{S'_0}^{S_1} F_{Stim}(r, t) dr dt - \int_{S'_0}^{S_1} F_{Inhibit}(r, t) dr dt > \alpha$$

OR

$$\sum_{n=1}^N \left[\int_{S'_0}^{S_1} F_{Stimulate}(n; r, t) dr dt - \int_{S'_0}^{S_1} F_{Inhibit}(n; r, t) dr dt \right] > \beta$$

The above still has no physical meaning. Now let us consider T Cell Affinity. As Nicholich et al state:

Affinity refers to the steady-state association constant between a monovalent receptor and its ligand, in this case a single T-cell receptor (TCR) and peptide–MHC (pMHC) complex. Structural avidity is the steady-state association constant between multiple cell-bound receptors and ligands and is determined by the direct binding affinities of multiple TCRs to their pMHC complexes. Functional avidity depends on the relative kinetics of signalling that translate into measurable biological functions such as proliferation, cytokine production or cytolytic function. APC, antigen-presenting cell.

Now as Hsieh et al note:

TCR affinity: The strength of interaction between the T cell receptor and a single peptide–MHC complex.

As an abstraction that may be fine but as something used in a measurement and equation it is highly deficient.

Now as Daniels et al note:

To estimate the TCR affinity of the ligands comprising the selection boundary, we measured tetramer binding; which correlates with monomeric TCR–pMHC affinities, is performed on live cells and involves the participation of CD8. The binding characteristics of tetramers were determined on pre-selection OT-I double positive thymocytes at 37 uC. The dissociation constant (Kd) was calculated by nonlinear regression analysis and confirmed by homologous competition experiments. The tetramer binding curves for Q4R7 (weakest negative selector), T4 (border ligand) and Q4H7 (strongest positive selector) overlapped. Their Kd values (Q4R7, 4869.5 nM; T4, 55610.1 nM; Q4H7, 5169.1 nM; n57, P50.455) and their half-lives (t1/2) were not significantly different (Table 1). However, heterologous competition assays showed that Q4R7 was more efficient than Q4H7 at inhibiting the binding of OVA tetramers.

or perhaps they mean something akin to this:

$$\sum_{n=1}^N \left[\int_{S'_0}^{S_1} F_{Stimulate}(n; r, t) drdt - \int_{S'_0}^{S_1} F_{Inhibit}(n; r, t) drdt \right] > \beta$$

or

$$\frac{\sum_{n=1}^N \left[\int_{S'_0}^{S_1} F_{Stimulate}(n; r, t) drdt - \int_{S'_0}^{S_1} F_{Inhibit}(n; r, t) drdt \right]}{\sum_{m=1}^M TCR_{Affinity}(m) f(m)} > \lambda$$

Now we know that there is a threshold effect for activating and suppressing. Namely there has to be more activators than suppressors. Just what that balance is of course is uncertain. Again, the statement has no physical meaning.

They continue:

This can be further influenced by other elements of immunity, including tumour-derived immunomodulatory components, as well as by exogenous factors such as infection and exposure

to pharmacological agents. A given patient with cancer may have a low set point, making it easier to generate an anticancer immune response, or a high set point, which makes it more difficult.

The aim of immunotherapy is to increase F_{stim} , decrease F_{inhib} or increase TCR signalling to drive progression of the cancer-immunity cycle. These values are difficult to quantify with current techniques but represent a useful theoretical construct. It is probable that the cancer-immune set point of a particular person is already determined by the time of clinical presentation, driven by the inherent immunogenicity of the tumour and by the responsiveness of the individual's immune system. Although it is reasonable to assume that various lines of cancer therapy or changes in environmental factors might alter F_{stim} and F_{inhib} , such changes might only be transient. Often, the set point that is identified using pretreatment biopsies is similar to the set point determined by biomarker profiling from biopsies taken on progression after therapy. Likewise, despite the continued accumulation of mutations in a tumour as a function of time, primary and metastatic lesions can exhibit similar immune profiles. The features that determine the set point may therefore reflect genetic factors that are specific to a given tumour, the genetics of the person with cancer, or the extent to which antitumor immunity had developed initially. Conceivably, immunotherapy may work as a consequence of either its direct effect on F_{stim} and F_{inhib} (that is, by assisting the completion of a single revolution of the cancer-immunity cycle) or its ability to alter the set point (for example, by propagating the cancer-immunity cycle, which enhances the cancer-specific T-cell response). Although largely conceptual, the idea of a set point provides a framework to help organize the torrent of clinical and biomarker data that will emerge over the coming months and years. The number of targets that could prove effective for cancer immunotherapy is great; the number of potential combinations of therapeutic agents that are directed against these targets (or combinations of such agents with conventional standard-of-care agents) is even greater.

Thus, let us try and construct meaning which may be measurable and verifiable as well as actionable. Consider the following model:

1. Let us assume we have a tumor cell. Let us assume there are N possible activator ligands and M inhibitor ligands.
2. Let us assume that for each of the above ligands we have on a T cell some receptor. If there is a ligand without a receptor we shall ignore it.
3. Assume we can count and differentiate the differing ligand-receptor possibilities on a cell.
4. Now calculate the following:

$$\frac{\sum_{k=1}^K \alpha_k N_{activator,k} - \sum_{j=1}^J \beta_j N_{inhibitor,j}}{\sum_{k=1}^K N_{activator,k} + \sum_{j=1}^J N_{inhibitor,j}} \leq \lambda$$

Namely, we count the number of different activators and the number of different inhibitors and then weight them by some metric, yet to be determined, and then weigh them by the total present.

This approach may have merit. The weights may be unity, but that is a mere guess. The weights may be reflective of the enzymatic consistency of the contact. Frankly we just do not know but it is worth exploring.

We now return to following Chen and Mellman and their observations. They note:

The role of the immune system in cancer remained unappreciated for many decades because tumors effectively suppress immune responses by activating negative regulatory pathways (also called checkpoints) that are associated with immune homeostasis or by adopting features that enable them to actively escape detection. Two such checkpoints, cytotoxic T-lymphocyte protein 4 (CTLA4) and programmed cell death protein 1 (PD-1), have garnered the most attention so far. CTLA4 is a negative regulator of T cells that acts to control T-cell activation by competing with the co-stimulatory molecule CD28 for binding to shared ligands CD80 (also known as B7.1) and CD86 (also known as B7.2). The cell-surface receptor PD-1 is expressed by T cells on activation during priming or expansion and binds to one of two ligands, PD-L1 and PD-L2. Many types of cells can express PD-L1, including tumour cells and immune cells after exposure to cytokines such as interferon (IFN)- γ ; however, PD-L2 is expressed mainly on dendritic cells in normal tissues. Binding of PD-L1 or PD-L2 to PD-1 generates an inhibitory signal that attenuates the activity of T cells. The 'exhaustion' of effector T cells was identified through studies of chronic viral infection in mice in which the PD-L1/PD-1 axis was found to be an important negative feedback loop that ensures immune homeostasis; it is also an important axis for restricting tumour immunity.

They then proceed to characterize three differing states of tumors with respect to their T cell response. They are:

1. Inflamed Tumor: This a tumor with lots of cells and penetrating the tumor space.
2. Immune Desert Tumor: This is a tumor with lots of cells but no significant penetration of the tumor space.
3. Immune Excluded Tumor: This is a tumor with a paucity of any T cells present.

Now we consider the descriptions as presented by Chen and Mellman:

The first profile, the immune-inflamed phenotype, is characterized by the presence in the tumour parenchyma of both CD4- and CD8-expressing T cells, often accompanied by myeloid cells and monocytic cells; the immune cells are positioned in proximity to the tumour cells. Samples from inflamed tumors may exhibit staining for PD-L1 on infiltrating immune cells and, in some cases, tumour cells. Many proinflammatory and effector cytokines can also be detected by mRNA analysis in these sections of tumors. This profile suggests the presence of a pre-existing antitumor immune response that was arrested probably by immunosuppression in the tumour

bed. Indeed, clinical responses to anti-PD-L1/PD-1 therapy occur most often in patients with inflamed tumors...The second profile is the immune-excluded phenotype, which is also characterized by the presence of abundant immune cells. However, the immune cells do not penetrate the parenchyma of these tumors but instead are retained in the stroma that surrounds nests of tumour cells. The stroma may be limited to the tumour capsule or might penetrate the tumour itself, making it seem that the immune cells are actually inside the tumour. After treatment with anti-PD-L1/PD-1 agents, stroma-associated T cells can show evidence of activation and proliferation but not infiltration, and clinical responses are uncommon. These features suggest that a pre-existing antitumor response might have been present but was rendered ineffective by a block in tumour penetration through the stroma or by the retention of immune cells in the stroma. T-cell migration through the tumour stroma is therefore the rate-limiting step in the cancer-immunity cycle for this phenotype.

Finally, the third type is characterized as follows:

The third profile, the immune-desert phenotype, is characterized by a paucity of T cells in either the parenchyma or the stroma of the tumour. Although myeloid cells may be present, the general feature of this profile is the presence of a non-inflamed tumour microenvironment with few or no CD8-carrying T cells. Unsurprisingly, such tumors rarely respond to anti-PD-L1/PD-1 therapy. This phenotype probably reflects the absence of pre-existing antitumor immunity, which suggests that the generation of tumour-specific T cells is the rate-limiting step. The immune-desert phenotype and the immune-excluded phenotype can both be considered as non-inflamed tumors.

Thus, this does pose the question; how does one identify these cells and how could one move one category to the other for better response? Frankly one asks just what is happening from one class to another?

Observations

Set Points, Check Points, and other elements of the control of the immune system as a mechanism to understand and deal with cancer has been evolving at a rapid pace. Where the Check Point field seeks new and effective ligand-receptor pairs, the Set Point field seems to examine the process in a more holistic manner. Perhaps that is an approach which would enable a more systematic approach.

Cell Maturation and Differentiation

How does this process change as a cell matures? What of cell differentiation. T cells like many of the lymphoid line go through varying degrees of maturation. Thus, we ask: what is the difference?

Stem Cells

We have discussed the stem cell constructs at length. In McGarty (Stem Cells) we have tried to bring some of these ideas up to data. The problem is that stem cells may very well have different markers than the cells we can attack with the tools at hand. Thus, attacking PD-1 and CTLA4

markers may work for the mass of the tumor and result in shrinkage but it may totally miss the stem cell. How best to address this is uncertain?

Therapeutic Dimensions

What are the therapeutic dimensions of this principle? We have discussed a few here but there are many which present themselves.

CAR T Cells

CAR-T cells are "engineered" T cells which are designed by use of such tools as a lentivirus to attack a specific malignant cell. They have been shown to be useful for hematological cancers and have been examined for solid tumors. As Ramachandran notes in his Thesis:

As the name suggests, a CAR is a chimera of domains from different proteins assembled together to create a functional receptor. These novel receptors initiate a functional downstream effector T-cell signaling pathway when they encounter target antigen, usually the TAA on a cancer cell. This gives the opportunity to engineer a large variety of TAA-specific receptors targeting a broad range of cancer types.

CARs typically contain four domains

(a) extracellular antigen binding domain: It confers the antigen-specificity to the engineered T-cell. A majority of the engineered CARs for cancer therapy have antibody-derived antigen binding domains called single-chain variable fragment (scFv). CARs containing a scFv extracellular domain retain the specificity of an antibody. A major advantage of having scFv extracellular domain is that it bypasses the need for antigen presentation by MHC-I on tumor cells, as antibodies directly bind to cell surface antigens. (b) Spacer or hinge region: It gives flexibility and length to allow proper dimerization of scFv, thus improving its stability. The most commonly used spacer regions are derived from IgG Fc CH2-CH3 domains, CD28 hinge domain and CD8 α spacer domain (c) Transmembrane domain: It determines the stability of CAR expression on cell surface. The most commonly used transmembrane regions are derived from CD3 ζ CD4, CD8 and CD28 molecules 138 and (d) Cytoplasmic signaling domain(s): This region has the domains that provide the necessary downstream signaling for T-cell effector functions. CARs are classified into different generations based on the number of cytoplasmic signaling domains namely first, second and third generation CARs. First generation CARs have only one cytoplasmic domain, usually T-cell activation signaling domain (CD3 ζ chain). In addition to the T-cell activation domain second generation CARs have one extra co-stimulatory signaling domain, e.g., CD28, 4-1BB, ICOS or OX40 and third generation CARs have two extra co-stimulatory domains...

In a recent Technical Note McGarty has further developed the CAR-T cell concepts for both hematological and solid tumors. CAR-T are engineered to specific targets. The question then is; can a better understanding of set points allow for improved targeting for CAR-T cells or are CAR-T cells perforce of their design not really useful for attacking solid tumors?

Dynamic Models

The enzyme kinetics of the reactions on the surfaces of T cells and APC or tumor cells are critical. We have almost always assumed that once a protein is bound it stays. Yet we know it is not the case. Furthermore, when understanding the set point model, if we have a paucity of activators on a T cell it will not function. If the paucity is due to enzymatic action, then perhaps we can indirectly address the low level by increasing the retention via enzyme kinetic improvement.

Pathway Factors

The pathway factors are both integral to immunotherapeutic approaches, they facilitate the process inside a T cell for example, but they may also be poorly understood. Let us briefly review that issue. We must look at pathways from the perspective of the T cell and the tumor Ag presenting cell.

1. From the T cell perspective we have internal genetic pathways which facilitate the process of cytokine release. If there are faults on the pathway, then we would not expect the T cell to function. Thus, we may ask if these are somatic defects or a result of some change in the T cell.
2. From the perspective of the tumor cell, we know its pathways have usually been altered. Then does this altering result in the excess expression of inhibitors or the suppression of activators. Do the pathways alter the MHC I presentation efforts?

Both dimensions are worth examining.

Political Factors

A recent National Academies Report by Balogh et al present several policy issues regarding immunotherapy. The report was meant to present a simplified overview of immunotherapeutics as well as present some key policy issues. Concerns regarding costs, patient value, physician-patient expectations were discussed. Also, was a discussion on evidence based approaches. The problem is that the experience is limited and the costs high. Furthermore, what seemed not discussed was the fact that the complexity of this field is great and the depth of understanding by physicians quite limited. One could say that most Oncologists are trained to administer chemotherapy, and have a limited if not aged understanding of the immune system.

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Labels: [Cancer](#)

THURSDAY, FEBRUARY 2, 2017

[MANUS, A POINT IN TIME](#)

Manus is one of the Admiralty Islands north of New Guinea. I find the current debates, I guess one can call them that, of interest.

First, Manus is north of New Guinea. It is part of the Admiralty Island and was one of the major bases during WW II.



At the southern end of the above is a tip of Australia. Manus was a major repair depot during WW II. That was after MacArthur managed to secure New Guinea from the Japanese. Now it is a relatively deserted island with what appears is a prison.

As the [NY Times](#) states in a video:

Here is what daily life looks like for an Iranian dissident at an Australian-run camp on Manus Island.

[The Guardian](#) has a more detailed discussion:

Those who try to come by boat – who are more likely to be from poorer and more troubled countries – have been assured by Canberra they will never come to Australia. Australia needs the people on the islands of Nauru and Manus to be removed from them – the policy is morally reprehensible and illegal. Domestic politics has made this hard – and this is why the US stepped in.

Frankly how people got sent to Manus is itself problematic. It is a tropical island which was brutally fought over during WW II.

Below is my fathers Destroyer in Manus in November 1944 after the Battle of Leyte Gulf. (DD-649, USS Albert W. Grant). At that time Manus was a major repair depot. Sadly the ship in the background was an ammunition supply ship and shortly after this photo it exploded killing dozens. Manus has a bit of a spotted history.



The issue is; why choose Manus? Having a spot in the Pacific rear its head again is quite interesting. Especially since men like my father and his crew mates had bloodied themselves saving Australia from Japanese atrocities. Strange how the world turns.



Labels: [Commentary](#)

SUNDAY, JANUARY 29, 2017

[DOING AN EXPERIMENT](#)

There are two extremes in doing an experiment. The Classic approach is to examine the literature, discuss with colleagues, take a few preliminary steps, then go step by step recording the results in your Lab notebook.

The second approach is to take that piece of shiny sodium and flush it down the toilet and run like hell. That way you get to see what really happens.

So if you want to, well say drain your sewer system, just toss that chunk of sodium and flush. Then you get to really see what happens.

Just a thought.

And for those Fine Arts majors who have not a clue of what I am saying try Wikipedia.



Labels: [Commentary](#)

TELLING PEOPLE HOW TO LIVE

The [NY Times](#) has some writer who discusses how to "take the care keys" away from a relative. This is a touchy topic. One the one hand we have 80+ folks who are often brighter and more considerate than their great grand children. Then we have some older person whose vision gets no higher than the horn on the steering wheel and moves like a snail but without any awareness of their surroundings. So who gets to decide?

The author writes:

My now-car-free relative is not the sort to sign up for one of those 55-plus communities promising sunshine, gardens and golf. Retirement was an eventuality that inspired in him not relief but dread. Fiercely independent, an old-school intellectual and, frankly, a bit of a loner, he insists on remaining in his suburban home ("I will die in this house" typically ends any conversation in which I suggest a move) — even if that home is slowly becoming a dangerous place for him to be in.

The issue here is; who gets to decide what to do? Does this author believe that she has total authority, that at some age we deny people autonomy, even if at no risk to others?

Autonomy has been a value for Americans since the founding, but since the Left has come along in a Nanny State, they get to decide and tell others what they should do, and in turn decide what is best.

There is an interesting article in the [Deep Code](#) blog which is worth reading. The author states:

So, for example, if the Deep State uses its power advantage as a way to stall until until it can innovate a collective intelligence advantage, it has a decent chance. (Of course, becoming a decentralized collective intelligence is going to be really hard for the actual individuals who make up the Deep State to understand and accept.) But watch out as the conflict evolves. As the Insurgency cuts down and unplugs legacy power structures (e.g, the media, the intelligence agencies) and replaces them with more fluid and innovative approaches (e.g., gab.ai and Palantir) the balance will begin to tip quickly. If the Establishment cannot stave off the Insurgency in the next 4–5 years, that phase of the war will be over.

I will not de-construct the above, but what it is saying is that there is a massive change afoot. Taking the keys away from Grandpa, letting Grandma just die, may be the final throes of the Left. It is not the Right taking over, it may be a totally different movement. Strangely enough, the very protests we see well formed and assembled with pre-printed signs, may be the very catalyst for this alternative to move ever so fast. Perhaps Marx had a point, namely thesis, anti-thesis, synthesis, but that such a process continues without a stable point.

Taking Grandpa's keys may be the last straw and the first act.



Labels: [Commentary](#)

FRIDAY, JANUARY 27, 2017

CALIFORNIA?

In 1861 there was a bit of a mess up started by states leaving the Union. Somehow if they could not get their way, well you know the story. Now along comes California.

It appears that [yescalifornia](#) is a move to leave the Union. They state:

*In the Spring of 2019, Californians will go to the polls in a historic vote to decide by referendum if California should exit the Union, a #Calexit vote. You will have this historic opportunity because the Yes California Independence Campaign will qualify a citizen's initiative for the 2018 ballot that if passed would call for a special election for Californians to vote for or against the independence of California from the United States. **This is a very important question.** It is the responsibility of this campaign to explain what a yes vote will mean for you, your family, your community, our state, our country, and our world. We have designed this website to answer many of these questions and look to you to ask more. "As the sixth largest economy in the world, California is more economically powerful than France and has a population larger than Poland. Point by point, California compares and competes with countries, not just the 49 other states."*

Not clear who these folks are. But perhaps we could sell it off to the highest bidder. Perhaps China would want California. Russia once had an interest, then again Mexico could get a claim in as well.

Knowing California, this may very well pass. Then think of it, all those Apps would be in a foreign country and we could block them. Make our children go back to reading books, doing real work.

There may be something here for everyone. Keep tuned.



Labels: [Politics](#)

THURSDAY, JANUARY 26, 2017

THE COST OF A WALL

Now I have never built a wall, at least a big one. You see I have a little wall, around my daylilies, to keep out the deer. It does not keep out the squirrels, rabbits, chipmunks, and nothing keeps out the fox. You see, foxes are really smart, and they are fearless. My fox walks by and smirks, yes, smirks at me. Fortunately his possible meals are all up in trees. But my wall, I put it in myself, holds out those evil deer.

Now don't ask me how much the wall costs. I just went to Home Depot, loaded the car with wall building stuff, really fence stuff, and then put it up. And waited. It worked. It kept those deer at bay.

Now as to the southern wall. I have not a clue. But the Press today is quoting MIT at \$25 billion.

So I thought that it would be useful to see what the source was. I know something about building stuff. I built cable systems, cellular systems, fiber systems, some in over 20 countries. I know building some stuff. I also knew then when back at MIT students and even some faculty would wander into the field of costing things. Like how much a fiber to the home would cost. Then I asked such things like; where is the franchise cost, the pole attachment costs, the right of way costs? Ooops, since they had no experience they had no clue. So their analysis was usually off.

So when I heard about this MIT cost estimate I went on a trip to the source. It appears to be a [Technology Review](#) piece. Now Technology Review used to be the alumni magazine until some twenty years or so ago it was taken over I believe by some group who turned it into one of those technological sheets that are mostly ads plus writings from a variety of folks telling us about the future. My copy generally sees the trash before it is opened. So when I saw that the reference and source was Technology Review I got suspicious.

Now, further the writer, I gather, is from a left leaning think tank in DC and as best as I can gather has never "built" a wall, at least a big one. The author states:

That fits with what structural engineers have told me: the total cost of highways and other megascale projects in the U.S. is generally two to three times the material costs. That makes a 1,000-mile wall pencil out at \$27 billion to \$40 billion.

That is a bit of a range. So let me see. It was not MIT but Technology Review. It was not an expert in walls, but some staff person at a think tank. It was not a detailed analysis but at best a set of guess works and then a multiplier. And the answer is somewhere between \$27B and \$40B. Try that on an MIT problem set.

Even [NPR](#), that bastion of totally correct reporting has stated:

Were he to, in fact, try a wall, the cost could be much higher. One estimate from MIT found that a 1,000-mile wall would cost anywhere between \$27 billion and \$40 billion.

If NPR had at least noted from its hyperlink it was Technology Review and NOT MIT, then it would in my opinion have been true reporting, not what seems to be the latest flurry of in my opinion could be considered and element of "fake news".

So let's talk to someone who has built things, real things. Like, I don't know, perhaps the Press could find a real person like that.



Labels: [Academy](#), [Commentary](#)

[THE CAMPUS CAULDRON](#)

Back in the 60s, when one opposed the Vietnam War, there were clear reasons. One was you, if you were male, had a good chance of getting killed. Half a million at a time were sent there and the strategy and reasons were anything but clear.

Now we have the clamor over the current President. As noted I have no horse in the race but as an observer the intensity of the opposition is, well just to say, kind of over the hill.

In The Tech, the MIT student newspaper, which even during Vietnam walked a middle road, extolling the concert for the coming weekend, not bubbling over in terror because Johnson or Nixon sent more troops. But now in [The Tech](#) they writer notes:

Many recount losing friends, being insulted, or being yelled at after having revealed their political beliefs. They've said that MIT professors have publicly criticized their candidate, their party, or their beliefs. Many recall hateful post-election rhetoric, such as assassination wishes on the "Share your hopes" posters put up in Lobby 7.

Imaging "assassination" wishes posted in the main entry way, and among these wishes many were apparently lauded by the general statements of the President of the Institute.

What do they say about the odors of dead fish? Just a thought. How do computer scientists and molecular biologists get so vitriolic? One need look no farther, I believe, than the exploding administration overhead.



Labels: [Academy](#)

MONDAY, JANUARY 23, 2017

[TRAFFIC MERGING](#)



The Canadians are polite to an extreme, I guess, and so notes [The National Post](#). You see when they notice a one lane notice, they all slowly and politely get into one lane a mile or so ahead of the merge. The paper notes:

Virtually every traffic scientist agrees Canada is absolutely awful at merging through bottlenecks.

In fact, it's hard to imagine how we could be worse. At the first sign of a lane coming to an end, the Canadian strategy is to immediately cram into single file and abandon the soon-to-run-out lane. Then, as cars slowly inch ahead through the gap, they zealously defend the sanctity of the

line by aggressively blocking the entry of any and all late mergers.

Now the write suggests what he calls a "zipper merge" which is what we in New York City call "alternate merge". It is what we do at the Holland, Lincoln tunnels and the GW Bridge. If we did not then the city would come to a halt. In fact in all of NYC we alternate merge. It is not just polite, it is survival.

Now for those of you who travel out of NYC in the State, I have been told by New York State Troopers, the last remaining Praetorian Guards in the US, that there is no such thing as an "alternate merge". The NY State Police say you MUST stop in the ending lane until there is NO traffic in the traveling lane, and then you may enter! Yep, bring half the world or more to a standstill. These guys must live in some holler in the Catskills. But they are 6'5" and walk holding the handle of their 9 mm on their hips. So, despite the fact that the law they say we must comply with does not exist, they are the law!

The Paper continues:

"By working together, by abandoning our individual preferences and our distrust of others' preferences, in favor of a simple set of objective rules, we can make things better for everyone," wrote Tom Vanderbilt in the 2008 book Traffic. Jurisdictions have tried with varying success to convert their citizens to the gospel of the zipper merge. Starting in the early 2000s, the state of Minnesota has been the U.S. standard for the zipper merge, rolling out pro-zipper merge signage and public relations campaigns. Since 2015, the City of Saskatoon has been pushing the zipper merge as a method to reduce congestion.

Perhaps if we are in the process of renegotiating NAFTA we could train the NY State Police in polite driving, and practiced in New York City. Who said we are rude?



Labels: [Commentary](#)

SUNDAY, JANUARY 22, 2017

PROTESTS: THEN AND NOW

Well back a hundred years there was my Grandmother, Hattie F. Kruger, before marrying my grandfather. Shortly after this photo, she is 3rd from right, President Wilson had them thrown in the Lorton Prison and there they rotted till he felt the public pressure. The he declared War on Germany.



Here are her great-granddaughter and great-great-granddaughter. They came and went by bus, the capes were, I gather, gifts from some one upon their arrival. They made it back home without a stop in Lorton.

I will let you all figure what has changed.



Labels: [Commentary](#)

[COME THE ECONOMISTS](#)

Again come the economists. This time with pets. Simply put, they argue that health care for pets is cheaper than for humans.

The NY Times reports:

“These commonalities made us think that something else may be behind the rapid growth in human health care spending,” said Amy Finkelstein, an M.I.T. economist and one of the authors of a recent study on pet care. She, along with her co-authors Liran Einav and Atul Gupta of Stanford, tried to find what that something else could be in their study on pet health care presented at the American Economic Association annual meeting in Chicago. “We often blame generous insurance and significant public sector involvement, but those are absent from pet care,” Ms. Finkelstein said.

Some health economists say generous health insurance and significant government intervention in the health care market promote unnecessary spending. They note the United States spends more of its G.D.P. on health care than other similar advanced economies yet does not exhibit broadly better health outcomes, a sign of inefficiency. But other economists argue that health care is so valuable that we might reasonably spend even more on it than we do today. Which camp is right?... “It makes you think that the emotional nature of the treatment decision may be important in explaining high and sometimes heroic end-of-life health care spending,” Ms. Finkelstein said, “whether on your dog or on your mother.”....Though you might reasonably avoid pet care insurance, you really can’t do that with human health insurance. Human and pet health care may have some commonalities, but this isn’t one of them.

Well folks the answer is real simple. If your dog or cat is terminally ill you "put it down". Cheap and does not require the excessive costs of hospitalization in final days. We used to let humans stay at home for their final days. But that too has ceased. If your pig or goat or sheep is terminal you may bring it down and render it, make some money on the carcass. Sorry, but it was an economic decision.

First, animals are not humans. We can legally "put them down". The ACA somewhat thought of that but never implemented it. The close as the got was in doing away with PSA testing, that was acceptable, so instead of biopsies and surgery, you have bone mets and death. After it is just a man. Rover has more dignity!

I wonder if the researchers ever spent time on a farm? I never saw many in Cambridge.



Labels: [Health Care](#)

SUNDAY, JANUARY 22, 2017

[DOWN THE RABBIT HOLE](#)

There is an old technique in interrogation or in avoidance called "Down the Rabbit Hole". This means you get a white rabbit, dress them up with a pocket watch and let them run down a rabbit

hole. People then follow and the issue is following the white rabbit. While at the same time you are left to do what you wanted yet no longer having a tone of watchers, in fact of the watchers are dumb enough then they all go down the rabbit hole. Sound familiar? Think!

But now perhaps re-reading Alice would help on many fronts.

"It's no use going back to yesterday, because I was a different person then."

"But I don't want to go among mad people," Alice remarked.

"Oh, you can't help that," said the Cat: "we're all mad here. I'm mad. You're mad."

"How do you know I'm mad?" said Alice.

"You must be," said the Cat, "or you wouldn't have come here."

"Why, sometimes I've believed as many as six impossible things before breakfast."

"Would you tell me, please, which way I ought to go from here?"

"That depends a good deal on where you want to get to."

"I don't much care where –"

"Then it doesn't matter which way you go."

And so forth.

Remember; "Nothing is necessarily what it appears to be." And if you really want to find out what is happening, do not go down the rabbit hole. Stay and watch what is happening.



Labels: [Commentary](#), [Political Analysis](#), [Politics](#)

ARE WE THAT DUMB?

The Telegraph published a piece on the impact of Technology and Income Inequality as spoken by the Chosen Few at Davos. They state:

A regular refrain was that governments and technology firms are not going to be able to solve many of the imminent problems that the world faces on their own; they are going to have to work together. Joichi Ito, the Japanese entrepreneur, activist and director of the MIT Media Lab pointed out that this will require groups with fundamentally different world views to collaborate. "Typically the people who are focussed on computer science and AI don't like the messiness of the real world," said Ito. "Most engineers don't understand the law; most engineers don't understand why governments exist." MIT even has a Charm School that tries to equip students with the skills to become future tech leaders and better deal with the real world of non-geniuses.

Now the Media Lab always held a rather strange position at MIT. Half real and half just Demo. Back in the 80s I spent time and donated funds to try to get them to break bread with EECS to no avail.

But the above remark is frankly a personal insult. Engineers deal with the "real world" every day.

They deal with patents, contracts, budgets, investors, lawyers, environmental controls and regulations. Perhaps a 19 year old does not but Engineers for the most part have to bridge the gaps to create and sustain something.

Engineers do Term Sheets, NDAs, Patent Filings. The lawyers take what they do and as good scribes reduce it to writing suitable for filing. To say "most engineers don't understand why government exists" is in my opinion absurd to the extreme. As for the MIT Charm school, whatever that is, perhaps Alumni should rethink the Alumni Fund. The Charm School may be a reflection more of the Administration than the reality of the working world.

I suppose, in my opinion and based upon my experience, the dicta from this Media Lab employee is more reflective of his world view than reality. For how did MIT alumni set up so many companies if we all are dullards requiring "Charm School".



Labels: [Academy](#)

TUESDAY, JANUARY 17, 2017

[HOW NOT TO RUN A VC ENTITY](#)

MIT had announced its Engine Initiative, an intent to have a \$250 million fund to invest in start up based upon the technology coming from the Institute. I never saw this as a positive, in fact it can have great down side effects.

Today they announced the "[Team](#)" to oversee this effort. You really cannot make this up.

My first question would be:

"Have any of these people ever run a start up?"

I would strongly doubt it. Then when you see all of these people, first it costs money, lots of it to keep all these folks going. That drives up tuition. Second, massive committees like this never get anything done. The Soviets had dozens of Five Year Plans, see where that landed them.

There is a wealth of VC entities just around the corner. Why do something like this. The assembly of this massive team clearly demonstrates that many have not a clue.



Labels: [Academy](#)

MONDAY, JANUARY 16, 2017

[PROBLEMS WITH PEER REVIEW](#)

There has always been a potential problem with Peer Review. Namely the Reviewers are not always pristine. The latest example is extraordinary.

In the [Annals of Internal Medicine](#) an author harmed in the process writes:

Dr. Doctor, I am aware that you recently admitted to wrongly publishing, as your own, a scientific research paper that I had submitted to Annals of Internal Medicine. After serving as an external peer reviewer on our manuscript, you published that same manuscript in a different medical journal a few months later. You removed the names of the authors and the research site, replacing them with the names of your coauthors and your institution. It took 5 years from conceptualization of the study to publication of the primary analysis (1). This study was my fellowship project and required a lot of work. It took effort to find the right research team, design the study, raise the funds, get approvals, recruit and create materials for study participants, run the diet classes, conduct the study visits, compile and analyze the study data, and write the initial report. The work was funded by the U.S. government and my academic institution. The secondary analysis that you reviewed for Annals used specialized methods that took my colleagues many years to develop and validate. In all, this body of research represents at least 4000 hours of work. When you published our work as your own (2), you were falsely claiming credit for all of this work and for the expertise gained by doing it. As you must certainly know, stealing is wrong. It is especially problematic in scientific research. The peer-review process depends on the ethical behavior of reviewers. Physicians and patients depend on the integrity of the process. Such cases of theft, scientific fraud, and plagiarism cannot be tolerated because they are harmful and unethical. Those who engage in such behavior can typically expect their professional careers to be ruined: Loss of reputation, loss of employment, and ineligibility for future research funding are the norm. Coauthors are also collaborators in the fraud, and such losses potentially apply to them as well. All the previous publications of those who steal others' work become suspect, and it reflects poorly on their training institutions, current employers, collaborators, and mentors.

It seems that one of the Reviewers just took the paper and put names on it. Legally this may be a bit more than plagiarism, especially if it relates to Government funded work.

I wonder how this one will turn out. Sorry for the original author!



Labels: [Academy](#), [Peer Review](#)

FRIDAY, JANUARY 13, 2017

HAPPY FRIDAY 13TH!

Friday the 13th of a January has always been an interesting day personally. So I look forward to the next few hours!

Cheers to all!



Labels: [Commentary](#)

TUESDAY, JANUARY 10, 2017

DISINTERMEDIATION

Some thirty seven years ago I discovered disintermediation. Some call it "creative destruction". Simply it is the process whereby an existing channel of distribution, say selling shoes, gets changed. So we go from a system where to obtain a pair of shoes we go to a shoe maker, who measures our feet, asks us what type of leather we want and then after some long period we get our shoes.

In this world, which actually existed, we may have one or at best two pairs of shoes. First they are expensive and second shoemakers can just make so many.

Switch to Amazon. I can log on look for what I want and then get it delivered the same day. Also the price is such that I may have a dozen or more shoes. Athletic shoes, beach shoes, dress shoes, hiking boots, snow shoes, and a second or third pair of dress shoes. Lots of shoes.

What happened. Disintermediation. The distribution channel changed. The nexus between maker and consumer was dis-intermediated by multiple parties including Amazon.

Now go to the current Twitter President. And the Movie Elite. Back in the old days of cobblers, the Movie Elite had a hand in glove relationship, symbiotic as it was, with the Broadcast media. If it were NBC or ABC or whatever, some movie elite could make a statement about a politician and the networks would carry it and if the politician did not like it the best they could hope for was some Page 10 note commenting on such.

Now with Twitter, I don't use it so I am relying on the media, true, fake and otherwise that it exists, the movie elite and the media elite get dis-intermediated. Like the old cobbler, they get shouted down by the person with some 140 characters!

These folks have not yet realized that the game has changed. Communications channels are ever more fluid and can be rapidly dis-intermediated. RT knows this better than China Daily. Trump knows this better than the Elites.

It will be interesting to see how this changes. Oh and yes, since I have never seen a football game and have no idea about this martial arts thing, I boxed as a young man, but only until my nose was broken three times, I have no Ox to be gored in this fight. One player brings all the power of the Elites, the other brings Twitter. So who do you think will win?



Labels: [Political Analysis](#)

MONDAY, JANUARY 9, 2017

THEY ARE AT IT AGAIN!

Prostate Cancer is a multifaceted malignancy. BRCA2 genes can make the result explosive and lead to rapid death. Many however are indolent. Knowing how to select which is which has not yet been achieved.

In a recent article a physical writes in [Health Affairs](#):

The indolent nature of many prostate cancers has heightened concerns that harms from treatment may outweigh those from the disease and has resulted in a growing consensus in favor of less aggressive screening and treatment. We sought to understand the population-level impact of this consensus on the treatment of prostate cancer. Using national Medicare data for the period 2007–12, we assessed treatment rates among men with newly diagnosed prostate cancer. We identified both population-based rates (which are sensitive to changes in diagnosis and treatment patterns) and rates among diagnosed men (which are sensitive only to changes in treatment patterns). We also assessed trends in treatment among men with a high risk of noncancer mortality, who are unlikely to benefit from treatment. Population-based treatment rates declined by 42 percent, while rates among diagnosed men declined by only 8 percent. Treatment rates among men with the highest noncancer mortality risk and regional variation were unchanged. These results suggest that decreasing rates of diagnosis, changing attitudes, and guidelines calling for reduced prostate-specific antigen screening, not changes in practice patterns among specialists treating diagnosed men, drove the decline in population-based treatment rates. Compared to policies that emphasize volume, those that emphasize value in specialty care have the potential to exert stronger effects on practice patterns.

Read the last sentence carefully. Value. It is like Quality. It has not absolute meaning and it would appear that as it is in the eye of the beholder and not the patient, well you guess it. That was the core of the ACA. Not any per-existing condition, but who gets to decide who lives and who dies.

Now read [Science Daily](#) which reflects on this article:

The researchers recommend new payment models or other policies that emphasize value of care over volume, which might provide more incentive for specialists to choose observation over treatment. They also urge participation in quality improvement initiatives, such as the Michigan Urological Surgery Improvement Collaborative, which strive to provide high quality, evidence-based care.

In addition, research continues to uncover new clues to identify which men are at highest risk of aggressive prostate cancer and could most benefit from screening and treatment. "That's really the concern here. We know prostate cancer is a deadly disease in some men. We need better tools to identify which men should be screened and among those diagnosed, which men should be treated aggressively. This is still a black box. It's that uncertainty that leads to different approaches to treatment based on how different physicians view the risk. If we get better predicting who's at highest risk, we can more accurately tailor screening and treatment,"

The statement is in my opinion grossly arrogant. The physician gets to decide if the patient should be treated? Really? What about the patient. After all he has paid for this. So we just let him die because some academic decides to do so.

Why does the ACA need to be repealed and redone? Life versus Death, the patient versus the system.



Labels: [Cancer](#), [Health Care](#)

[CHINA AND TRUMP](#)

The current Administration seems fixated on the power of RT to influence Americans. Then there is such sites as China Daily which lays bare threats and uncertainty.

[China Daily](#) states:

...professor and chair of the department of political science at the University of St. Thomas in Houston, Texas, said: "Trump is about to create a very difficult period in China-US relations, one that may rival that of the 1950s and 60s. I am deeply concerned that Trump is rapidly moving US foreign policy toward a deep Cold War mindset regarding China. "My profound fear is that Trump has surrounded himself with anti-China hardliners who have little experience with or expertise on China, have rarely, if ever, visited the country, and have little understanding beyond textbooks and oped pieces of the nuances and subtleties of China's history, culture, and political system."

I am not aware of this Professor of what appears to be a small Catholic college in Texas, but it seems that he has become a statement maker for the Regime. Surprised no Harvard, Stanford, Yale or Princeton types.

In contrast the article continues:

...deputy director of research at the School of Regional and International Studies at the Far Eastern Federal University in Vladivostock, Russia, said the exchange of goodwill between Trump and Moscow signals subtle changes in Russia's ties with China. According to public opinion surveys, Russia was the only country to prefer Trump over Hillary Clinton, the Democratic Party's presidential candidate. "Since 2012, ties between Moscow and Beijing have been expanding and deepening, especially in the political-military domain," Lukin said. If Moscow normalizes relations with Washington, "the Sino-Russian partnership will continue, with the emphasis shifting to economics and trade", he added.

How much of this is game playing and muscle stretching and how much reflects a fundamental change is yet to be played out. China and Russia have had a tenuous relationship at best over the decades. You cannot buy anything Made in Russia at Walmart but there are still tons of Made in China.

It is surprising that the organ that the Chinese use to send out a message use Academics so far

from the base. Vladivostok is not Moscow, but it is quite reputable. Houston is not Cambridge yet it is no where close to Vladivostok.

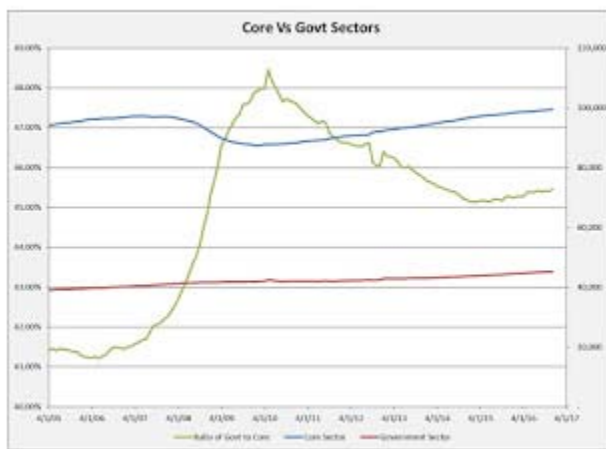
One should ask; what this message means and to whom was it directed?



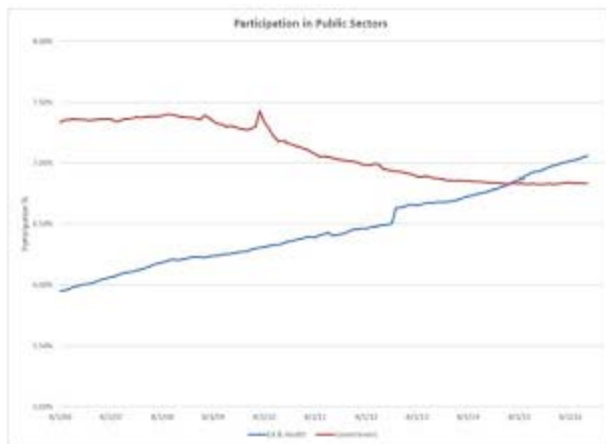
Labels: [Academy](#), [China](#), [Politics](#)

[MORE ON EMPLOYMENT JANUARY 2017](#)

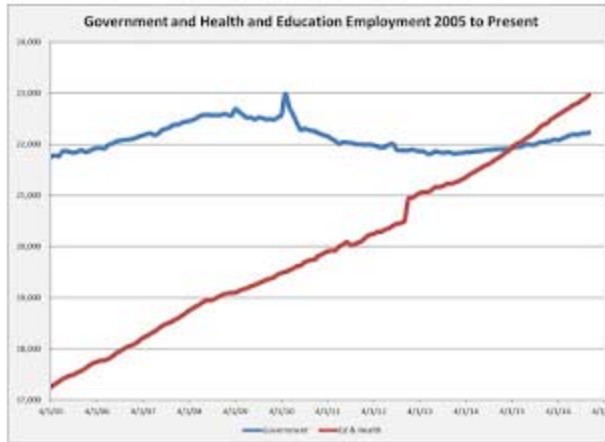
Last Friday the Government announced the latest Employment Stats. As usual we noted the mass amount no longer in the work force but we now take a look at details.



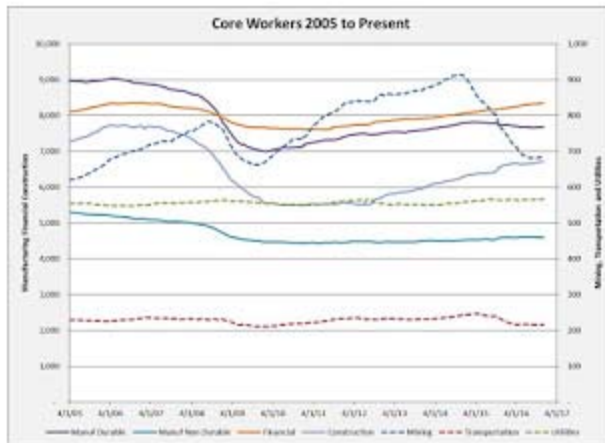
The above is a plot of Government or Government related employment versus non-Government. It dropped for a while but we note it climbing again. This chart shows that as that climbs then more people doing real work are having to be taxed for people doing Government supported work.



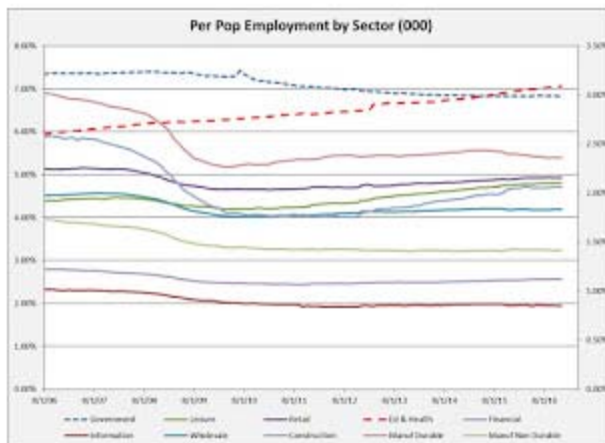
Again we show this as a Public versus Private sector breakout.



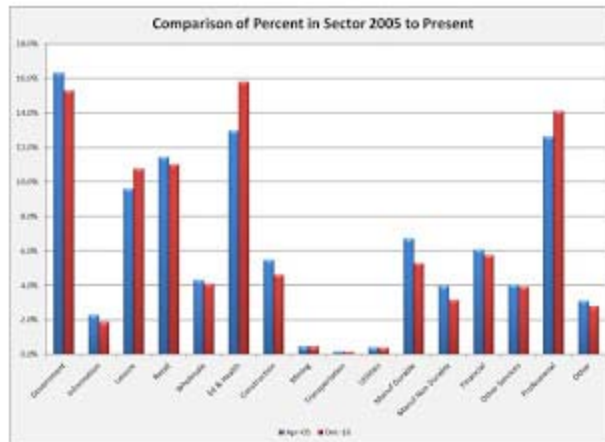
Looking deeper the real reason is the explosion of employment in Health Care. Clearly the AMA has created a massive number of jobs, most at the lower end, and in turn these jobs are paid for from a taxation base. Unfortunately that is all being borrowed. Compare this to the JAMA analysis presented earlier.



The above is a listing of the Core workers during this period.



The above is detail per pop. Finally below we compare before the Collapse and now.



The above is a picture of the change in our employment structure.



SUNDAY, JANUARY 8, 2017

[YOU BROKE IT, NOT BREXIT](#)

And I thought the US Academy was in a state of collapse. But the [Telegraph](#) depicts the UK Universities as follows:

But students at a prestigious London university are demanding that figures such as Plato, Descartes and Immanuel Kant should be largely dropped from the curriculum because they are white. School of Oriental and African Studies (SOAS)'s student union is insisting that when studying philosophy "the majority of philosophers on our courses" should be from Africa and Asia.

The article continues:

Sir Roger Scruton, the philosopher, said the demands suggest "ignorance". "You can't rule out a whole area of intellectual endeavour without having investigated it and clearly they haven't investigated what they mean by white philosophy," he told The Mail on Sunday. "If they think there is a colonial context from which Kant's Critique of Pure Reason arose, I would like to hear it."

Knowing Scruton, and he is brilliant, he has more than a point. The irony is that these individuals led to the very creation of a civil society.

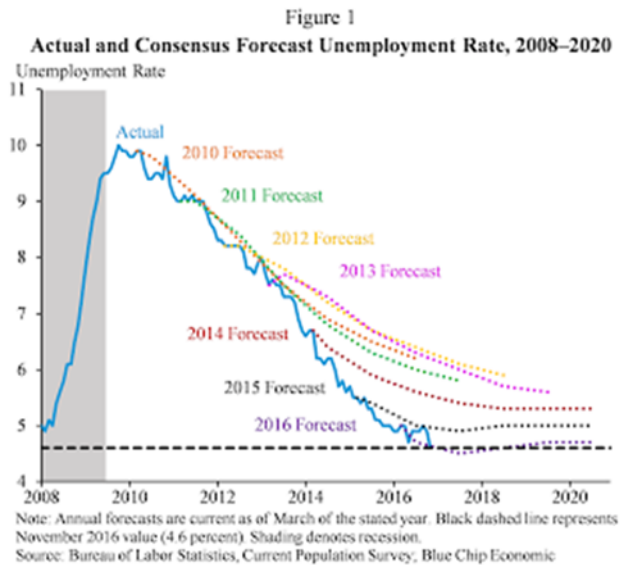


Labels: [Academy](#)

[FACTS AND THEN THERE ARE PARTING MEMOS](#)

For those who may have been examining this Blog over the past eight plus years one of our topics was the Romer Curve, which was the projection of unemployment

Now from the still current [Administration](#) comes a rewriting of history.



They state:

From its peak, the unemployment rate recovered to its pre-recession average in mid-2015 and continued to fall, standing at 4.6 percent as of November 2016. This rapid decline came far more quickly than most economists predicted: as recently as March 2014, private forecasters expected the unemployment rate to remain above 5.0 percent until at least 2020 (Figure 1). Meanwhile, the labor force participation rate, which has been subject to downward pressure due to the aging of the U.S. population, has been broadly stable since the end of 2013, as the strengthening labor market recovery has led workers to enter (or reenter) the workforce, offsetting downward pressure from demographic trends.

To examine the facts just go back and look at my Romer curve analyses. At NO time did any data appear as indicated above. By month we tracked the actual versus the Romer projections. Even using the recalculations which employed massive numbers removed from the possible employment roles.

History is written by the victors. Not clear yet who they may be but when data such as the above is presented when the real data based on the Romer memo disputes it, I truly wonder. But alas, they are but economists. Worse yet, they are politicians.



Labels: [Political Analysis](#)

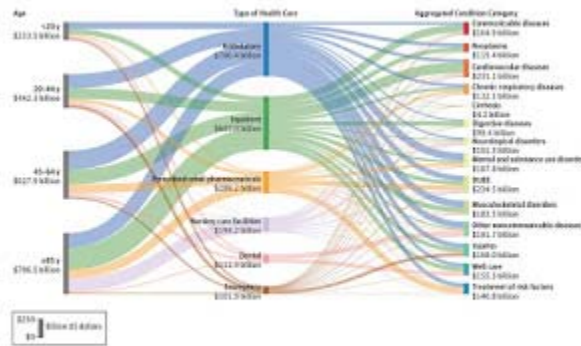
[INTERESTING DATA](#)

[JAMA](#) has an exceptionally interesting piece on Health Care costs and changes. The authors state:

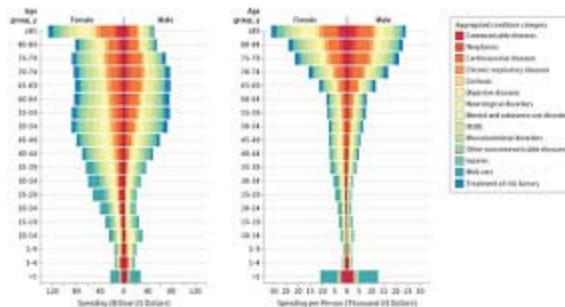
From 1996 through 2013, \$30.1 trillion of personal health care spending was disaggregated by 155 conditions, age and sex group, and type of care. Among these 155 conditions, diabetes had

the highest health care spending in 2013, with an estimated \$101.4 billion (uncertainty interval [UI], \$96.7 billion-\$106.5 billion) in spending, including 57.6% (UI, 53.8%-62.1%) spent on pharmaceuticals and 23.5% (UI, 21.7%-25.7%) spent on ambulatory care. Ischemic heart disease accounted for the second-highest amount of health care spending in 2013, with estimated spending of \$88.1 billion (UI, \$82.7 billion-\$92.9 billion), and low back and neck pain accounted for the third-highest amount, with estimated health care spending of \$87.6 billion (UI, \$67.5 billion-\$94.1 billion). The conditions with the highest spending levels varied by age, sex, type of care, and year. Personal health care spending increased for 143 of the 155 conditions from 1996 through 2013.

The following chart is quite interesting, albeit open for some discussion.



DUBE is Diabetes and a collection of other things. Frankly I would have liked to see T2 Diabetes separate but I suspect it and its sequellae are all over the chart. The greatest sum is in the 65 and older as one might suspect.



The above is interesting since it depicts annual costs total and per person by age and by disorder. Surprisingly older women are more costly than older men. Also as one would expect over 85 is costly. However I would expect that if one looked at the distribution it would be some 80:20 rule, namely 20% of these people account for 80% of the cost.

Finally the data below is of interest, which is a chart of Public Health spending.

Table 6. Largest 20 Public Health Spending Conditions for 2015 in the United States*

| Rank [†] | Condition | 2015 Spending (Billions of US Dollars), \$ | Annualized Rate of Change (2000 to 2015), % |
|-------------------|--|--|---|
| 1 | All causes | 34.23 | 2.65 |
| 2 | Alcohol [‡] | 3.52 | 4.97 |
| 3 | Lower respiratory tract infections | 3.28 | 15.48 |
| 4 | Diabetes (type 1 and 2) | 2.93 | 14.11 |
| 5 | Other infectious diseases (bacterial and viral) [§] | 2.87 | 3.25 |
| 6 | Hepatitis | 2.28 | 6.71 |
| 7 | Protein and carbohydrate (respiratory distress and asthma (severely)) | 2.28 | -4.07 |
| 8 | Varicella | 2.15 | 14.95 |
| 9 | Tuberculosis (not drug-resistant) | 2.14 | 9.18 |
| 10 | Alcohol poisoning | 2.08 | 9.18 |
| 11 | Tuberculosis | 2.08 | 3.68 |
| 12 | Alzheimer's | 2.08 | 3.68 |
| 13 | Neurological disorders (including MS) | 2.08 | 3.68 |
| 14 | Brain cancer | 2.08 | 30.01 |
| 15 | Alzheimer's | 2.07 | 6.02 |
| 16 | Low back and neck pain | 2.14 | 6.76 |
| 17 | Tuberculosis | 2.14 | 6.02 |
| 18 | Self-harm | 2.14 | 14.11 |
| 19 | Other mental disorders (eating problems and anxiety disorder) | 2.13 | 3.00 |
| 20 | Furcra, bronchitis, and lung cancer | 2.13 | 7.48 |
| | Top 20 causes | 32.84 | 5.19 |

*Public health spending by condition in 2015 for 20 conditions with the largest spending in 2015, reported in XPS US-0000.

[†]Ranked from largest spending to smallest spending. [‡]Value is 0.0 in the Supplement table as condition and uncertainty intervals are at zero.

The ones with the greatest change are of most interest. Such as breast cancer with an annualized cost increase of 30%! I really do not know what to make of this one. But worth reporting.



Labels: [Health Care](#)

FRIDAY, JANUARY 6, 2017

SMART PHONES

I had the opportunity to view the Senate hearings yesterday to see the latest dance about the camp fire. What struck me, and this now must reflect age, was as the DNI was speaking one of his aides apparently was continuously on his smart phone and both chuckling and sharing it with a colleague.

In the old days if that happened the employee, yes a Government employee we pay for, would be seeking alternative occupations.

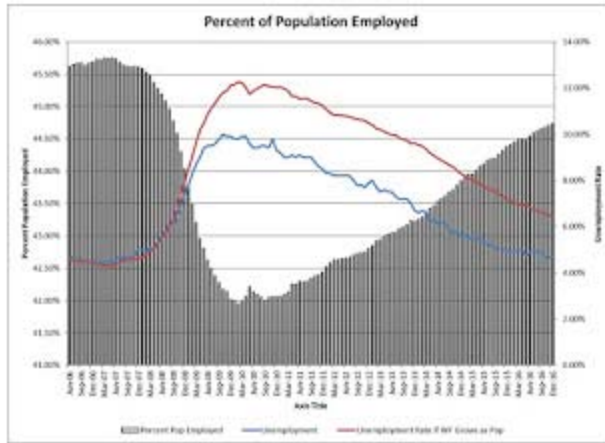
But I gather the messages were more important than the content of the briefing.

Just an observation. Oh well, they are on their way out any way.

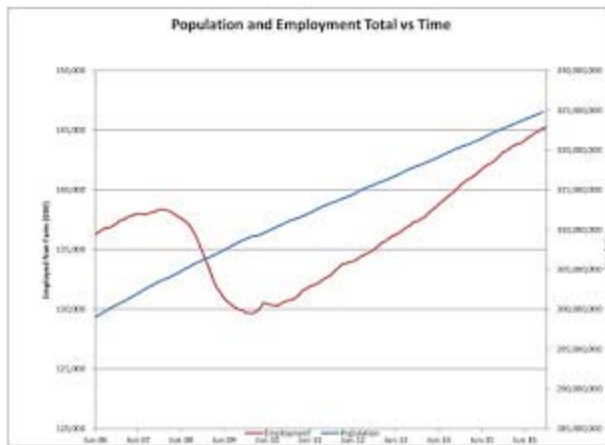


Labels: [Commentary](#)

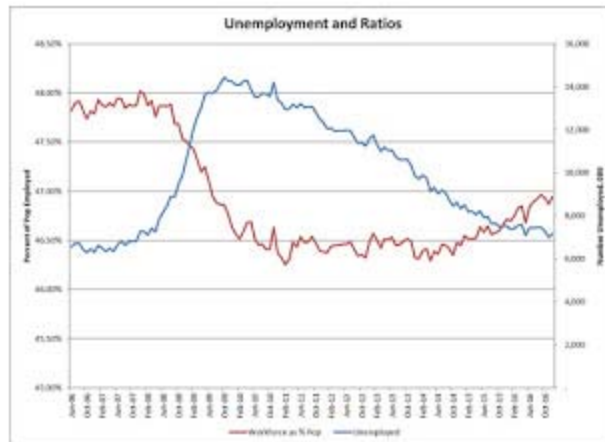
EMPLOYMENT JANUARY 2017



Employment is increasing but we still have a significant amount no longer in the base. It should reflect a 7% + unemployment rate if we maintained the base as it was in 2006. Even then it had dropped from 2000.



One can see the growth in employment and population. The latter growth is the problem in a sense that we do not have the old percent in the employee pool. Thus the 4.7% is truly deceptive as we have been showing for the past eight years.



The above does reinforce this issue. The workforce as a percent of population is still well below what we started with.

We will examine the details later.



Labels: [Economy](#)

WEDNESDAY, JANUARY 4, 2017

[IT IS CALLED A BUS](#)



Perhaps I have too much time. But I have been reading the MIT News Office documents, it seems to be in my opinion a Politburo type now. The one which caught my eye today was the "car pooling" idea for Manhattan. You see I actually drove a cab for a short while, as the front seat driver with an uncle, briefly mind you, and I am back and forth and am an avid subway user. Nothing better than the Bway line from 34th to 42nd at rush hour. It makes Tokyo look genteel. You want diversity, get on that train. And yes, the East side Lex line is just as bad.

Now to the MIT folks. They state in the [MIT News](#) blurb:

Led by ... MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL), researchers developed an algorithm that found 3,000 four-passenger cars could serve 98 percent of taxi demand in New York City, with an average wait-time of only 2.7 minutes. "Instead of transporting people one at a time, drivers could transport two to four people at once, resulting in

fewer trips, in less time, to make the same amount of money,” “A system like this could allow drivers to work shorter shifts, while also creating less traffic, cleaner air, and shorter, less stressful commutes.” The team also found that 95 percent of demand would be covered by just 2,000 10-person vehicles, compared to the nearly 14,000 taxis that currently operate in New York City. Using data from 3 million taxi rides, the new algorithm works in real-time to reroute cars based on incoming requests, and can also proactively send idle cars to areas with high demand — a step that speeds up service 20 percent, ...

First, people want to go to different places. If you want to join in there are buses. If you want to get there fast there is the subway. If you want to go really fast, try a helicopter. The copter can get you from one point to another fast but it does not deliver you to where you really want to go, no landing spot.

Now for the above. "Shorter hours" means less pay. I guess these wizards have never really worked on the streets of New York. The traffic problem is simple. No alleys. Thus all the trucks double and triple park during rush hours and traffic stops. You even stop the bus.

Some how the above study seems to have spend no time finding our how people get around New York. The 95% coverage makes a tone of illogical assumptions in my opinion.

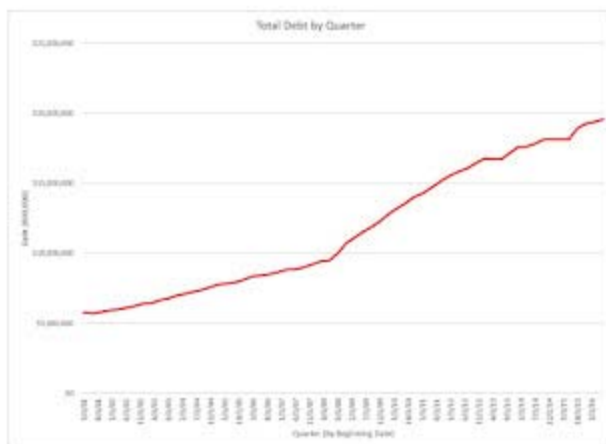
Thus in my opinion and in my almost 75 years of experience, having been born and raised here, traffic is driven by individual decisions, not group decisions. Just spend time on the cross town S line from Times Square to Grand Central. There are millions of individuals just passing by. Stop that individuality, in my opinion, some half thought out academic illusion, and you destroy what makes New York work. If not the world. This is not a world of neat computer science. This is mass humanity.

Stay in Cambridge, please. Oh yes, and try and find a parking spot in Kendall Square!

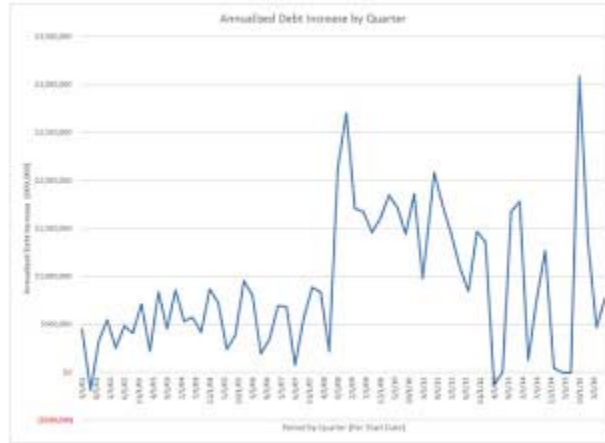


Labels: [Academy](#)

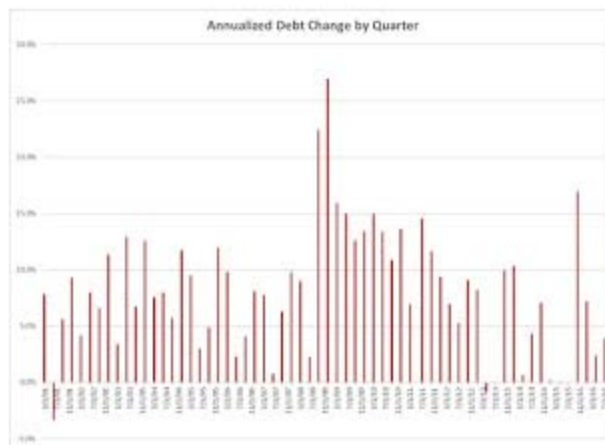
DEBT: IT JUST KEEPS GOING UP!



The total debt keeps rising with no end in sight. The above is through Q3 2016. Most likely we are well above \$20 trillion.



The above is the annualized changes by Quarter, The surprise was a year ago where we saw a \$3 trillion annualized increase! One wonders where the Press is on this one. Clearly this is more important than some less than competent IP server manager and their employer.



Finally the above are the Quarterly annualized increases. This is well ahead of any GDP changes. The blame is on Medicare and Social Security. But frankly many of us paid into and continue to pay into a system whose returns to us are negative to say the least. Where is the money going folks!



Labels: [Economy](#)

TUESDAY, JANUARY 3, 2017

CYBER SECURITY

In the recent complaints about invasion of cyber networks, the DNC and Burlington Power, we see in all cases human failures on the party attacked. Whether it is use of personal or entity computers to access what should not be accessed, like web sites, images, attachments, it is generally the blatant carelessness and/or stupidity on the part of those invaded.

Cyber security has a multiplicity of ways to block intruders and even more so to attempt to overcome the incompetence of the users. We briefly review some of them.

1. Encryption

Encrypting messages is straightforward. There are a multiplicity of relatively secure means to achieve this. All this does is take what is created and allow it to be opened and used only by whom it was intended. It does not mean however that the receiver cannot then take it and let it become open due to their incompetence. Even if it is of printed form it can be reproduced and sent onwards.

2. Authentication

Authentication is the process of making certain that the entity seeking access is both authorized and who they say they are. Over the decades I have examined a multiplicity of authentication systems. All have some issues but many present viable necessities.

There are many authentication options now available, especially biometric ones. Many have evolved from the intelligence sector and can be readily applied in commercial applications. These authentication mechanisms can be used on both transmit and receive so that encrypted files require a high level of authentication. However, like all of these issues, the device which opens the file, after being authenticated may not be secure! It can be an endless chasing of the tail.

3. Outbound Control

Sending messages from a secure location to another secure location requires that the data being sent and its destination is authorized. One means of doing this is to employ a DPI, deep packet inspection, where not only are IP addresses checked but packets are fully inspected. That means that an approach to send packets to some acceptable address via a tunneling mechanism, then sent elsewhere, could be determined. Also examining the type of data being sent and profiling it to IP address can also be accomplished and determine if data is being improperly downloaded.

In addition means to determine lists of insecure or threat IP addresses or even more complexly profiles of outbound traffic that meet threat profiles. Namely traffic that may be sending files which should not normally be sent to locations that may not be acceptable. This would mean an intelligent DPI process.

4. Inbound Control

This is the process of monitoring where traffic is coming from is critical. One can also use DPI here as a means to assess not only where the traffic is from, but what the traffic is. Messages have profiles and they should be used to throttle access.

5. Usage Monitoring

The key question is often; what is being used on the network? Thus, monitoring what applications are being used is essential. This may be complex but as with others it can be accomplished.

6. User Monitoring

Users have profiles. They have jobs that requires certain behavior at certain times. They type in a certain manner. Back in the days of Morse code one could identify a distant operator by their key usage patterns. The same can be done by keyboard, mouse, and other I/O interfaces. When they change then one must immediately suspect something and remediate.

7. Usage Flagging

Usage profiles can be developed. Metrics describing users can be developed and once a usage profile is aberrant then immediate remediation is necessary.

8. Network Segregation

In the later 1980s the ARPA Net was split into a commercial and military net. The result purportedly was a separate and non-connected set of IP networks. In the late 1990s when I deployed my Central and Eastern European nets I did so over independent private fiber links. One could have a secure and isolated network.

9. Private Networking

A key element in security is separating the network. Network segregation is the ultimate in that construct but a less costly and somewhat effective method is private networking. Take the power grid as an example. Any power company who controls their networks via some IP methodology should do so only on a separate secure private network. Lease circuits, block any outside access, and separate all facilities so that the control backbone is NOT a part of any public access. Any company utilizing the public side of the Internet for control of critical assets is asking for a disaster to occur.

10. Secure Operating Systems

Many of the concerns are from the outside in. However back in the 1970s there was a major concern from the inside out. Namely having a secure operating system. Who wrote the OS, what is hidden inside the chips, the file manager. Remember the chips come from a potential adversary. The OS may have bits and pieces from generations of old code.

Furthermore, this issue of security demands a secure platform in toto. Namely, having the right person, decrypt the secure data on what would be an insecure platform defeats the purpose. This is the classic issue of Red and Black environments. This is an old paradigm where everything secure was held within a protected environment with no communication between it and the outside world. However, this is quite difficult to achieve in current day operations. Namely,

people all too often want to use their own computers or devices and it is at this point that security can and is often breached. It can be a secure person in a secure environment but with an insecure terminal.

11. Paper Trails

In the old days, we had paper. The paper was numbered, it was kept in a secure environment, and there was theoretically no means to copy it. Yet good spies would find a way to compromise the situation. But paper had its worth. A security check of a safe at random times allowed for some semblance of security. However, under the right circumstances one could photo the document if surveillance was inadequate. This could be mitigated by having multiple individuals in at the same time. However, that also could be compromised. Yet paper did eliminate a multiplicity of risks that electronic access presents.

The classic exception to this is in the tale of the Falcon and the Snowman, the story of the son of an FBI agent working in a secure facility at TRW who managed to feed the Russians massive amounts of data. The reason, just sloppy security controls.

12. Real Time Security Audits

Security audits were and still are essential. Trust goes just so far. When establishing a security policy and protocol one must further be certain people understand their responsibilities, that they are checked on meeting them and that there are substantial and immediate consequences for failure. Collusion with the auditors represents a risk, but it would require substantial efforts.

13. Real Time Network Monitoring

Networks should be monitored. Monitored for use, users, usage. Who is sending and receiving what and when and from/to whom. Profiles count and looking at the network as a totality is critical. Furthermore, there must be some sequestering of the network. The old aphorism, "Don't use pay toilets" reflects the fact that various infections can be obtained from truly open environments. If anyone, and especially unknowable actors can access the same facilities as the secure users, there is no security.

14 Training and Punishing People

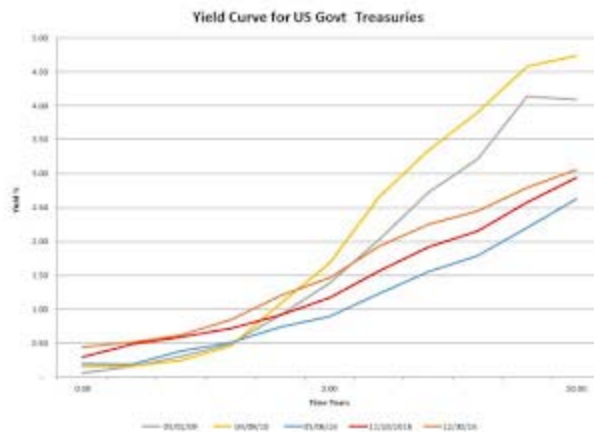
Ultimately security of any type depends on people. As someone once said to me; "Trust no one, not even your father!". Brutal but all too often true. The tales of the Communists from Cambridge, Burgess et al, is a tale of assuming the "good old boys" or "one of us" means something. People range from stupid, to arrogant, to incompetent, to downright evil. They do not wear signs telling us what one or combinations they present. We all too often have to assume the worst. Trust is the basis of betrayal.



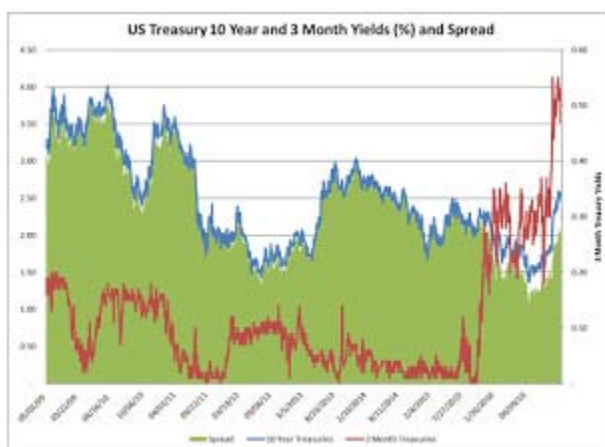
Labels: [Security](#)

MONDAY, JANUARY 2, 2017

INTEREST RATES



The Treasury yield curve is increasing again. The spreads have taken a substantial change.



This will be a harbinger for this year.



Labels: [Economy](#)