
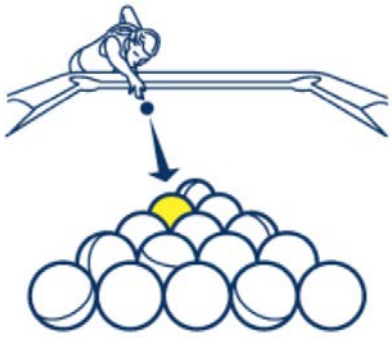


A <u>Big Break</u> is needed to resolve the Bone Headed confrontation between The Unstoppable Force (IROM) versus The Immovable Object (FDA)

The previously indistinct lines separating vague government policies and well defined private interests in cellular medicine are finally coming into focus. Previously, the factions on both sides had been practicing relative "peace"- that break in time between all-out war in which everyone stands around reloading, steeling their swords and reinforcing their castle walls and populating their moats with alligators and piranhas.

The next few decades in medical breakthroughs will be an interesting competition between expensive drugs and inexpensive cells taken from the patient's body. In some ways, this battle will define how we as a society deal with healthcare costs, regulation and affordability in the 21st century. Regrettably, the powers that be here in the early part of the century are doing a great job of keeping cheaper and safer cells from patients, in favor of more expensive and often more side-effect laden drugs. What's finally decided in key FDA hearings this year will impact every American's healthcare bill for the foreseeable future.
(Regenexx)

KEY RECENT DEVELOPMENTS:

1. **Stem Cell Malpractice Begins**
   https://www.linkedin.com/groups/4464752/4464752-6102956527268741123
   http://www.ipscell.com/wp-content/uploads/2016/01/BioheartLawsuitTEXT.pdf
2. **FDA moves to crack down on unproven stem cell therapies**
   http://www.statnews.com/2016/02/08/fda-crackdown-stem-cell-clinics/
3. **FDA warning letter issued to Irvine Stem Cell Treatment Center 12/30/15**
   http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm479837.htm
4. **Are Stem Cells the Future of Medicine?**
   http://www.worldhealth.net/news/are-stem-cells-future-medicine/
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5. **Stem Cells – Investors Making a Fortune?**
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Federal regulators are preparing to crack down on scores of clinics across the United States that offer pricey stem cell therapies for conditions ranging from autism to multiple sclerosis to erectile dysfunction without, they say, "any scientific evidence that they work".

As many as 200 "stem cell clinics" have cropped up in recent years, offering injections, facelifts, and treatments for a number of devastating conditions. They initially avoided heavy regulation, in part because they use cells extracted from a patient's own body and just as importantly because they don't do much to those cells (minimal manipulation) before reinjecting them.

But the Food and Drug Administration recently issued draft guidelines clarifying that the stem cells used in most clinics are "drugs" and, as such, require a rigorous (read that expensive and time consuming) approval process before they can be used in patients.

A public hearing has been set for April 13, 2016.

The last all-out war between Allopathic Medicine and the FDA occurred in the 1990's. It lasted about a decade, but ultimately with the support of U.S. legislators (elected officials), the in-vitro fertilization crowd successfully defeated the FDA's (unelected bureaucrats') idea that women's ovaries/eggs were "drugs" that needed to be regulated from Washington D.C. In the interim, what has resulted is "siloing"- that being the establishment of silos of knowledge and opinion, comfortably impenetrable by outside ideas.

Anyone who has played billiards knows that when the balls become sequestered into unworkable clusters, what is needed is a big BREAK. And this is precisely what is needed now with regard to the loggerhead that has developed as a consequence of the growingly impenetrable silos that constitute the cellular medicine community, Big Pharma and the federal government. The practice of Interventional Regenerative Orthopedic Medicine (IROM) may serve as the cue ball careening on a collision course to break up the solidified silos of Big Pharma and the Food and Drug Administration (FDA).

All of this headline grabbing FDA mischief pushes even further to the background the ongoing touchy feely, "less is more" concept that is the World Health Organization. The WHO is an organization having equally lofty and seemingly undoable goals of other similarly "sanctioning organizations" like, say, NATO. The WHO has been advocating- hoping really hard for- an environment that encourages interprofessional education (IPE) to help improve health information management (HIM). The idealized idea being that IPE is an approach to education that "occurs when two or more professions learn about, from and with each other to enable effective collaboration to improve health outcomes".

I don't know about YOU, but just WHO do they think they are to push HIM on US? Can these dinosaurs actually believe that what our health care system needs are more energized versions of the same old tired, binary concepts of Allopathic Medicine- i.e. drugs and surgery? Without the slightest acknowledgement of cellular medicine, the "Fred Flintstones" and "Barney Rubbles" of medicine are pushing some esoteric dream of "HIM without walls".

"THEY" apparently believe that our health care dilemma can be easily fixed essentially by holding meetings (the one word that would explain why mankind will never meet its potential- meetings). They propose to coax all the occupants out of their existing impenetrable silos and getting them to decrease wait times and improve electronic documentation of the same old tired concepts of Allopathic Medicine. No mention of how safe, inexpensive and effective cellular medicine therapies could almost instantaneously effect the correction of medicine, but (unfortunately?) without all those government mandates and lavish resort meetings.

Guide to Life: How to Properly Break in Pool

By J. TRAVIS SMITH

Being loud is usually obnoxious, but when it comes to the break in billiards, it's completely necessary. No one is guaranteeing you'll have Tom Cruise's "sledgehammer break" from ***The Color of Money*** (more likely you'll end up ripping a hole in the table), but perfecting a good break isn't as difficult as it looks. Below is a short guide to breaking in 8-ball — if you're playing 9-ball, you probably don't need a guide.

1

Don't break your shaft. The speed and power necessary for a good break make it an easy way to bend or utterly destroy your pool cue. For increased speed, most players use a separate, lighter cue for breaking. Grab the house cue off the wall and chalk the tip — it's probably already been through hell anyway.

2

Allow me to break the ice. You want the rack to be frozen — meaning all the balls are touching each other — otherwise half the balls won't move.

3

Spot the ball, form your bridge. Even among professionals the spot of the cue ball varies widely. Some place it on the head spot (the center point of the half of the table from which you break, a.k.a. that little dot that's probably worn to shit), others a few inches off the rail (the padded wall enclosing the playing area). As long as it's on or behind the head string (the midline running the width of the breaking half, you need a damn glossary for this game), it's really up to you. Just place it where you're most comfortable and where you'll avoid scratching off the break (pocketing the cue ball and losing a turn). If you can, use a closed bridge — in which your index finger wraps around the pool cue — in order to keep the cue from pulling up during the shot.

4

Stand and deliver. During the game, keep your legs spread, knees bent and body low for the most accurate shots. However, for the break shot you want to straighten up a little so you can generate more power. When breaking, keep your grip loose and slowly draw back the cue, then drive forward with both your hand and hips simultaneously. When the cue tip makes contact with the ball, your hand should be at about your hip and your forearm should be perpendicular to the floor. Don't lock your wrist. As you follow through, your dominant foot will most likely kick up a bit from the force of the shot. Ideally, you want to leave the cue ball near the center of the table for your next shot, so aim slightly below the center of the ball so that it "deadens" after breaking the rack.

5

Aim for solid contact. There is no disagreement among the pros: always aim to hit the front ball in the rack "full face". Hitting the center of the ball best translates the force of your shot to the rest of the rack, effectively spreading the balls and maybe pocketing a few. Optional: If you are wont to impress your friends, aim for the second row of balls in the rack. You're more prone to scratch this way, but with the right angle and enough luck, you can hit the eight-ball in off the rack and win the game (some tournaments don't recognize this rule).

The FDA recently underscored their new approach in a warning letter it sent at the end of December to a network of stem cell clinics in California, New York, and Florida. Regulators advised the owner that he needed FDA licenses and approval to sell and use stem cells, which the agency classified in the letter as "biological drugs". Such licenses would require evidence that stem cell treatments are both safe and effective — the sort of proof that takes drug companies many years of clinical trials to obtain, at a cost of millions of dollars.

What appears to have precipitated this confrontation was a combination of exuberance and concern:

- Patient exuberance (exciting, promising results) and concerns (lawsuits precipitated by perceived broken promises and poor results)
- Physician exuberance (safe, effective procedures) and concerns ("status quo" physicians questioning the science and safety)
- Societal exuberance (hope of resolving existing Health Care problems) and concerns (fear by the "status quo" of resolving existing Health Care problems).
- The fires of change flamed by the winds of societal self-interests (miracle cures, doctors claiming fame, stem cell investors standing to make a fortune, etc.).

OVERVIEW OF KEY RECENT DEVELOPMENTS:

1. **Stem Cell Malpractice Begins**
   https://www.linkedin.com/groups/4464752/4464752-6102956527268741123
   http://www.ipscell.com/wp-content/uploads/2016/01/BioheartLawsuitTEXT.pdf

A malpractice suit was just filed in Florida for the injection of adipose SVF for macular degeneration. **All practitioners of cellular medicine and biologics should be very concerned about using therapies and protocols that are not backed by registry data that tracks complications and then publishes that data in the peer reviewed literature.** Cellular medicine practitioners can expect to see more of this in the next few years, increasing trepidations and anxiety while raising concerns as to whether their cellular medicine practices are protected or are vulnerable.

The **Biologic Orthopedic Society (BOS)** is a group of professionals dedicated to advancing the research and development of biologic treatments for musculoskeletal injuries and disorders. The following are comments posted on a recent BOS blog pertaining to the revelations of this recently filed lawsuit:

- *There is a time and place for everything, even a malpractice suit. This was the proper setting. If we fail to police ourselves, the legal profession will do it for us but their way is painful and expensive*

- *This could easily be a slippery slope for many clinicians. There is remarkably little data to support most of what is being marketed and promised to patients. I am a believer in the science that stem cell treatments are and will be beneficial in multiple situations including many in which we have no good current treatment. I think that physicians and scientists have to be allowed to push the envelope to discover what to do and how to do it. What is the correct formula and can that be replicated? I think that the FDA has a right to be concerned about what is going on in the market but I am concerned that the new guidelines will not only impair these types of clinics but also legitimate investigation and legitimate innovation. We cannot advance the*

science without risk and consequences. The threat of an onslaught of negligence litigation will just create another barrier to the successful adoption of this technology.

- *We tried many years ago with ICMS (International Cellular Medicine Society) to put in a minimum set of guidelines, that went something like:*

  1. You must have strong animal data that the exact cell type your using helps condition X
  2. The patient must have no good options
  3. An IRB should be used for investigative care
  4. You need to be a specialist in the area you're treating (i.e. no cosmetic surgeons injecting knees or MSK specialists injecting wrinkles)
  5. You need to track patients in a registry
  6. You need to report your results on-line and in the peer reviewed literature where appropriate
  7. You must use a strict candidacy grading metric-good, fair, poor like any other medical procedure

  Since then we've had nonspecialist or the wrong specialist docs injecting God knows what, God knows where, publishing nothing, tracking nothing, and treating everything!

- *It's not a biological issue it's bad medicine. I completely agree about tracking, tracking, tracking. This requires relentless effort to ensure those treated stay connected. What i am not sure about is how this data will have any impact when the big event is only 60 days away. I have written many legislators and was called by one congressman office. I was instructed to write next week to his DC office to arrange a meeting. Not sure what that would do either but putting a human side on the issue might help gain support. The treatment for those with few if any options and most being years before they may choose arthroplasty…*

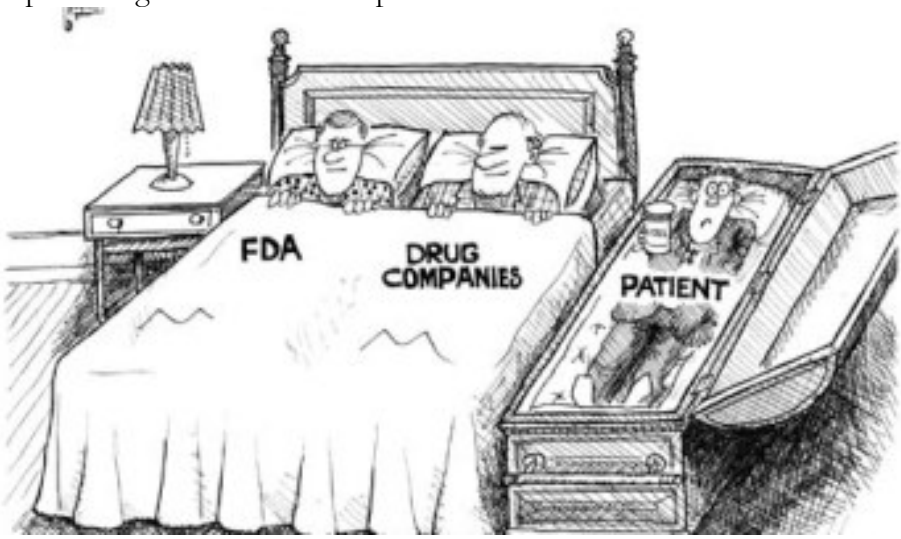
- *The biggest issue here for me is that there is no animal modelling that I can find that would show that stromal vascular fraction is helpful in macular degeneration. In fact, when you broaden the search to adipose MSCs (isolated and culture expanded) and macular degeneration in PubMed, there's one lab article on differentiating (in culture) adipose MSCs to RPE cells using a very specific cocktail. All the rest are again lab papers or opinion pieces. This is a nice review article:* ***http://www.ncbi.nlm.nih.gov/pubmed/25609937*** *on the concept (that doesn't use adipose MSCs). I think the issue here is you had a clinic run by business people convince an ophthalmologist to do this with a patient. The doctor didn't know enough about stem cell biology to realize that SVF is a different animal than adipose MSCs that are isolated which is a different animal from bone marrow MSCs and RPE cells. Now the ophthalmologist and the business group that made the SVF is involved in a big malpractice brawl.*

- *For the RCT only crowd-orthopedic surgery will have to cease tomorrow, as almost all of it has no RCTs-see http://www.regenexx.com/bmj-chimes-scandalously-poor-evidence-for-orthopedic-surgery/*

  Also see-http://www.regenexx.com/has-medical-research-become-faith-based-religion/ for an RCT on parachute use.

2. **FDA moves to crack down on unproven stem cell therapies**
   http://www.statnews.com/2016/02/08/fda-crackdown-stem-cell-clinics/

One of many examples of the government's intentions in 2016 is made undeniably clear based on a lengthy FDA issued warning letter dated December 30, 2015. A not so Happy New Year was issued to members of the Cell Surgical Network® (CSN). The letter was apparently prompted by an FDA investigation of that clinics use of SVF. The warning letter informs the CSN practitioners in no uncertain terms that the SVF utilized by these centers are believed to have violated several of the FDA guidelines pertaining to "minimal manipulation".



http://stemcellrevolution.com/about-us/founders/

As excerpts from that lengthy FDA warning letter indicate, in no uncertain terms, the SVF preparation utilized by this member of the Cell Surgical Network® (CSN) is not considered to be in compliance with FDA regulations as "the practice of medicine" (please do not skip over the 6th item in the follow list of FDA complaints, that clarifies that should the practitioners not comply within 15 days they could face seizure and/or injunction):

1. *"Your SVF product is intended to treat a variety of diseases and conditions, including, but not limited to, autism, Parkinson's disease, pulmonary fibrosis, chronic obstructive pulmonary disease (COPD), multiple sclerosis (MS), cerebral palsy, and amyotrophic lateral sclerosis (ALS), and is therefore a drug under section 201(g) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) [21 U.S.C. 321(g)] and a biological product as defined in section 351(i) of the Public Health Service Act (PHS Act) [42 U.S.C. 262(i)]. It is also a human cell, tissue, or cellular and tissue based product (HCT/P) as defined in 21 CFR 1271.3(d)".*

2. *"In addition, your SVF product fails to meet 21 CFR 1271.10(a)(2)'s criterion that the HCT/P be "intended for homologous use only, as reflected by the labeling, advertising, or other indications of the manufacturer's objective intent. As a result, your SVF product cannot qualify for regulation solely under section 361 of the PHS Act and 21 CFR Part 1271".*

3. *"Please be advised that in order to lawfully market such a biological drug product, a valid biologics license must be in effect [21 U.S.C. 355(a); 42 U.S.C. 262(a)]. Such licenses are issued only after a showing of safety and efficacy for the product's intended use. While in the development stage, such products may be used in humans only if the sponsor has an investigational new drug (IND) application in effect as specified by FDA regulations [21 U.S.C. 355(i); 21 CFR Part 312]. Your SVF product is not the subject of an approved biologics license application (BLA) nor is there an IND in effect".*

4. *"We acknowledge receipt of your written responses for CA, FL and NY, all dated October 2, 2015, which seek to address the inspectional observations on the Form FDA 483's issued at the close of the inspections. We have reviewed*

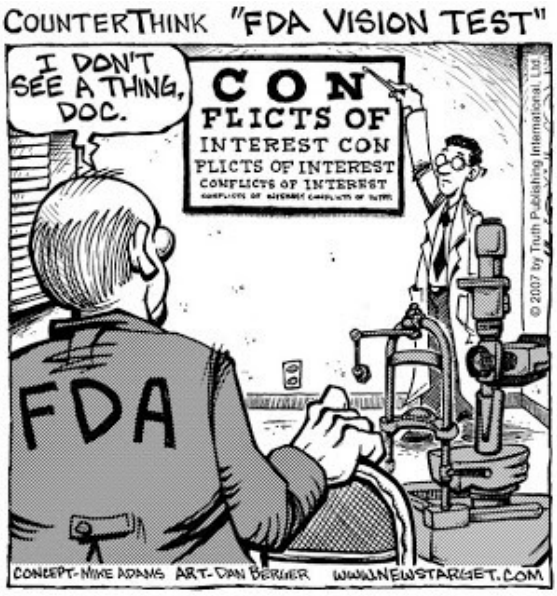
your responses and have concluded that they do not provide sufficient detail to fully assess the adequacy of your corrective actions".

5. *Neither this letter nor the observations noted on the form FDA 483, which were discussed with you at the conclusion of each inspection, are intended to be an all-inclusive list of deficiencies that may exist at your facilities.*

6. *"You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such actions include seizure and/or injunction".*

http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm479837.htm

The FDA has begun to go after adipose SVF clinics again. This doctor was part of CSN and claimed that since he didn't have a lab and was operating clinical trials that he was exempt from the FDA regulations. Apparently not. Realize that this is where it gets interesting as there is no way that operating out of a surgery center this doctor can meet cGMP (current good medical practices) guidelines and even if he does, he is still manufacturing a biologic drug without FDA approval. It appears that **many warning FDA letters will be issued to many SVF clinics this year.** If cellular medicine practitioners are using SVF, they best not believe the fairy tale that they are immune. No matter whose course they took, they are exposed.



<https://www.linkedin.com/comm/nhome/?midToken=AQH_IsfBee7wXQ&trk=eml-b2_anet_digest_of_digests-null-3-null&trkEmail=eml-b2_anet_digest_of_digests-null-3-null-null-byjjz%7Eijhepgmk%7El9>

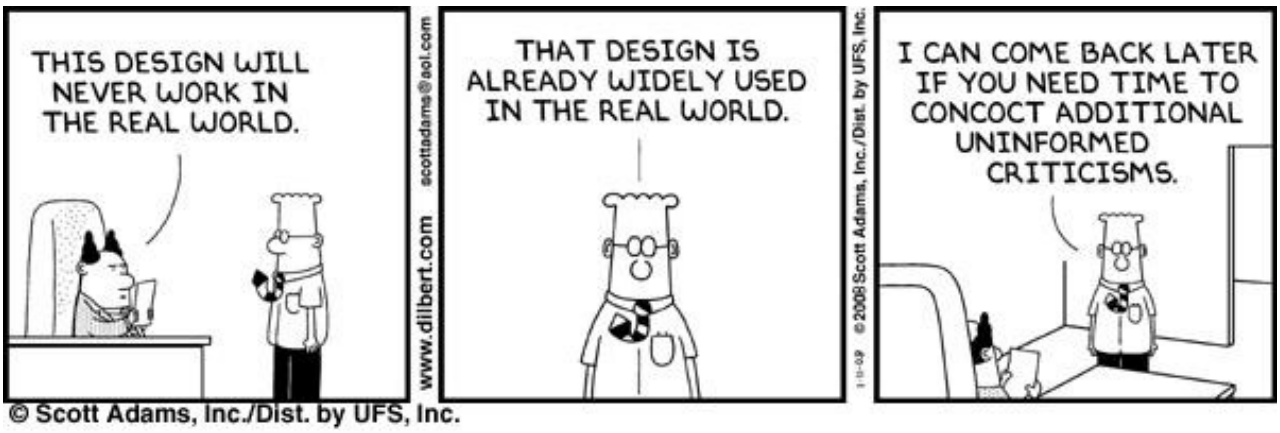
We learn best when we study our failures. So let's try to turn this unfortunate setback for the practice of cellular medicine into a teaching moment. The untoward outcome of the self-inflicted FDA audit for this aggressive and wayward group was predictable based on reviewing the time line and sequence of events. The founding members had initially obtained approval of their initial protocol by a well-recognized and reputable IRB (institutional review board).

But the group shortly thereafter ran afoul of their IRB commitments, including but not limited to changing and expanding their protocols along with adding co-investigators without submitting their

names and credentials to the IRB. The group then began granting non IRB approved credentials (suitable for framing, apparently) to physicians that paid the growingly rogue group for a brief "visiting fellowship". When confronted about this illegal practice by local watch dog groups as well as the IRB in question, the group did not acquit themselves adequately.

After the reputable IRB withdrew the group's certification, the group then formed their own IRB, through which they passed their growingly questionable (according to the FDA) protocols. These short cuts allowed the group in question to continue their questionable practices and pricing until the FDA showed up unannounced at their door (as is standard practice for FDA audits).

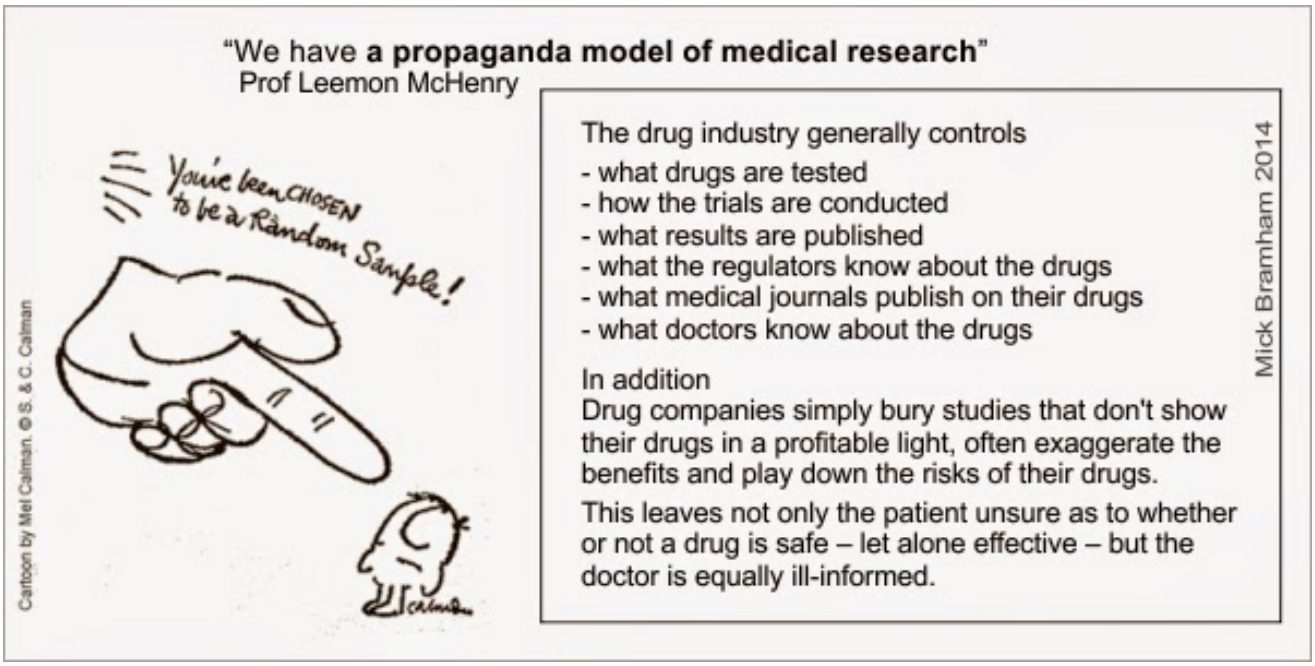
The answer, as far as the honest and forthright practitioners of cellular medicine is concerned, is to simply have all protocols and patient consent forms approved by a reputable IRB and have the patients entered into and followed by a HIPPA compliant patient registry. The currently uneven and often outrageous pricing for biologic procedures will ultimately be corrected by the simple marketplace rules of supply and demand. But the



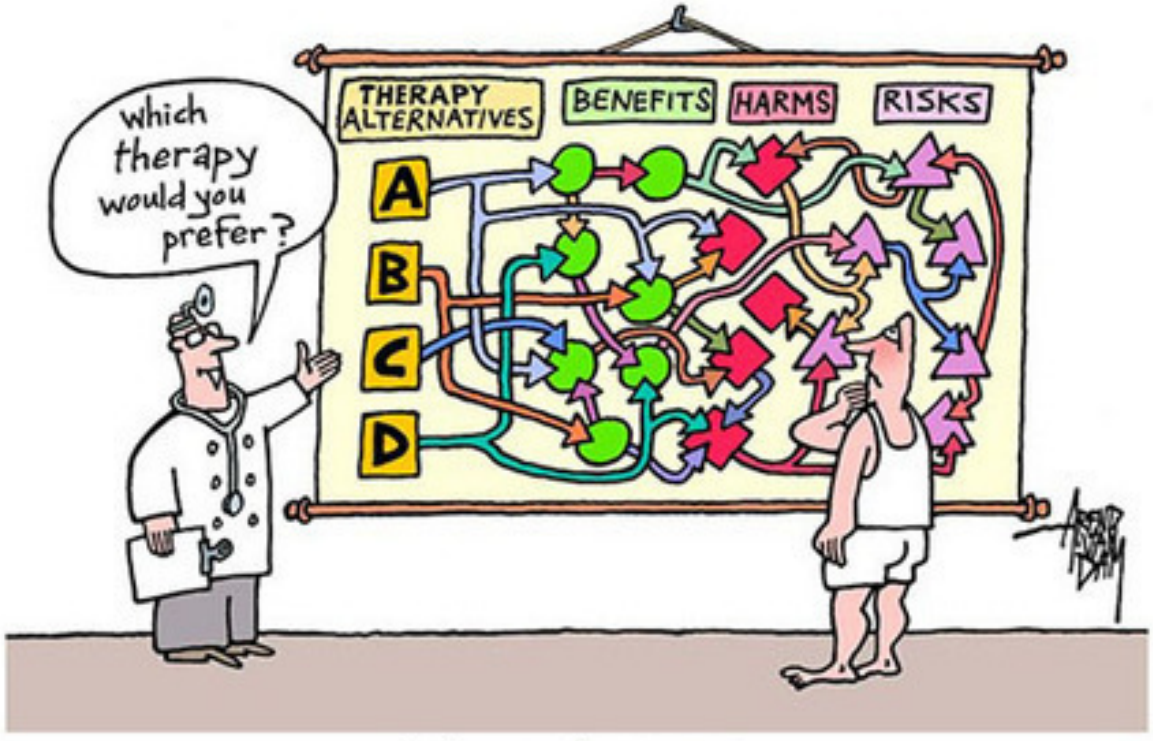
The FDA, knowingly or otherwise, has succeeded in saturating the "ether" known as biologic medicine with uncertainty.

Physicians have a long history of reverting back to tribalism when challenged, thereby the vagaries of FDA guidelines inject fear and confusion into the various silos of the cellular medicine community.

In the beginning of any new concept there are always early adopters, some of whom put themselves out as all-knowing leaders in their burgeoning fields of endeavor. Often these all omnipotent individuals lead some of the lesser informed followers (early adopter wanna-be's) down the prim rose path (i.e. a course of action that seems easy and appropriate but can actually end in calamity). It is not surprising that people when confronted with fear and desperation often turn to soothsayers that they don't fully understand. The above FDA audit brings to light but one such example of self-appointed leaders who brought shame to themselves and scrutiny to the practice of cellular medicine.



The questionable conduct and unquestionable commercialism practiced by this recently investigated group of clinicians brought unnecessary and potentially ruinous attention to themselves and their "visiting fellows". And ultimately, those self-appointed "leaders" in cellular medicine only helped the FDA to maintaining the uncertainty and perpetuating the confusion that continues to cloud the practice of cellular medicine as a whole.



informed consent

What is lamentable is that this did not have to happen. The record shows that this particular group applied for and was granted IRB approval early in their initially innovative and above board cellular medicine practice. The individuals who were the pioneers of the group were (based on their C.V.'s) distinguished in their own medical specialties. But, apparently they made the all too common mistake of over estimating one's past exemplary training and positive experiences. Thus, ill-fated confidence made them believe that positive prior achievements in their Allopathic Medicine practices would extrapolate into equally laudable successes in the practice of cellular medicine.

The truth is that it is very difficult to tell a priori who might or might not become a leader in a particular field or endeavor. The business world, just like the field of medicine, is replete with examples where former vice chairmen, CEO's or "founders" of corporations ultimately make unwise decisions leading to the downfall of their businesses. It is actually very difficult to tell from someone's background whether or not a particular person will become and remain a successful leader.

3. **FDA warning letter issued to Irvine Stem Cell Treatment Center 12/30/15**
   http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm479837.htm

4. **Are Stem Cells the Future of Medicine?**
   http://www.worldhealth.net/news/are-stem-cells-future-medicine/
   http://daytrader.com/ob-stem-cells-investors-making-a-fortune-1/

5. **Stem Cells – Investors Making a Fortune?**
   http://daytrader.com/ob-stem-cells-investors-making-a-fortune-1/

A huge windfall profit could be waiting for smart investors looking to capitalize on biotech companies making big strides in the stem cell therapeutics space. These biotech companies are starting to gain massive investor interest in trading circles and social media alike. Until recently these little biotech companies have been flying under the radar, but just over the last few weeks this has started to change. This attention may be because these companies are playing in a segment of the market that has the potential to change the way modern medicine is practiced forever.

Investors believe they are being given the equivalent of the opportunity to be one of the initial investors in Amazon, or Google, or Microsoft, or even Wal-Mart when they were just coming onto the market and shares were going for just a fraction of what they are today. Investors are always searching for overlooked companies that have the potential to drastically increase in value, but with thousands of companies trading over the counter, it can seem overwhelming to find that small microcap positioned to be "The Next Big Thing."

But investors now believe they have come across something that simply cannot be overlooked. These typically small biotech companies appear to be in the right market at the right time. And investors believe that the biotech space that could be poised for unprecedented gains and the timing could very well be perfect.

http://www.regenexx.com/your-own-cells-are-a-drug-you-may-lose-the-right-to-use/

The FDA has proposed regulations that, if adopted into law, will no longer allow "stem cell" therapy to be considered "the practice of medicine".

PRP (platelet rich plasma- not technically "stem cell" therapy) is still considered by the FDA as "the practice of medicine" and thus remains under the auspices and control of the State Medical Societies in which the PRP is administered. However, in certain states (Texas, for instance) there is a recommendation that physicians utilizing PRP and other cellular medicine procedures should do so under the guidelines of an approved IRB (institutional review board). Be that as it may, PRP has been specifically excluded from discussion at the upcoming public FDA hearing on April 13th, 2016.

This recent notification from the FDA indicates that they are focusing on "stem cell" therapies, particularly SVF (stromal vascular fraction), believing that the enzymatic separation of the human mesenchymal stem cells (hMSCs) from fat obtained via liposuction represent a "drug". If the FDA is successful, SVF will no longer fall under the definition of "the practice of medicine". The FDA has been signalling over the last two years that SVF should not only be disqualified from being classified as "minimal manipulation" but in addition, they believe that SVF does not meet the FDA requirements of "homologous use".

In other words, the liposuction procedure in which fat (and accompanying hMSCs- i.e. SVF) that is removed from the hips, for instance, cannot be reintroduced into any other site in that patient (i.e. the face or breasts). Doing so, according to the FDA, violates the "homologous use" requirement of "minimal manipulation", and (in their opinion) such SVF tissue represents a "drug". And as such, SVF cannot be administered without FDA approval (meaning practitioners must apply for an IND (investigational new drug), be approved and participate in a "drug trial" under strict FDA guidelines- and at enormous expense).

The FDA also has long been signalling that (in their opinion) the enzymatic (chemical) separation of the hMSCs from the liposuction derived fat constitutes producing a "drug". However, hMSCs that are separated mechanically (without enzymes) utilizing vibration and centrifugation, are classified by the FDA as a "fat graft", which does (for now) fall under the definition of "minimal manipulation", thus "fat graft" is considered "the practice of medicine" (and not a drug- for now).

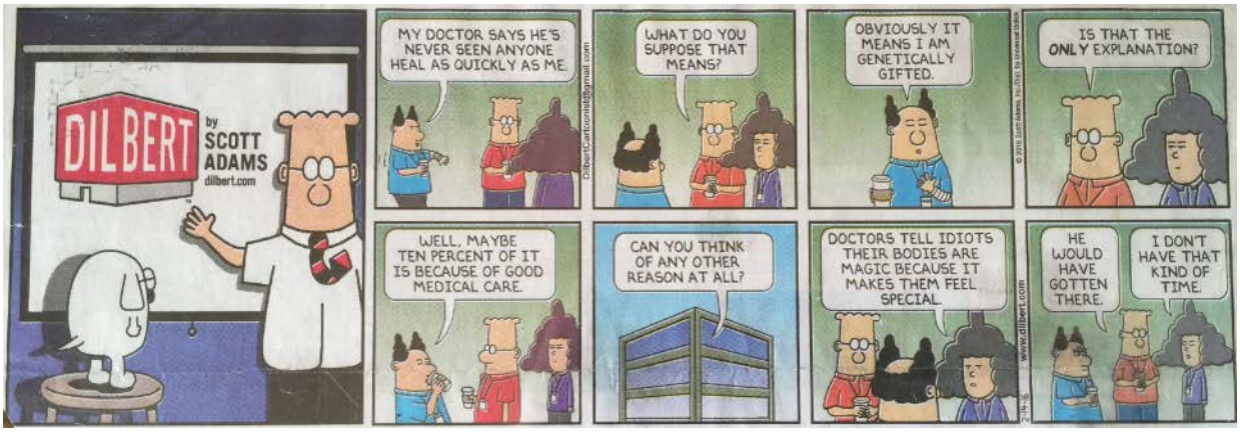
Practitioners who do not believe or understand how committed the FDA had become to stopping the use of "stem cells" in the United States need only visit the FDA's ***Inspections, Compliance, Enforcement, and Criminal Investigations*** section of their website:

http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm479837.htm

Occasionally, individuals are parachuted into situations that they know very little about, but are able to get their bearings extremely quickly, deal with imperfect information and then apply their unique and grounded point of view to bring that endeavor to a successful solution. But more often than not, particularly in Medicine, what is needed to successfully navigate the treacherous and turbulent waters of change is an Integrative Medical Organization that is willing to provide up to date training and guidance based on unlimited sources of information. The American Association of Orthopedic Medicine (AAOM) is the most successful of those organizations because of placing a premium on continuously nurturing and incubating individual cellular medicine practitioners who will ultimately become their next leaders.

The AAOM provides this structure and credentialing for practitioners, while the ICMS (International Cellular Medicine Society) provides the guidelines and certification for the protocols and consent forms for cellular medicine clinics. It is less effective for individual physicians to perform a new procedure or to try to introduce a new wrinkle into the existing practice of Allopathic Medicine.

Individuals, more so than organizations, tend believe that they are "winning"; a dangerous and arrogant practice. But the consistency and stability provided by the AAOM and the ICMS help to avoid the propensity to 'ease back' or to perpetuate old habits, behavior so common to humans when they start believing their own press clippings, becoming complacent, no longer seeking new paths, losing that hunger to blaze new trails.



On the other hand, the AAOM and the ICMS are only as good as the next generation of practitioners that join the organizations; which will be the sole determiner (not the FDA) of when, where and what the next advancement will be in cellular medicine.

Those impatient practitioners of cellular medicine need only be reminded that Einstein spent 15 years proving his theory concerning space, light and gravity until he finally made a discovery that disputed Newton's existing Laws of Physics. And only recently, over 100 years later, were Einstein's original theories proved. As it turned out, gravity was initially Einstein's nemesis, but finally (a few weeks ago) science recorded the first concrete documentation of his theories on gravitation. But despite lack of "definitive proof", even non-physics types understood that because of gravity, all things will fall down to Earth if not properly constructed. Similarly, Medicine too will fall if it violates not only the laws of medicine but the laws of corporations and realities of business evolution.

And if one believes the self-aggrandizing fallacy that every single company, practice and practitioner is going to be an enormous success, then Cellular Medicine will succumb to the same fate as the dot com industry in the 1990's, and they all will undergo enormous setbacks. But, this fate may be avoided if the leading organizations in cellular medicine can encourage individual practitioners to be more discriminating and cautious, and to be less "too big for their britches". Relationships are built on making and keeping promises. If the products or services of a cellular medicine practice does not meet those expectations, it will fail, just like any other business that does not fulfil its promises. But the fact that patients are making the conversion from unknowing commodities of expensive stem cell therapies to citizen scientists will see to it that reluctant physicians will be held accountable (as buried but clearly mandated in the statutes of the **Accountable** Care Act).

Although the early adopters have their challenges, there are subliminal obstacles to success that are due to late comers. Many late stage investments are not really investments; they are just disguised forms of debt. And, unlike the high risks borne by early investors, the late comer's "investments" are

very well protected. The early adopters, brandishing an almost delusional optimism, tend to live on the financial "bleeding edge" while the second wave of investors enjoy living on (and falsely bragging about living on) the "cutting edge" of a technology or development. The practices (like the businesses) that fail will be those that deny reality, not utilizing their money or resources wisely, operating on the idea that there are endless shortcuts to success.

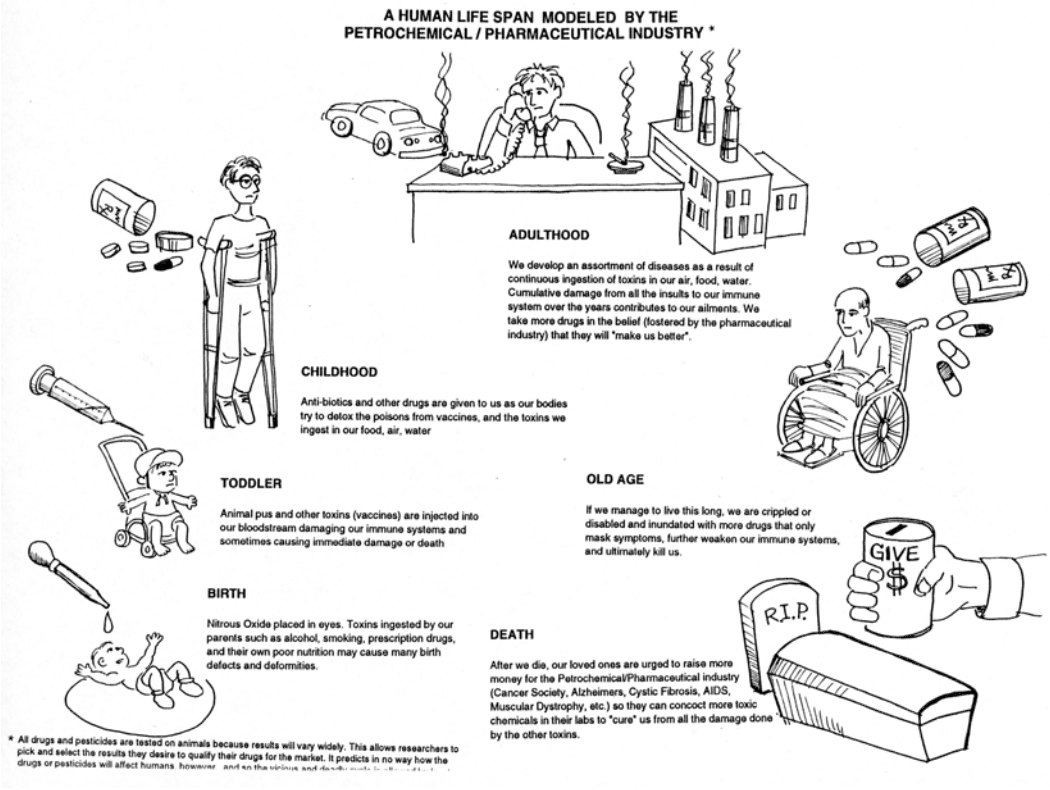
Human frailties remain the primary challenges to mankind accepting Mother Nature's gifts of cellular medicine; which if accepted will result in the correction of medicine. The major human shortcomings include greed, pride-fullness and avarice; thus never forget to "**follow the money"**.

The FDA is inexorably addicted to and influenced by the money (and power) bestowed upon them as a consequence of their pivotal role in approving drugs by the pharmaceutical industry and toys from the device industry. However, doctors and patients have unavoidable financial influences as well. In 2016 the **"Affordable Care Act"** raises the maximum out-of-pocket limit for an individual Marketplace plan to **$6,850** and **$13,700** for a family plan.

In order to survive, doctors (or their staff) need to know how to collect co-pays, cash and deductibles or face losing patients. **Money has become the most sensitive subject with patients and the #1 reason for dropping out of care.** Thus, most of patients want to continue to receive care, but if physicians don't have solutions for them, they will create their own by not showing up

and canceling because of monetary concerns. Reasonably priced, safe and effective cellular medicine therapies are the obvious answer.

Despite all the early and ongoing mistakes by practitioners, one of the things cellular medicine as a whole is getting right is that it is a response to a growing insatiable consumer demand for biologics. And despite the bedlam that we all read about the FDA, the FDA is not changing its stripes or stance on anything that threatens what they perceive as their unbridled control over medicine. Hence the Unstoppable Force of cellular medicine is colliding with the Immovable Object of the Food and Drug Association. Sometimes teaching turns into an intervention, and that is what is in order for this conflict.

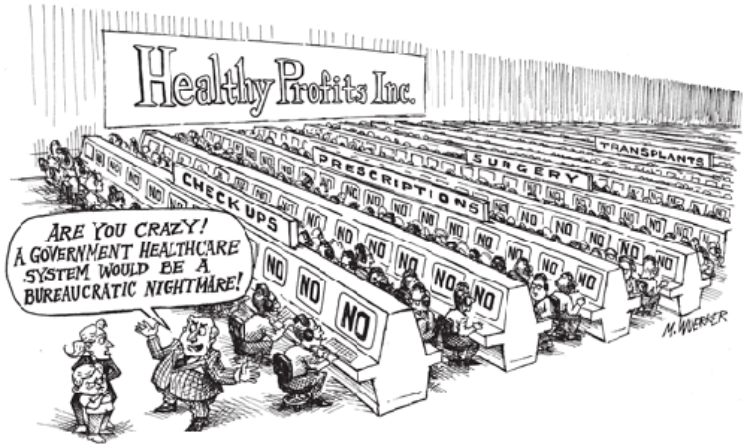


Thus far, the FDA is predictably taking the predictable stance that; 'you cellular medicine practitioners turn over to us all of your names and all of that which you have and we will examine it and tell you which of it is legitimate'. Further, the FDA believes that they alone will determine who the leaders of the biologic medicine community should be. But the problem is that the unwieldy and fuzzy polices of the FDA are no different than the unintelligible tax code, and even when practitioners of cellular medicine try to act in direct accordance with the bylaws, there is no guarantee that they won't find themselves in the middle of a career destroying audit.

The FDA seeks out bastions within the "at risk" Allopathic Medicine community who are most fearful of the ability of biologics to replace the growing dysfunctional, dangerous and expensive brand of medicine to which they must pledge allegiance (the binary drug or surgery approach). And although representing the minority of health care physicians, the AMA and the AABB are held up by the FDA as the approved groups in charge of the practice of medicine. Meanwhile, regenerative medicine practitioners, chiropractors, manual therapists and naturopaths are deemed to be out of

the mainstream. There has even been talk of "physicians" going on strike, or unionizing to fight the insufferable changes that have been put upon them.

But this FDA rubber stamping group does not represent the majority of health care providers by a long shot. In fact, the dues paying memberships of the AMA and many of the specialty societies of Allopathic Medicine are plummeting. Thus, there is no "nationwide" or "majority" group of physicians that will continue to blindly follow or perpetuate the will of the FDA. In fact, if what is fair and equitably is allowed to happen, the "independents" in the health care community will make the final determination, almost certainly overriding the will of the FDA and the status quo Allopathic Medicine community.



An overreaching and narrow definition of "homologous" is counterproductive with emerging trends in biologics. All of these techniques show great promise, safety, low risk of adverse events and data supporting positive outcomes where other standards of care have failed. Is the FDA truly interested in homology or limiting use of biologics?

Fat pads do exist natively in joints such as the elbow, knee, lumbar facets and ankle to name a few. Fat pads are cushions as one function, but not the only function. To say transferring fat into a joint is not homologous is a limiting viewpoint simply because the fat is aspirated from the belly or an area that happens to provide cushion, does not mean that the only function is to provide a cushion; in fact, it is scientifically proven that subsets of cells resident in the adipose fat are not primarily involved in cushioning at all. Most likely, in the future, as more and more studies now being completed are published, all the activities that cells in tissue perform won't be limiting homology to a superficial understanding of an example of a most obvious function, (but not the only or perhaps the most important function).

The health care reformation put forth by non-physicians in Washington D.C. has been naively focused on delivering the same old expensive and ineffective "status quo health care" in a faster, better documented and more efficient way- but it's still the same old health care. But as patients, continue to "Google" they will choose not to participate in the status quo system.

It always takes courage for those pioneers of change to accomplish their goals. And the truth is that, in Medicine, the old school is being threatened both by the "new school" and their patients.

And in the most successful cellular medicine practices, the "new school" makes sure that employees are given a good salary, an honorable mission statement and a friendly work environment conducive to productivity.
Parenthetically, even while old school practitioners of Allopathic Medicine continue to drag their heels and deny the correction of Medicine led by biologics, the leaders in the health care industry have read the writing on the wall (and in the blogs).

For instance, after losing a substantial settlement for continued and recurring complications caused by hip joint replacement, the *Stryker* company is now embracing Interventional Regenerative Orthopedic Medicine (IROM). *Stryker* is acquiring the rights to market for the Italian company, *Lipogems*, which have patented a technology to produce an FDA acceptable "fat graft" material. A global settlement for patients who had complications involving defective Stryker Rejuvenate and ABG II Hip replacements was one of the largest of its kind, with 1.4 billion dollars in restitution to injured individuals throughout the United States. **The FDA originally approved those hip prostheses, bringing into question their dubious success regarding their unrelenting involvement in orthopedics.**

Adipose tissue contains multipotent elements with phenotypic and gene expression profiles similar to human mesenchymal stem cells (hMSCs) and pericytes. The *Lipogems* product is a fat tissue derivative with the characteristics of a "minimally manipulated" product that can be readily injected in an autologous fashion in the donor subject. The overall procedure is fast, safe, does not require stem cell expansion or manipulation, and therefore, it is not subjected to the governmental regulatory restrictions imposed by current Good Manufacturing Practice (cGMP). Although the Lipogems fat graft uses mild mechanical forces in a completely closed system, avoiding enzymes, additives, and other manipulations, **thereby falling under the FDA definition of "minimal manipulation", practitioners should be cognizant of the impending FDA concerns regarding "homologous" use.**

The FDA also appears to have their sites on controlling bone marrow derived stem cells (BMAC) and amniotic tissues/cells.

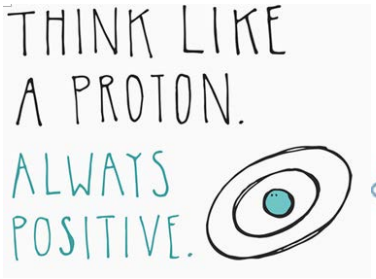
In summary:

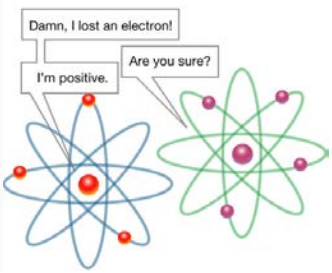
1. **PRP and mechanically derived "Fat Graft" are not currently considered a drug by the FDA, and therefore remain under the scrutiny of the State Medical Boards (no change in the current understanding - "status quo").**
2. **Many warning FDA letters will be issued to many SVF (stromal vascular fraction utilizing enzymatic fat separation) clinics this year. So, for instance, if cellular medicine practitioners are using SVF, they best not believe the fairy tale that they are immune. Based on FDA actions, no matter whose training course SVF practitioners took, they are exposed. BMAC and amniotic tissues may also come under closer FDA scrutiny.**
3. **The AAOM is in the process of generating a white paper that outlines the minimum standards of care with regards to regenerative medicine practice pertaining to maximizing cleanliness and maintaining sterility of the clinics and labs during regenerative procedures- all of which is designed to decrease exposure of clinicians to governmental audit or sanction.**
4. **SVF, BMAC and amniotic tissue/cells are being challenged by the FDA, and practitioners utilizing these tissues need to either attend and testify, or at least submit a comment to the FDA challenging this attempted change/control from Washington with regard to the growing practice of cellular medicine.**

https://www.gpo.gov/fdsys/pkg/FR-2015-10-30/html/2015-27703.htm

ICMS (International Cellular Medicine Society) proposed set of guidelines to minimize risk of FDA sanctions:

- **Protocols for investigative care should be submitted for IRB approval.**
- **Investigators should have strong animal data that the exact cell type their protocol utilizes helps the condition they propose to treat.**
- **The patient should have no good options (or the only option is surgery).**
- **Practitioners need to be specialists or be receiving specialty training in the area they endeavor to treat (i.e. no cosmetic surgeons injecting knees or MSK specialists injecting wrinkles without those practitioners having undergone specialty training).**
- **Investigators (practitioners) need to track patients in a registry.**
- **Investigators (practitioners) need to report their results on-line and in the peer reviewed literature where appropriate.**
- **You must use a strict candidacy grading metric- good, fair, poor - like any other medical procedure**





The following is my response to the FDA notifying that I will be in attendance at their public hearing in April

This is to notify the FDA that I will be in attendance at the upcoming FDA public hearing pertaining to the FDA's proposed new stem cell therapy policies.

I serve as the Chairman of the Institutional Review Board for the International Cellular Medicine Society, and for several years I have had the privilege of reviewing countless worldwide protocols pertaining to the use of biologics, including the cellular medicine therapy that the FDA is currently investigating.

I am available to present our view point that the administration of autologous cells under the long existing and exhaustive FDA guidelines of minimal manipulation is by definition "the practice of medicine", and therefore fall under the auspices of the state medical societies, not the federal government.

As the Chairman of a large review board, we have been called to adjudicate any complications that occur within the ICMS approved protocols, and I am happy to report that there have been no serious adverse events (SAE's) attributed to the administration of approved cellular medicine products. This negligible complication rate speaks volumes about the safety of these procedures, particularly compared to the increasing, often devastating complications related to dangerous pharmaceuticals and surgical procedures.

The literature on cellular medicine shows a time graft demonstrating a logarithmic growth, and the ICMS and the American Association of Orthopedic Medicine (AAOM) are leaders in training physicians and publishing the papers showing the effectiveness of these safe and relatively inexpensive biologic therapies.

There are many state legislatures now passing laws to allow state employees to have a choice between cellular medicine therapies versus pharmaceutical and surgical procedures. We have shown in our state that last year if the 213,000 state employees would have been given the option, they would have chosen cellular medicine therapy over joint replacement, the result would have been a 90% savings to the state's private medical option.

I look forward to the opportunity to testify at the public hearing in defense of leaving physicians in charge of the practice of medicine, and I will encourage the FDA to maintain their focus on their regulatory mandate to keep us all safe from toxic and dangerous drugs and risky surgical procedures and medical devices as we navigate this ongoing correction of Medicine.

The key to the initial success, as well as the long term outcome of any medical therapy, and specifically cellular medicine procedures, is both the pre and post procedure patient assessment and rehabilitative care.

First off, without determining at the outset the **"diagnosis, diagnosis, diagnosis"** (thank you for teaching me that Anette), the therapy will be a crap shoot.

What follows is a 6-point guideline for that I use for regenerative injection therapy, and note that the role of the "injectionist" is relegated to number 5, followed only by the glaringly underestimated importance of patient follow-up via a registry (number 6).

But no matter what is injected or how it is injected, imaging guidance or no, there must be both the dignity of a proper diagnosis and diligent follow-up.

Co-Guidelines

Regenerative Injection Therapy (RIT)
Buffered 5% Dextrose (D5W)
and/or
Platelet Rich Plasma (PRP)
Interventional Regenerative Orthopedic Medicine (IROM) Practice

6 Co's of MAXIMIZING EFFECTIVENESS OF RIT

1. **Co**llaborate with patient's Primary Care Provider (PCP)
2. **Co**ordinate with patient's Chiropractor and/or Manual Therapist to ensure the patient the dignity of a proper diagnosis.
3. **Co**llate existing health care records with all prior medical and surgical history with an updated pharmaceutical history and hormone status.
4. **Co**rrelate prior imaging studies with appropriate up-to-date imaging to arrive at the correct diagnosis.
5. **Co**mmunicate overview of regenerative injection therapy (RIT) in sync with patient's understanding of their existing health care regimen (making clear that RIT is 'in addition to', not 'instead of' the patient's existing and evolving 'patient specific' integrative health care regimen).

6. **Co**mplete patient registry following RIT.

Number 1 in the guidelines involves collaborating with the patient's primary care provider (PCP). **The patient-centered medical home (PCMH)** is the offspring of the **Affordable Care Act** that, among other things, mandates that going forward Primary Care physicians must acquire and store all patient electronic health records (EHR). The mandate was presumably designed to encourage us to provide high-quality care, but achieving a PCMH practice has required an expensive and cumbersome organizational overhaul.

In a given year, Medicare patients see on average two different primary care physicians and five specialists working in four separate practices. For many patients, they rarely find a primary physician who can remember them from visit to visit, let alone come to know them in depth or with any meaning or relevancy. Our approach to this disjointed healthcare is Integrative Medicine.

Our goal is to organize like-minded individuals to help transform the discipline of family medicine. We are introducing the concept of primary care in conjunction with pain medicine and Regenerative Injection Therapy (RIT) practice. We are showing how safe and relatively inexpensive Cellular Medicine treatments can successfully meet the needs of our patients in this changing health care environment. We no longer place the total focus just on our practitioners, but also on our allied health care providers, office staff and most importantly on our patients (patient centered care infers the patient must assume responsibility and commitment to their health care).

Patients will seek out those practitioners who both provide the services they want and those who perform those services well. **Our regenerative medicine practitioners are educated and trained by the American Association of Orthopedic Medicine (AAOM). Our biologic regenerative therapy protocols are approved by the Institutional Review Board (IRB) of the International Cellular Medicine Society (ICMS). And our patient consent forms and clinics are certified by the ICMS.**

Practitioners who are appropriately trained as well as having their cellular medicine protocols and clinics approved by an IRB will go a long way toward minimizing their exposure to FDA audits, warnings and sanctions. Anyone favoring the "mission creep" in which the FDA is moving toward a position of having the authority over everybody while answering to nobody, need only visit their local DMV (Department of Motor Vehicles)

Number 2 coordinate with patient's Chiropractor and/or Manual Therapist to ensure the patient the dignity of a **proper diagnosis**. We cannot understate the importance of having the patients evaluated and treated before and after their regenerative injection therapy by their Chiropractors, Physical Therapists or Manual Therapists. Practitioners who skip this key step in the treatment of their regenerative medicine patients will not have the outcomes of those who understand the importance of pre and post procedure therapy **(IROM is 'in addition to', not 'instead of' the patient's existing and evolving 'patient specific' integrative health care regimen).**

Chiropractic medicine had its start in the United States in 1895. It is unique amongst the healing arts in that it is a **non-drug (non-pharmaceutical) based profession**. Chiropractic physicians are

Physical Medicine Specialists who treat the whole body with particular emphasis on the spine. The vast majority of all spinal manipulation throughout North America is provided by chiropractic physicians.

Numerous studies over many decades have demonstrated both cost effectiveness, as well as clinical efficacy of chiropractic medicine.

- Chiropractic medicine is a cost effective option having been proven efficacious in the management of musculoskeletal issues.
- Chiropractic physicians understand the significance of PRP therapy and embrace it as another non-pharmaceutical option in the management of patients with musculoskeletal issues.

Number 3 collate existing health care records with all prior medical and surgical history with an updated pharmaceutical history as well as nutritional and hormone status. Our pain patients' records will reveal extensive non-surgical "management" with ineffective steroids and narcotics. In addition, pain patients are particularly susceptible to having undergone unnecessary and ineffective surgical procedures that must be taken into account when planning for IROM.

Number 4 correlate prior imaging studies with appropriate up-to-date imaging to arrive at **the correct diagnosis.**

A patient with no confidence in the diagnosis will have no confidence in the therapy. And what we are beginning to see is that poor outcomes may precipitate anything from patient complaints to Medical Boards to malpractice lawsuits. And, despite the proven safety and enormous potential of cellular medicine injection therapy and its potential to change medicine, without pre injection work up and post injection follow-up, the outcomes won't be maximized.

Number 5 communicate overview of regenerative injection therapy (RIT) in sync with patient's understanding of their existing health care regimen **(making clear that RIT is 'in addition to', not 'instead of' the patient's existing and evolving 'patient specific' integrative health care regimen).**

Number 6 complete patient registry following regenerative injection therapy (RIT).

The best defense when the FDA shows up one Monday morning and knocks on the clinic door, is having the cellular medicine being practiced in an OSHA compliant clinic under an IRB approved protocol and patient consent form, accompanied by an electronic patient registry (all of which are obtainable from the ICMS- International Cellular Medicine Society).

We are moving into the world of accountability- **Accountable Care Act**- although you might not want to peruse all those thousands of pages of the Obamacare legislation, suffice it to say that the law makes it explicitly clear that **we are moving into a world that however and whatever we decide to do for or to our patients, we are going to be held accountable.**

Inaccurate is the popular belief that "stem cell and biologic medicine represents the wild west". That metaphor infers the adage that in the wild west "it was easier to ask for forgiveness than for permission". Nothing could be further from the truth. Anyone who has dealt with the federal government (IRS audit?) knows that bureaucrats do not simply accept an apology for breaking their "laws". And anyone who believes that pleading ignorance with the "I didn't know the law" excuse is going to exonerate them from FDA sanctions is as delusional as the motorist who tells the state trooper – "I didn't know the speed limit".

For the Regenerative Medicine practitioner, the correction of Medicine may ultimately assure that the first "shot" is reimbursed, but anything that follows will be the responsibility of the "accountable" health care provider. And that is what regenerative medicine is all about.

Until next time:

David L. Harshfield M.D., M.S.
Chairman - IRB International Cellular Medicine Society
Member of the Board of Directors- AAOM

Subject: AAOM Call to Action - FDA Stem Cell Hearings

SPECIAL ANNOUNCEMENT

The World Authority on Orthopaedic Medicine

Orthopaedic Problems, Innovative Solutions, Since 1983

Dear Colleagues,

Call for Action regarding the FDA proposed new stem cell therapy policies

The AAOM is joining forces with other organizations in a **Call for Action regarding the FDA's proposed regulations regarding stem cell therapies in the practice of medicine.**

Please read about the Call for Action below and do your best to support this "grassroots" response to the FDA's proposed new stem cell therapy policies. We feel very strongly that the FDA proposed guidelines overstep their regulatory mandate and may interfere with the "practice of medicine", by interjecting themselves into the physician–patient covenant, interfering with the patient's right for treatment, and, in the case of autologous cells, placing restrictions on a person's own healing capacity.

The first big deadline is January 8th

Individuals who wish to attend or present at the FDA public hearing concerning four (4) draft guidelines before they are accepted as final regulations must register by sending an email to CBERPublicEvents@fda.hhs.gov **on or before January 8, 2016,** and provide complete contact information, including name, title, affiliation, address, email and phone number.

The goal is to have 10000 people registered in the next week. Please reach out to patients, politicians, Industry, Hollywood, NFL, NBA, physicians and all concerned groups to register. Of course registering is not a commitment to attend but 10000–20000 registrants will get the attention at the FDA. We will, of course, then have some time to prepare and coordinate our message and begin to deploy our various leverage points.

Thank you for your attention and action regarding this very important matter.

If you have to go fast go alone, but if you have to go far go together.

Meaning all those who feel they need to go fast risk the ire of the FDA, while those who want cellular medicine to endure need to stick together.

Brad Fullerton, MD, President AAOM

Information about the DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 1271

[Docket No. FDA–2015–D–3719]

Draft Guidances Relating to the Regulation of Human Cells, Tissues, or Cellular or Tissue–Based Products; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notification of public hearing; request for comments.

For more information **visit**.