Our Patient's Autologous Stem Cells are Drugs: The FDA Moving down a Dangerous Slippery Slope

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Adult autologous stem cells (A-ASC's) show great promise in research and early pre-clinical/clinical use. These cells have the potential to revolutionize medicine by differentiating into repair tissues or exerting paracrine effects to assist in tissue healing.[1] What you may not realize is that a herculean power struggle going on behind the scenes where the Food and Drug Administration (FDA) is now claiming, through the "canary in the coal mine" of stem cells, to have authority over your medical practice. If left unchecked, the next logical step in this regulatory pathway appears to be dividing certain pain procedures into those that require federal regulation and those that do not.

In 2005, the FDA dramatically, and quietly, changed its regulatory approach with potential to upset the "great wall" between medical practice and mass drug production. In this year, the agency made changes to the 361 Public Health Service act to classify certain A-ASC's (based on more than minimal processing) as a biologic drugs requiring pre-market, federal approval before use for sale in interstate commerce.[2] Before 2005, this drug production status could have only applied to allogeneic tissues (i.e. cells that were mass produced in a vials for mass distribution). After 2005, this was applied to all human tissue. Since that time the agency has clarified that it considers "more than minimally manipulated" autologous tissue and cells to be biologic drugs.

The agency has traditionally gone to great lengths to differentiate *one on one* medical care risks (over which it has no authority) from *one on many* drug and device production risks (it's congressional mandate). However, after this subtle change in its regulations, the agency drew a regulatory, public health risk line through a one on one autologous tissue risk for the first time. For example, instead of only claiming authority over mass produced donor cells in a vial, the agency asserted authority over the re-implantation of the patient's own tissue. This change, may sound esoteric at first, yet by this regulatory sleight of hand, the agency gave itself the authority to regulate medical practice risks (one on one risks).

This wall between the agency and the practice of medicine has been defined by many court cases, but the case the agency brought against an Alabama physician (*United States v. Evers*) is illustrative. In this case, Dr. Evers was prosecuted by the government for using prescription drugs off label. The judge sided with Dr. Evers and explained why the FDA should not interfere with the practice of medicine. For example, the Court noted that a drug's package insert is not the most up-to-date information on the drug's uses. New uses are often discovered, reported through medical journals or seminars, and may become widely used in the medical profession; however, the drug manufacturer may not have sufficient financial or other interests to pursue FDA approval for the new uses. Further, if a doctor must prescribe and treat only within "federally sanctioned" methods, this would result in medical stagnation at the best, as physicians await drug manufacturers' initiative and FDA approval.[3] The court reasoned, ***"A***

free, progressive society has an enormous stake in recognizing and protecting this right of the physician."

The best everyday example of the line FDA has drawn between one on one medical care risks and one on many public health risks, is how it currently handles compounded pharmaceuticals.[4] In the Compliance Policy Guideline for compounding pharmacies, the agency states that since it doesn't regulate the practice of medicine or pharmacy, that it will only attempt to interfere in this relationship if a pharmacy is compounding drugs in advance of receiving a prescription, manufacturing on a commercial scale, or compounding drugs for resellers or for wholesale use. In essence, the FDA will only intervene if the pharmacy crosses the line and departs from filing a single patient's prescription and starts mass manufacturing of lots of drugs. However, the agency has not shown the same digression in its regulatory framework for autologous cell therapy and this marks a stark change in agency policy toward physicians. Since A-ASC's can only represent a one on one medical care risk because they are derived from the same patient in which they will be re-implanted, FDA, has now arbitrarily drawn the risk line through this one on one medical care risk and assigned it a mass production, public health risk status.

By declaring regulatory authority over autologous tissues based on the degree of processing of those tissues, the FDA has inserted itself into the practice of medicine by declaring that processed in a certain way, our patient's body parts are drugs. In the same way that the agency in *Evers* (above) declared it had authority over how drugs should be prescribed, it has now declared authority over what constitutes a drug in the first place. This problem with this stance is further illustrated by a recent U.S. district court decision which stated that genes (and by extension stem cells) are laws of nature and therefore cannot be patented.[5] This patent case creates clear precedence that the cells or genes in our bodies are not property of the biotech industry (devices or drugs) to be registered in the federal patent office, but body parts no different than a knee or an elbow. Nobody invented autologous stem cells, nor genes, nor knees or elbows.

A recent publication on autologous stem cell treatment risks shows these risks to be substantially less than traditional one on one surgical care.[6] Even if for other applications the risk is more than reported in this study, how does any aspect of an autologous one on one medical care risk transform that risk into a one on many batch drug production risk? Stated another way, can a medical procedure, no matter how unfamiliar, ever have the same widespread public health impact as drug production? As an example, we would all agree that a bad batch of mass produced drugs or devices would have serious and far reaching public health implications. A single bad batch of drugs may make many patients ill in all 50 states (a one on many risk, hence the reason we have an FDA in the first place). However, no aspect of a single medical care procedure, can be morphed into this kind of magnified public health impact. The surgery a patient chooses to undergo, the IVF fertility treatment, the testosterone use from a compounded prescription, are all one on one medical care risks, which the doctor and patient discuss, and the patient either chooses to accept or avoid. They are not, by their one on one nature, national public health epidemics to be regulated at a federal level. Some one on one medical care risks are quite

serious and some are miniscule; for example certain types of cardiac surgery have high morbidity or mortality rates while other types of cardiac procedures such as an EKG, have negligible risks. The medical care system goes to great lengths everyday to mitigate these risks. However, drawing an arbitrary risk line through these procedures (or others in the future), allows FDA to divide medical care into a type that requires federal regulation and a type that does not. If this is allowed, since all one on one procedures by their definition are medical practice, the FDA is by default regulating the practice of medicine. Autologous cellular therapy is just an example, no matter where we draw this risk line through the one on one delivery of autologous cells, we still end up with a one on one medical practice risk and not a magnified, mass production, public health risk. For example, the use of the patient's own autologous cells is not a risk to all patients or many patients, just one unique patient, just like all the other medical care risks discussed here. Finally, to illustrate the problems with drawing the risk line through a medical procedure, consider a recent publication showing that a routine MRI magnetic field changes the biologic characteristics of stem cells.[7] Before the publication of this paper, the agency defined a biologic drug by cell processing that changed the biologic characteristics of the cells, however, this research confirms that a routine MRI changes the biologic characteristics of the cells. Do the "less than minimally manipulated" stem cells injected into the patient become federally regulated drugs after a routine MRI?

In summary, the assertion by FDA that certain processing steps for autologous stem cells turns those cells into a one on many drug production risk is not supported by an additional public health impact beyond any other one on one medical care risk. Furthermore, the agency's decision to insert itself into the practice of medicine by drawing a line through one procedure, sets a dangerous precedent. Where does this line get moved to in the future? Do certain compounded drugs get assigned a drug manufacture risk? Certain fertility procedures? Certain high risk surgeries? Certain high risk surgeries involving cells? Congress has prohibited the agency from having any authority over the practice of medicine and as discussed, there is great societal benefit in keeping it that way.

If you have an interest in supporting safe A-ASC use, sign up at http://www.cellmedicinesociety.org/

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