Q: WHEN IS BONE MARROW NOT AN ORGAN UNDER THE NATIONAL ORGAN TRANSPLANT ACT?

DECEMBER 2, 2011 • BY HANK GREELY • COMMENTS [2]

Hank Greely, Director, Center for Law and the Biosciences

A: When the stem cells that make up the crucial part of bone marrow transplants are harvested by peripheral blood stem cell apheresis – or so says the Ninth Circuit.

Yesterday, December 1, the Ninth Circuit released its decision in Flynn v. Holder. (The opinion can be downloaded here – look for December 1, 2011 and Flynn v. Holder.) A variety of plaintiffs sued the government, claiming that the criminal provisions of the National Organ Transplant Act (“NOTA”) were unconstitutional as applied to bone marrow donations. The plaintiffs included patients who need bone marrow transplants, parents of sick children who need or may need bone marrow transplants, a physician whose patients need bone marrow transplants, and a California not-for-profit corporation, MoreMarrowDonors.org, that wants to create a program to provide financial incentives (scholarships, housing allowances, gifts to designated charities, and so on) to encourage people, particularly of minority and mixed-race backgrounds, to donate marrow.

The Act makes it a crime “for any person to knowingly acquire, receive, or otherwise transfer any human organ for valuable consideration for use in human transplantation if the transfer affects interstate commerce.” The Act defines human organ as “the human kidney, liver, heart, lung, pancreas, bone marrow, cornea, eye, bone, and skin, and any other human organ specified by the Secretary of Health and Human Services by regulation.” By regulation, HHS has added “intestine, including the esophagus, stomach, small and/or large intestine, or any portion of the
gastrointestinal tract.” Neither the Act nor its implementing regulations includes blood, blood products, eggs, sperm, or hair, among other things. (The Act also excludes from its definition of valuable consideration any “reasonable payments associated with the removal, transportation, implantation, processing, preservation, quality control, and storage of a human organ or the expenses of travel, housing, and lost wages incurred by the donor of a human organ in connection with the donation of the organ.”)

The district court dismissed the complaint for failure to state a claim upon which relief could be granted. The Court of Appeals, in a unanimous decision, reversed in part. Judge Linfield wrote the opinion, joined by Judges Goodwin and Graber.

A couple of biomedical facts are necessary to understand this fight. First, the cells in our blood system come in many different varieties (red cells, T cells, B cells, platelets, macrophages, and many others, most with many importantly different subtype). All of these cells have limited lifetimes and so they are constantly being replaced by new cells, produced mainly in our bone marrow. Most of the cells in the bone marrow, however, are not responsible for making new cells. The cells that do make new blood cells are hematopoietic (“blood forming”) stem cells. There are various kinds of hematopoietic stem cells, ranging from the least differentiated, which can give rise to all the kinds of blood cells, to various intermediate-stage stem cells, each of which can give rise to only some of our kinds of blood cells. These hematopoietic stem cells are generally located in the bone marrow, but they can “break free” and float in the bloodstream. The production of these stem cells, and their migration into the bloodstream, can be encouraged by various drugs, including notably “granulocyte colony-stimulating factor” (GCSF).

The second important point is the difference between taking out cells by aspiration as opposed to by apheresis. When bone marrow is donated by aspiration, the traditional way of extracting bone marrow, a long needle is poked into the donor’s bone (usually the hip) and some of the bone marrow is sucked out. Apheresis instead pulls cells from the circulating blood. Apheresis has long been used to pull out particular kinds of blood cells, such as platelets. The donor sits in a reclining chair for several hours, with his blood system connected to an apheresis machine, which pulls the sought-after cells from the circulating blood.

The plaintiffs argued that the criminal provision of NOTA violates the Equal Protection Clause, because, without a rational basis, it treats bone marrow transplants differently from blood, sperm, or egg “donations,” for which compensation can be paid. The Court was not entirely sure whether the plaintiffs were challenging the statute’s application to any bone marrow donations or just those done through the technique of apheresis. The Court held that the statute may constitutionally regulate the donation of bone marrow through aspiration and it recites various policy and philosophical distinctions that Congress might have rationally relied upon to criminalize bone marrow donation by aspiration.

The Court’s opinion leaves open the possibility that a ban on bone marrow donation by apheresis unconstitutionally violates the Equal Protection Clause and that the
dismissal of the complaint on that argument was inappropriate, but the Court proceeds to make that issue moot. It concludes that NOTA does not, in fact, prohibit bone marrow donation when done through peripheral blood stem cell apheresis. It points out that none of the soft, fatty marrow tissue (think of the tasty stuff inside the bone in the wonderful Italian dish, ossobuco) is actually removed – or otherwise touched – in apheresis. Instead, cells are taken from circulating blood, just as cells are taken from circulating blood in all the many kinds of blood donation allowed by the Act. Congress could not have intended specifically to include peripheral blood stem cell apheresis as bone marrow donation, because the procedure did not exist at the time. As Congress excluded blood itself, all of which is formed in and, at some point, is part of, the bone marrow, the Court concluded that hematopoietic stem cells, extracted from circulating blood by apheresis, are not bone marrow for purposes of the Act and therefore that the ban on paying for bone marrow does not apply to them.

As the Court summarizes its decision, with a nice bit of linguistic discussion,

It may be that “bone marrow transplant” is an anachronism that will soon fade away, as peripheral blood stem cell apheresis replaces aspiration as the transplant technique, much as “dial the phone” is fading away now that telephones do not have dials. Or it may live on, as “brief” does, even though “briefs” are now lengthy arguments rather than, as they used to be, brief summaries of authorities. Either way, when the “peripheral blood stem cell apheresis” method of “bone marrow transplantation” is used, it is not a transfer of a “human organ” or a “subpart thereof” as defined by the statute and regulation, so the statute does not criminalize compensating the donor.

(LOVE the reference to “brief”!)

Frankly, this seems sensible to me. It will be interesting to see if the government seeks to appeal this decision further. There is no circuit split (yet?), so that reason for Supreme Court interest does not exist. And, of course, the Secretary of HHS could, presumably, amend the regulations to include these cells as a covered organ, as the regulations now expressly cover intestinal organs. I hope the government does not try to stop these efforts; not only could they provide much needed transplants for very sick people, but they could also be a real world experiment in various incentive schemes for organ donations. Those have been talked about for a long time, but have not been feasible (in the United States) because of NOTA’s criminal prohibition.

In the longer run, this may have some implications for regenerative medicine more generally. If, rather than transplanting a kidney, one uses stem cells from a donor to “build” a kidney for transplant, this decision might be relevant – at least as long as the stem cells were derived from some tissue (like blood) not covered by the Act. (Of course, when a stem cell donor would be needed and when such a donor would demand payment are interesting questions.)

So, it’s a narrow decision, but an interesting one – and one that might have broader...
implications. And it will let us see just what the Obama Administration thinks about incentives for some kinds of organ or cell donations.

Hank Greely

Director, Center for Law and the Biosciences

PS. My thanks to Ben Hippen at UNC, whose post on the very useful MCW-Bioethics listserv alerted me to this case.

Alex Capron says:

December 2, 2011 at 12:50 pm

This, as one expects from you Hank, a clear description and analysis of the case. But I was puzzled by your approval for the decision. The focus of NOTA was not only the form that an organ takes or the manner in which it is obtained for transplantation. Rather, NOTA was written to prevent the development of a market in organs for transplantation based on three propositions: that having a market will not increase and in fact may decrease the availability of organs for transplantation, that paying people to part with their organs for money (or other “valuable consideration”) will result in the poorest and most vulnerable people becoming the organ bank for those who can afford transplants, and that payments for body parts amounts to turning human beings into market commodities. The manner in which an organ exists in the body (whether all in one place or distributed) and the manner in which it is removed from the body were certainly not central to NOTA’s rationale or objectives. Therefore, the development of apheresis as a means of harvesting peripheral blood stem cells as an alternative to aspiration is simply another means of obtaining a portion of the bone marrow which is a change no more relevant than the many other developments in organ transplantation in the past 27 years.

What is relevant is that bone marrow transplantation is a form of treatment where the risks of financially motivated “vendors” are actually greater than with other organs because the preparation of the recipient (through irradiation of the bone marrow) occurs much longer before the harvesting and transplantation of the bone marrow than is true with transplants of solid organs. The risk of a “hold up”—which always exists but is certainly much greater with a donor who motivation is money rather than concern about the life and well-being of the recipient—ought to give anyone pause.

At several points in your commentary you make reference to what might have led
Congress “to criminalize bone marrow donation by aspiration.” The plaintiffs would like to create the sense that NOTA has to be struck down (at least—or for the moment—as to PBSC aspiration) in order for live-saving transplants to go forward. But that’s not the case, because Congress never did any such thing as to any transplant procedure. What it did was to criminalize payment for the organ, for the reasons I have already mentioned, and thousands of transplants occur every year despite NOTA. We certainly need more efforts to increase donation of all organs (especially from deceased donors, as to heart, liver and even kidney, but also from living donors, especially as to bone marrow). The HHS “Collaborative” produced a large up-tick in the rate of donation beginning a decade ago, and it needs to be reinvigorated, with new “best practices.” But all the existing arguments against developing a market in organs continue to exist and apply to bone marrow as much as any other organ for transplants. Some supporters of the plaintiffs in Flynn v. Holder are rejoicing precisely because they see it as the death knell for the NOTA payment-prohibition, which they will achieve by turning their present arguments on their head: if we can pay for something as innocuous as donating bone marrow through apheresis, then how can we leave donors of kidneys and liver lobes, who bear a much greater burden, with no compensation? And if the payment system does not have the effect of reducing the supply of bone marrow (or only has the effect of greatly increasing the cost of bone marrow for transplants while somewhat increasing the available supply), they will argue that NOTA is without a policy rationale—though the harm to the supply was only one, and probably the least important, of the rationales for the statute.
The 9th Circuit panel arrived at an unwise decision based on its fascination with a change in technology. I’m sorry to see you agree with the judges.

Alex

Reply

Louis Weltzer says:
December 13, 2011 at 9:40 am
I am an attorney and a recent stem cell donor, so I have been following Flynn v. Holder with some interest. My concern has been that if compensation is permitted for stem cell donation, the United States may not be able to participate in international donor registries which prohibit such compensation. Do you have any information about how this decision may affect such participation?

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