Using Birth Tissues in Spine Surgery

By Robin Young

Maybe it's a Texas thing, but more and more spine surgeons are buying and using pieces of donated placental tissue as an adjunct to their spine surgery.

In fact, Texas is probably the one place in the United States where recycled placental tissues are finding the most wide spread surgeon acceptance although, to be sure, many spine surgeons around the U.S. are also intrigued with this idea of overlaying a piece of placental tissue over their surgical site.

Here's what's going

on. **Full Disclosure**

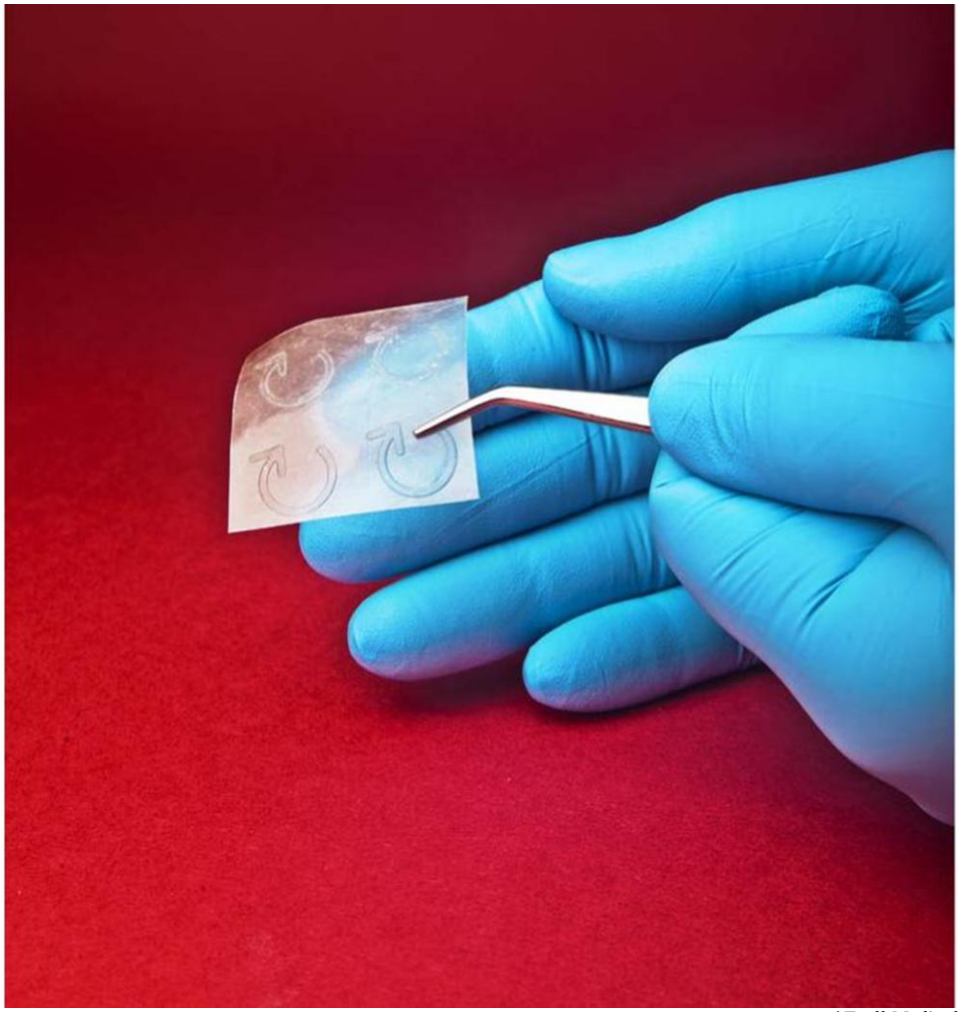
One of the suppliers of birth tissues for use in surgery is a company I founded—AFCell Medical. So, full disclosure, I have a vested interest in this subject. But, having said that, this article is applicable to any company in this arena and for any physician who would like to understand why there is an upsurge of interest in these tissues.

Say, You Doing Anything With That Placenta?

Placentas have been the subject of lore and speculation for thousands of years and are afforded special status in a variety of cultures. Charles Dickens's fictional character David Copperfield, in fact, was described as having been born with a caul. Everyone in those days knew that a "caul" was good luck. A "caul" is the dry remnant of their fetal membrane, also known as the "sely how." Among its mythical benefits was that it was able to save sailors from drowning.

In time, fetal membranes lost their mythical power in most Western cultures and became nature's refuse. But, over the course of the last 100 years a growing body of clinical research has been describing the use of placental tissues in a wide range of wound repair and surgical applications.

The concept that placental tissues could conceivably have value for physicians in wound repair or surgery probably comes from its function as part of the overall pregnancy system. Placentas cover and protect embryos throughout their development. They protect babies from infection or rejection and they help to sustain and nourish the fast growing baby with nutrients and oxygen. Placental tissues also remove carbon dioxide and waste materials by



AFcell Medical

"filtering" or "sieving" them through the placental tissues.

After the baby is born most hospitals inspect the placenta to make sure it's not missing any pieces, so that none is left in the uterus and then incinerate the tissues as a medical waste. Some hospitals will keep the placenta for a week or so in case anything is wrong with the baby so that tests can be run on it to figure out what the problem is. Then they also incinerate it.

The First Recorded Use of Placenta in Surgery

But clinical interest in placentas has always been high. About 100 years ago, Stern and Sabella, working together in 1913, treated and independently reported the use of "amniotic membrane" on burned and ulcerated skin surfaces. The intact amniotic tissues were applied to skin burns and ulcers and then further covered with warm paraffin and dressings. After 48 hours, the dressings were removed and the amnion had integrated with the patient's tissues. Stern and Sabella reported that the patients lacked infection and experienced a marked decrease in pain and an increased rate of re-epithelialization of the traumatized skin surface.

Twenty-two years would pass before another researcher would study the use of amniotic tissues for wound repair or surgery and publish the results. Brindeau in 1935 and Burger in 1937 reported using amnion for vaginal reconstruction surgery. They reported that the tissues restored function for the patient and nine months after surgery showed normal epithelial cells. Burger then conducted further experiments in rabbits, dogs and cats and reported that when amnion was used in dura matter defects that no adhesions formed.

Scheffer Tseng

Between 1980 and 2000, there were more than 50 clinical papers published in a wide variety of peer review journals which described, mostly in the form of case reports, the use of placental tissues in burns, ulcers, abdominal surgery, spine surgery and ocular repair.

In the late 1990s, Dr. Scheffer CG Tseng, an ophthalmologist and faculty member at the University of Miami, Florida, applied for HCT/P (human cell tissue products) regulatory status for the use of amniotic tissues in ocular repair.

If there is a "father" of the use of placental tissues in wound covering or surgery it is Dr. Tseng.

In 1999, the FDA's tissue reference group looked at Dr. Tseng's application to have amniotic tissues for ocular repair designated a human tissue transplant and rejected it saying, "Amniotic membrane for ocular surface reconstruction is considered a tissue under the current regulations at 21 CFR Part 1270, but the intended use would be non-homologous when 21 CFR Part 1271 becomes effective."

Dr. Tseng appealed that ruling and argued that amniotic tissue functions as a cover to encase amniotic fluid and a developing fetus and therefore using it to cover the eye WAS homologous use.

The FDA agreed and a year later the Tissue Reference Group (TRG) of the FDA reversed the prior ruling saying: "Allogeneic amniotic membrane for ocular repair is considered to be a section 361 HCT/P (reverses FY2000 decision). Amniotic membrane cultured with stem cells for ocular repair is considered to be a biologic product subject to INDs and BLAs."

The two key points made by the FDA was that amniotic membrane is a covering BUT that it must be acellular.

The FDA TRG's Subsequent Rulings

Since then, the FDA's Tissue Reference Group has refined what "homologous use" of amniotic tissues means saying: "Allogeneic dehydrated and decellularized amniotic membrane is considered a 361 HCT/P if the product's advertising is restricted to homologous use for a wound covering. Wound repair or wound healing would be non-homologous uses, and when advertised as such, the product could not be considered a 361 HCT/P." – 2002 TRG ruling.

In 2003 the TRG said: "Decellularized particulate human placental connective tissue matrix intended to replace or supplement damaged or inadequate

integumental tissue is considered a 361 HCT/P."

In 2004, the TRG clarified its 2003 ruling saying: "Allogeneic dehydrated and decellularized amniotic membrane is considered to be a minimally manipulated 361 HCT/P when the product is intended to be used as a wound covering. When intended for wound repair or wound healing, additional characteristics of the HCT/P are relevant (e.g., the presence of cytokine-containing cells). Since dehydration and decellularization alter these relevant characteristics, dehydration and decellularization constitute more than minimal manipulation and the product, when intended for wound repair or wound healing, would not be considered a 361 HCT/P."

Clinical Papers

Using Google Scholar to search for articles which use the term "Ocular Use of Amniotic Tissues", 10,300 citations pop up. The most cited article was written by Dr. Tseng (in conjunction with Drs. Prabhasawat, Barton, Gray and Meller). The article describes a study of 26 patients (31 eyes) with limbal stem cell deficiency and how using amniotic tissues improved their outcomes. Specifically, the article said: "Except for the 2 eyes with atopy, all amniotic membrane-covered surfaces showed rapid epithelialization (in 2 to 4 weeks) and reduced inflammation, vascularization, and scarring and the surfaces became smooth and wettable."

Since the late 1990s, literally tens of thousands of patients with a variety of ocular problems including caustic burns have been treated with recycled placental tissues. So well established is this practice that insurance carriers have published extensive policy state-

ments regarding the use of amniotic tissues.

Cigna Corp, for example, wrote the following earlier this year; "Amniotic membrane (AM), the innermost layer of the fetal membrane, exhibits properties that are helpful in wound healing, particularly of ocular injuries." – Then cited 62 clinical papers to support its conclusion.

Aetna Inc. wrote in a policy statement issued this past June: "Amniotic membrane-covered [ocular] surfaces have been shown to induce rapid re-epithelialization to a smooth and wettable surface and reduce inflammation, vascularization and scarring thus allowing successful surface reconstruction."

Four years ago a paper appeared in the *European Spine Journal* that used cross-linked amnion (CAM) as an anti-adhesive barrier in a laminectomy canine model. The authors, Tao and Fan, reported that using amniotic membranes to re-cover the surgical site post laminectomy "is an effective anti-scar adhesion material, which can decrease adhesion tenacity and scar amount in epidural space."

The authors also wrote: "Gross observation demonstrated that scar amount and adhesion tenacity of CAM group were significantly lower in comparison with those of FAM [freeze dried amnion membrane] and non-treatment groups. A white, slightly vascularized CAM layer covered the dura mater without tenacious scar adhesion. The histology analysis also indicated reduced fibroblasts infiltration and consequent epidural fibrosis, which were similar to the results of AFF (Autologous Free Fat) group. In conclusion, the CAM is effective in reducing epidural fibrosis

and scar adhesion after laminectomy in canine model."

Suppliers

The largest supplier of amniotic membranes for physician use is probably MiMedix Group, Inc., which is based out of a suburb of Atlanta, Georgia. Dr. Scheffer Tseng's company, Bio-Tissue and its orthopedic spin off Amniox Medical, Inc., are probably the second largest followed by my company, AFCell Medical, and then BioD out of Memphis. With the exception of AFCell Medical, all suppliers have their own sourcing and processing capabilities. AFCell Medical uses the Musculoskeletal Transplant Foundation to process its tissues and is the only company with issued patents covering its processing technology.

All of these companies supply an acellular product. One company, Osiris Therapeutics, Inc., does supplies a birth tissue product with all of the native cells, including stem cells, available.

Why Use it in Spine Surgery?

In many respects placental tissues are a form of fascia tissue. Fascia is one of the most important covering materials in the body and serves to protect virtually every structure in the body—bones, nerves, muscles, tendons, organs, the spinal cord and the brain. So when trauma or surgery disrupts that natural, protective fascia covering, amniotic membranes are structurally and by composition, extremely similar if not precise transplants.

In effect, placental membranes are a way of putting all the parts back the way the surgeon found them originally. ♦