Umbilical Cord Stem Cell Therapy

The Gift of Healing from Healthy Newborns

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Acknowledgments

The authors wish to extend heartfelt thanks to the following people whose direct or indirect input influenced the evolution and content of this book:

Fernando Ramirez, M.D., Director of the Spinal Cord Regeneration Center, Tijuana, Mexico; Frank Morales, M.D., Director of Rio Valley Medical Clinic, Matamoros, Mexico; Paul Sanberg, Ph.D., D.Sc., Distinguished University Professor, Director of the Center of Excellence for Aging and Brain Repair, and Associate VP/Associate Dean for Biotechnology Development at the University of South Florida College of Medicine; Kathy Mitchell, Ph.D., Associate Professor, Department of Pharmacology & Toxicology at the University of Kansas–Laurence; Norman Ende, M.D., of UMD–New Jersey Medical School; Lyn Darnall, M.A., M.Ed., statistician and senior science writer for Steenblock Research Institute; Dave Bloom, President of Bloom Public Relations (www.ournewsroom.com); Steven Goldfinch, VP of Cure-Source (www.curesource.net); Sheri Schultz, Ph.D., at Albert Einstein College of Medicine, NYC; Larry Howard, President of Weller Health Institute (www.wellerhealthinstitute.com); and Emer Clarke, Ph.D., at Stem-cell Technologies, Inc. (www.stemcell.com).
With love and appreciation to my wife, Noyemy; daughters, Karen and Amber; and my son, David Jr., who is serving his country proudly in Iraq (U.S. Army), for their support, encouragement, and sacrifices in all my endeavors down through the years including the writing of this book.

I also extend heartfelt thanks to all the researchers, physicians, therapists, and scores of patients who have helped transform vision into reality, and theory into milestones of progress for the betterment of the human condition.

—David A. Steenblock, M.S., D.O.
Dedicated to the pioneers—those stalwart souls who have chosen to step into the vast undiscovered frontier, to resist fear and persevere against all obstacles, and by doing so to move themselves and all of us ever forward.

Among them: my wife, Sachi Tsujii-Payne; my fellow traveler along the road of discovery, Dr. David Steenblock; Dr. Fernando Ramirez of the Spinal Cord Regeneration Center in Tijuana, Mexico; Dr. Frank Morales, Director of the Rio Valley Medical Center in Matamoros, Mexico; Steenblock Research Institute’s (SRI’s) statistician, Lyn Darnall; chemist Marie Colucci; lab tech Sue Hardin; biomedical engineer Kevork DerAlexanian; medical librarian Karen Sullins; volunteer E/S translator Grace Odgers; and the more than one hundred patients and parents and caregivers of patients who took an informed step into the land of promise, which is human umbilical-cord stem-cell therapy.

—Anthony G. Payne, Ph.D.
... science proceeds as a series of successive approximations.

—Edwin Powell Hubble
in *The Nature of Science and Other Lectures*, 1954
Authors’ Note

We are standing at the threshold of a new and exciting medical era—an era of regeneration, rejuvenation, and renewal in which stem cells will set the stage for healing and, in some cases, the restoration of injured, diseased, and debilitated tissues and organs. However, it would be premature to portray this emerging field as “miraculous” or “magical.” Stem-cell therapy is surely in its infancy, but it is rich with promise. And though it is buttressed by a tremendous body of scientific work, the therapeutic administration of stem cells is often empiric—meaning that there is often a lot of “give and watch” and “tweak and try again” (more commonly known as “trial and error”). This is a familiar and recurring theme in medicine.

In the pages that follow, we share some of the science that underlies stem-cell therapy and put a human face on this field with accounts of people who have benefited from human umbilical-cord stem-cell treatments. And, in providing this information, we encourage you, the reader, to take that bold first step into this vast and wondrous new medical frontier.
INTRODUCTION

A Brief History of Stem-Cell Therapy

The first recorded medical use of stem cells occurred about a century ago when doctors administered stem-cell-rich bone marrow by mouth to patients with anemia or leukemia. Although this attempt to cure or improve these conditions failed, scientists eventually were able to demonstrate that mice with defective bone marrow could be restored to robust health when injected with marrow taken from healthy mice. Quite naturally, this suggested that bone marrow could be transplanted from one human being to another.

This process, known as “allogeneic transplantation,” was attempted for the first time in people in the late 1950s in France. Patients with leukemia were given doses of radiation that wiped out their marrow, and this was followed by bone-marrow infusions. In many cases, their bodies made new marrow and began producing white and red blood cells, but all of the patients eventually died due to infections or a return of their cancer. All in all, almost 200 allogenic bone-marrow transplants were performed from the late 1950s through the 1960s, but without long-term success. However, transplantation involving identical-twin donors was fairly successful and thus served as a foundation for continued clinical research.

Getting a recipient’s body to accept and utilize donated bone marrow was an obvious challenge. In 1958, French scientist Jean Dausset identified the reason for rejection. He found that specialized proteins
exist on the surface of the majority of cells in an individual’s body, marking the cells and tissues they make up as unique to the individual. These surface markers were dubbed “human leukocyte antigens” (HLA antigens) or “human histocompatibility antigens.” It is these markers that make it possible for the immune system to determine what belongs and what doesn’t belong in an individual’s body. When the immune system encounters foreign markers, or antigens, on a cell, it generates antibodies and other substances to destroy what it perceives as an invader. Disease-causing bacteria, viruses, cancer cells, and foreign matter that breaches the skin are among the “invaders” that the immune system is designed to detect and eradicate.

This surveillance system helps defend the body against things that can cause it harm. This protective mechanism, however, is also behind a recipient’s rejection of bone marrow, which carries surface markers that say, “foreign to the body.” Therefore, it follows that the antigens on the donated bone marrow must closely match that of the recipient for a bone marrow transplant to take hold. Naturally, bone-marrow transplants between identical twins ensure a 100-percent match between donor and recipient. (Such transplants were among the first to be systematically performed in people.) In the 1960s, as physicians and researchers became more adept at determining HLA compatibility, they began to carry out successful bone-marrow transplants between siblings who were not identical twins.

In 1973, doctors at Memorial Sloan-Kettering Cancer Center in New York City performed the first bone-marrow transplant in which marrow from an unrelated donor was given to a five-year-old child with severe combined immunodeficiency syndrome (SCID)—a rare, usually fatal, genetic disorder in which the body cannot defend itself against germs. The child was given seven successive infusions of marrow, six of which did not fully “take.” The seventh finally resulted in engraftment, or acceptance of the donor’s cells, and thus brought about the restoration of normal red and white blood-cell-making function.

These early bone-marrow transplants basically brought about improvement in the recipients because of the stem cells contained in the bone marrow. The stem cells went to work in the recipient’s bones,
creating healthy bone marrow tissue, which is necessary for the production of red and white blood cells. In the case of leukemia—the overproduction of abnormal white blood cells by the bone marrow—physicians discovered that if the patient’s bone marrow is destroyed with chemotherapy (cell-killing drugs) and radiation, they could introduce donated stem-cell-rich marrow that would engraft (take hold) and create healthy bone marrow in the recipient.

Over the past thirty years or so, the use of stem-cell-rich bone marrow, as well as stem-cell-rich umbilical-cord blood, has proven a boon to the treatment of hematopoietic, or blood-related, cancers, especially acute myelogenous leukemia, Hodgkin’s disease and other lymphomas, and, most recently, multiple myeloma. This approach has also been used in the treatment of solid tumors such as breast cancer, as well as sickle-cell disease, thalassemia, progressive multiple sclerosis, systemic scleroderma, severe systemic lupus erythematosus, and severe rheumatoid arthritis.

Today, in the United States more than eighty diseases are in some way addressed by bone-marrow transplants and umbilical-cord blood treatments. It is, of course, the stem cells in bone marrow and cord blood that do the work when it comes to actually bringing about the repair, restoration, or healing of an organ or tissue. Logically, it follows that pure stem cells isolated from marrow or cord blood could be employed to bring about more sure or swifter healing responses in ailing people. Bone-marrow stem cells bear HLA antigens that require cross-matching in order to minimize the possibility of an adverse reaction or rejection. Umbilical-cord stem cells, on the other hand, appear to present less of a risk of rejection or adverse reaction. Many studies have shown that even when mismatched cord blood is given to patients, the reaction is generally mild and easily managed. (And interestingly, this immune response to the mismatched blood actually helps patients with leukemia fight their disease.) On the other hand, stem cells extracted from cord blood appear to carry an extremely low risk of rejection or of causing an adverse reaction. In more than 150 patient treatments involving human umbilical-cord stem cells tracked over an almost three year period by Steenblock Research Institute, no such
reactions were ever noted. (Growth factors in the vials containing the stem cells did cause some patients problems such as mild muscle tremors, but this side effect vanished once the lab responsible began washing out all the growth factors during the final phase of cell culture processing).

At the present time, the use of cord blood is permitted in the United States for only certain conditions and diseases such as leukemia and anemia (hematopoietic conditions). This reflects a belief among most scientists and physicians that umbilical-cord stem cells are limited to becoming red blood cells and certain immune cells. This commonly held notion is being challenged by a growing body of evidence that cord blood and cord-blood stem cells can help improve many neurologic, eye, and circulatory diseases and disorders, as well, but this proof is tentative and not yet compelling enough to convince the Food and Drug Administration (FDA) to approve or otherwise allow the use of cord blood or cord-blood-derived stem cell for these non-hematopoietic conditions and diseases. Therefore, for the time being, people seeking human umbilical-cord blood stem-cell treatment for neurologic, eye, or circulatory ailments must thus travel abroad to receive this treatment. It is a decisive move that for many is proving well worth the time and expense, as you will soon learn.
Stem cells—unspecialized cells that give rise to specialized cells—appear to be one of the body’s ablest tools for self-repair. When a disease or injury strikes, these cells respond to specific chemical signals and set about to facilitate healing by differentiating into the specialized cells required for the body’s repair—that is, provided they exist in sufficient numbers and receive the correct signals when disease or injury occurs. When they do not, the end result is an inadequate or compromised healing response. With regard to stem-cell therapy, there are a couple of ways to remedy this: (1) specific tissues can be grown from a patient’s or donor’s stem cells outside the body and then transplanted into the damaged or injured site; and (2) stem cells from a patient or a donor can be introduced into the body and their activity encouraged by removing impediments to new cell creation and proliferation, such as high levels of heavy metals, eating foods that support cell growth and multiplication, and taking select natural or pharmaceutical compounds that support and sustain these processes. In this way, stem cells can help restore damaged or diseased organs and tissue. Either way, the donor’s stem cells may also help the body to heal simply by getting it to create certain growth factors and other body chemicals that promote repair. These remedies are the essence of true regenerative medicine.
REGENERATION

The realization that certain cells in many, if not most, animals can generate and regenerate tissues and organs is an old one: Aristotle (384–322 B.C.), in his *Generations of Animals* and *History of Animals* observed that salamanders regrow amputated body parts. Around 77 A.D., Roman author and natural philosopher, Pliny the Elder, also wrote about a lizard's ability to regrow its tail. This phenomenon was later mentioned by Dominican friar and famed theologian Albertus Magnus during the thirteenth century. And, in the centuries that followed, many observations were made by various scholars, scientists, and writers concerning the regeneration of limbs by salamanders, of the liver in many animals including humans, of amputated claws of crayfish, and of deer antlers. However, Abraham Trembley (1710–1784) is generally held out by historians of science as having initiated the modern era of research on regeneration. Trembley performed experiments from 1740–1744 involving regeneration in the hydra, a Y-shaped freshwater animal. Some of these experiments included cutting the hydra in half and observing the growth of two complete hydras from the two sections. Trembley found that this regrowth effect also held true when he cut a hydra into four or eight or even more sections. He also painstakingly grafted parts of one hydra onto another and ultimately created a nine-headed hydra, not unlike the Greek mythical creature for which this little animal is named. The “how did it do it?” behind the hydra’s ability to regenerate is, of course, stem cells—however, this discovery would not be elucidated until the 1950s with the seminal work of embryologist Leroy Stevens.

Dr. Stevens linked tumors in mice (called teratomas) to embryonic cells that lack cell division “shut off” commands that occur naturally in the matrix that houses them in the embryo. Other researchers such as Dr. Gordon Barry Pierce found that once such cells were placed in their native environment (extracellular matrix, or ECM), they converted back to normal cells and then went on to become various tissues. Thanks to Dr. Stevens’s prolonged, intensive work with teratomas, it was clearly established that they sprang from cells that all others in a developing body stem from.
AN INSIDE LOOK AT STEM CELLS

At conception, a zygote (a single cell) is created from the fertilization of an egg, or ovum, by a sperm. This remarkable cell is totipotent, meaning that it is capable of generating every other cell of the human body to make a complete organism. The zygote (the fertilized egg) divides from one cell into two (about twenty hours after insemination), two into four (about forty-eight hours after insemination), and four into eight (about seventy-two hours after insemination). A sixteen- to thirty-two-cell embryo (about ninety-six hours after insemination) is called a morula. This is followed by the blastocyst stage (about one hundred fifteen hours after insemination). Then, cellular reorganization occurs during the gastrulation stage, resulting in two or three tissue (germ) layers as follows: the ectoderm (skin and nervous system), the endoderm (the lining of the gut and internal organs), and the mesoderm (muscles, bones, and heart). All of the cells have identical DNA. However, at this point in development, different genes in different cells begin switching on, leading to the development of the various organs of the body.

Stems cells of the outer ectoderm layer become specialized into brain and spinal-cord nerve cells with their supporting cells called “glia.” (The glia help nourish and protect the neurons, or nerve cells, by forming a layer of insulation around them, much like the insulation around electrical wires. The glia form the “white matter” of the brain and the blood-brain barrier.) Stem cells that come from the mesoderm manufacture red blood cells, white blood cells, and platelets, as well as bone, cartilage, fat, muscle, and skin. Stem cells of the endoderm develop into the cells of the digestive system and lungs.

In the early stage embryo, stems cells are pluripotent, which means they have the potential to give rise to every cell and tissue in the body, except the placenta. With the passage of time, stem cells in the various tissues and organs of the body become what scientists refer to as “terminally differentiated,” which means they are committed to a specific function. They are thus considered more limited in terms of the kinds of cells they can become and are known technically as “multipotent” stem cells.
Until recently, most scientists believed that differentiated cells could not deviate from their “cellular destiny.” For example, it was believed that one could not get an umbilical-cord stem cell to function like a neuron or nerve cell. However, recent laboratory research has cast serious doubts on this contention. In fact, it has been demonstrated that cord blood stem cells can be transformed into cells that behave like neurons. This is of great interest and utility to scientific researchers and the medical community alike.

**SOURCES OF THERAPEUTIC STEM CELLS**

Three are three basic sources of stem cells for therapeutic purposes: embryonic stem cells, adult stem cells (also called “somatic stem cells”), and umbilical-cord-blood-derived stems cells. Let’s take a look at each of these.

**Embryonic Stem Cells Derived from Aborted Fetuses or Fertilized Eggs**

In 1998, it was announced that two teams of scientists working independent of one another had succeeded in isolating embryonic stem cells: One was headed up by Dr. James A. Thomson, an embryologist at the University of Wisconsin, and the other by Dr. John D. Gearhart of the Johns Hopkins University School of Medicine in Baltimore. Dr. Thomson’s group went on to develop the world’s first human embryonic stem-cell lines. (When a given cell or set of cells is cultured to produce many new generations this chain of related cells is referred to as a “line.”) Since that time, much data has been amassed in international clinical studies on these remarkable cells. They have been documented as effective in the treatment of a whole host of medically challenging conditions in animal models, including stroke, diabetes, and certain heart and circulatory ailments. This is due to their capacity to regenerate the blood system, as well as every single organ, tissue, and cellular system.

Although stem cells derived from embryos have shown great prom-
ise in terms of their ability to bring about healing or restoration, their use poses numerous technical and scientific challenges, as well as ethical and political ones. (See Appendix A on page 139.)

**Adult Stem Cells Derived from Adult Tissue**

Adult stem cells, or somatic stem cells, are isolated from the tissues of an adult—for example, from the bone marrow or blood. There are a very small number of stem cells in each tissue, however, so once the adult stem cells are extracted, they need to be grown (cultured) in the laboratory to increase their numbers. The use of adult-derived stem cells is less controversial than the use of embryonic stem cells by far, but it is complicated by the fact that these cells may not afford as much clinical utility as embryonic cells, because they appear to be more restricted in terms of the cell types they can become. And while many adult stem cells can be turned into various cell types in the lab or coaxed to at least mimic other cell types without being exactly like them in all respects, it appears embryonic stem cells have a greater potential to become any cell in the body.

**Umbilical-Cord Blood-Derived Stem Cells**

Umbilical-cord blood-derived stem cells are harvested from otherwise discarded umbilical cords from natural full-term births. These cells are classified as “adult stem cells”; however, because these stem cells are only nine months old when the cord blood is harvested, they appear to have greater plasticity (the ability to generate differentiated cell types) and thus greater restorative and regenerative potential than stem cells derived from adult tissues.

The debate over using embryonic stem cells and the questionable effectiveness of adult stem cells have led many scientists and clinicians to concentrate their energies on cord-derived stem cells. In both animal and human use, human umbilical-cord stem cells (hUCSCs) have demonstrated great efficacy in promoting the healing of many conditions.
HOW THERAPEUTIC STEM CELLS AUGMENT THE HEALING PROCESS

Many scientists contend that when stem cells are injected or infused into a person, they tend to travel to those parts of the body that have suffered from some type of injury. At these sites of injury, the blood vessels typically have been damaged, narrowed, and constricted. These constrictions prevent the oxygen-carrying red blood cells from passing through to the tissues, which produces areas of reduced oxygen—a state known as “hypoxia.” Since stem cells are relatively large, they become lodged in these narrowed and constricted blood vessels (where the low levels of oxygen are just what stem cells tend to thrive in; see “Oxygen and Early Human Development” below). In addition, the endothelial cells that form the inner lining of the damaged blood vessels express certain biochemical signals including cytokines and growth factors, which have been shown in laboratory studies to attract stem cells to the site of damage. Theoretically, once the stem cells arrive at the site of damage, they go about differentiating into the specialized cells required for tissue repair.

Many researchers believe that as the stem cells divide into more specialized cells, they are able to transform into new blood vessels, neurons (nerve cells), muscle tissue, eye tissue, pancreatic tissue, kidney tissue, liver tissue, bone marrow, lung tissue, and so on, depending upon where in the body they wind up and also on the local tissue envi-

Oxygen and Early Human Development

In the early stages of human development, before the first stem cells have become specialized, they develop in a low-oxygen environment. As the embryo grows and the stem cells become specialized, they begin to require more and more oxygen. The more specialized the cell, the greater the oxygen required.
ronment, most likely due to the wealth of growth factors and other body chemicals that influence or govern many aspects of cellular activity contained in the tissues.

**CONCLUSION**

Ancient peoples observed instances of regeneration in animals, which inspired many ancient myths and esoteric medical practices but also formed the basis of modern research into this field. And, of course, they saw instances of their own bodies’ ability to renew and regenerate certain tissues such as skin and bone. Today, we know that at least some of this repair and regeneration is due to the activity of stem cells. Indeed, it appears that these versatile cells are one of the body’s most important built-in repair mechanisms. When disease strikes or we sustain an injury or cut, biochemical signals from the diseased, injured, or otherwise traumatized tissue sets the stage for marshalling stem cells to the “hot spot” where they apparently begin churning out compounds that help the body heal and, in some instances, actually are transformed into cells to replace those that are distressed or diseased.

Unfortunately, people’s own stem cell supply may not be sufficient to meet the demand posed by a major illness or injury, or else may not respond to signals emanating from the damaged organ or tissue. The aging process may also compromise stem-cell response and subsequent activity, and so may conditions such as heavy metal toxicity that might tend to thwart signal responses or interfere with their ability to migrate, engraft, and proliferate. In these instances, there are medically effective interventions such as heavy metal detoxification and nutritional support that can help make the tissue environment less inhospitable to stem cells, after which stem cells can be introduced into a patient’s body to help augment their own native stem-cell defenses. Human umbilical-cord stem cells are prime candidates for this purpose because they have a solid track record in terms of safety and at least preliminary evidence of being effective in helping the body deal with many health challenges.
The recognition that there is a connection between blood and healing, and blood and life, goes far back into antiquity. Myths were spun around this, such as the Babylonian tales of blood-lusting vampire-like spirits called Lilitu who prowled by night seeking to find, kill, and drain the blood of newborn babies and pregnant women. This particular myth is compelling because it reveals an early awareness of the life-giving power inherent in blood, especially that of newborns and expectant women. Today, we are fully aware of the tremendous value of blood transfusions in preserving life. We have also discovered that cord blood contains stem cells that can pull off many remarkable medical feats, such as helping to cure leukemia and remedy certain anemias. But how is cord blood collected and given to people with conditions that respond to it? And how do scientists go about removing the stem cells from the blood, expanding their numbers, harvesting, and preserving them? Let’s take a look.

THE COLLECTION OF UMBILICAL-CORD BLOOD
The blood from a single umbilical cord amounts to about a thimble or two in volume that contains between 100,000 and 300,000 stem cells. If prearranged with the hospital, the blood is collected from the detached cord within five to fifteen minutes following the birth of a
full-term baby. The cord blood is then transported to a cord blood bank where it is tested for communicable diseases such as HIV and hepatitis, processed further, frozen in liquid nitrogen, and stored in a cryogenic vault until needed (see “Umbilical-Cord Stem-Cell Blood Banks” below). The most recent studies suggest that frozen stem cells remain viable for up to eighteen years, if not longer.

THE EXTRACTION OF STEM CELLS FROM UMBILICAL-CORD BLOOD

Stem cells have distinctive biological surface markers (such as CD34 and CD133) that make it possible to extract them from umbilical-cord

Umbilical-Cord Stem-Cell Blood Banks

Once regularly discarded as worthless afterbirth tissue, more and more new parents are opting to send the cord blood or the entire cord from their newborn’s birth to a cord blood bank for testing and storage. The reason for this new trend is the increasing evidence that stem-cell-rich cord blood or cord stored today may come to the rescue of a child or family member later in life. This is especially true for families with a history of genetic diseases, such as diabetes or leukemia.

Many experts feel that this “biological insurance” is unwarranted except in cases where families are plagued by certain genetic diseases. However, despite this contrary opinion, in 2005, more than 50,000 new parents signed to have their newborn’s cord blood tested and stored at one of the dozen or so private cord blood banks in the United States. In other cases, parents choose to donate the newborn’s cord blood to one of the nearly two-dozen not-for-profit cord blood banks in the United States, such as those associated with the American Red Cross or the National Bone Marrow Donor Program. These banks make cord blood available to anyone in need. (See the Resources section.)
blood. These extracted cells are able to (1) divide into two equal cells (symmetrically), thus recreating themselves while preserving their multipotent capacity (self-renewal), and (2) through asymmetrical division, give rise to a variety of functional cells such as blood cells, immune cells, liver cells, and so on that serve a specific function.

New methods of separating umbilical-cord stem cells from blood components that cause rejection (a condition known as “graft versus host disease”; GVHD) have made it relatively easy to produce pure stem cells for use in animals and humans. (See “The Separation of Stem Cells from Cord Blood and Their Processing” on page 17.) The same cannot be said of embryonic and bone-marrow stem cells, or, to

What Do the “CD” and “+” and “−” Mean?

The designation CD stands for “cluster of differentiation,” a term that was coined to define cell-surface molecules that were revealed by the action of monoclonal antibodies—that is, antibodies produced in the laboratory that bind to a specific protein or foreign substance. For example, an antibody is created in the lab to a cell-surface molecule such as CD34. When the antibody finds this CD molecule, it latches on. The cell is positive for this CD factor—thus CD34+. When human umbilical-cord stem cells are selected out that are positive for a CD like 34, then we say the resulting collection of cells are CD34+. If cells are deleted that have a particular CD factor, thus leaving behind only cells that lack it—let’s say 44—then they are said to be CD44−. Why the numbers, you ask? Clusters of differentiation were assigned numbers such as CD1, CD2, and so on, relating to the order in which they were discovered. In general, each CD is associated with one or more functions, which were discovered through the effects of the antibodies on cell or tissue function.

With input from Steven Goldfinch, Vice President of CureSource, a cord-blood processing and storage firm (www.curesource.net)
a lesser degree, cord blood itself. These do contain elements that can provoke the recipient's body to reject them.

Traditionally, immunosuppressive drugs and radiation have been used prior to bone marrow and cord-blood transplants to lessen the chance of rejection. These pre-treatments are toxic to stem cells and new neurons. Both chemotherapy and radiation are associated with nerve damage and symptoms of memory loss, depression, and declines in IQ. By virtue of the fact that “purified” umbilical-cord blood-derived stem cells (separated from cord-blood components) are safe to use without immunosuppressive therapies, it follows that therapeutic use of these stem cells should be more effective. In short, instead of having large numbers of neurons killed off prior to giving stem cells as is the case with traditional stem cell transplant techniques, patients simply get an infusion or implant of hUCSCs and hopefully build on what they had (neurologically). And this is exactly what's being reported by physicians and researchers involved in treating patients and conducting clinical pilot studies outside the United States.

HOW UMBILICAL-CORD STEM CELLS ARE ADMINISTERED

Umbilical-cord stem cells are generally given by IV, either after a patient’s bone marrow has been destroyed (in the case of leukemia and sometimes advanced multiple sclerosis) using chemotherapy or radiation and post-transplant use of immunosuppressive drugs such as cyclosporine to reduce the risk of rejection—or it is given by IV alone.

Traditional Route—Bone Marrow Ablation and Use of Immunosuppressive Drugs

The standard, or traditional, method of performing stem-cell therapy for the purpose of treating blood-related diseases such as leukemia involves destroying the bone marrow of the recipient by use of chemotherapy and radiation, then giving stem-cell-rich marrow or umbilical-cord blood by IV. This approach is risky and requires extreme
care to avoid complications, including postoperative infections. (Remember, once the bone marrow is eradicated, the patient’s immune system is no longer functional.)

Here in the United States, the National Marrow Donor Program (NMDP) Registry (www.marrow.org/NMDP/registry.html) contains detailed information on more than 5 million volunteer bone-marrow donors and more than 28,000 donated cord-blood units (as of July 2003). The NMDP Registry is the largest collection of such donors in

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The Separation of Stem Cells from Cord Blood and Their Processing

One of the most effective ways to remove stem cells from cord blood is with a technique called “immunomagnetic separation.” This approach involves attaching ultra-small bits, or nanoparticles, of iron to antibodies that seek out and bind to stem cells that have a particular molecular marker, such as CD34 or CD133. These iron-tagged stem cells and the blood in which they are afloat are then subjected to a magnetic field. The iron-tagged CD34 stem cells adhere to the magnet, while the blood cells and serum and such do not and therefore can be flushed away.

After the blood cells have been drained away, the magnetic field is removed, thereby allowing the stem cells to fall into a waiting collecting dish. So simple, yet so elegant and effective! The stem cells are then cultured in a special solution containing nutrients and growth factors. After reaching a point whereby further expansion cannot be achieved without the cells differentiating—that is, turning into various types of cells—they are harvested, the growth factors are washed out completely, and they are then placed in vials along with a very small amount of a cryopreservative and frozen in liquid nitrogen. (The cryopreservative used is dimethyl sulfoxide [DMSO] and dextran, compounds that prevent the formation of membrane-rupturing ice crystals during freezing.)
the world, and boasts a network of donor centers and transplant centers in fourteen countries with cooperative agreements in existence with fifteen international registries. The NMDP helps coordinate over 170 stem-cell transplants each month and has racked up more than 16,000 total transplants since 1986, when the organization was founded.

**Low Adverse-Effects Route: Injection and IV Drip without Radiation or Chemical Ablation of the Bone Marrow and Use of Immunosuppressive Drugs**

Umbilical-cord stem cells can be given intravenously (IV drip), by subcutaneous injection, by implant, or by a combination of these approaches. An IV drip takes about thirty minutes, while an injection is completed in a few seconds. Implants including those made into the brain require that patients be hospitalized for anywhere from one day to several weeks. Stem cells introduced by IV drip or subcutaneous injection circulate in the bloodstream where they are exposed to chemical signals such as stromal-derived growth factor-alpha from injured, inflamed, hypoxic (low-oxygen), or diseased tissues. These signals act like homing beacons, calling the stem cells to the area. Implanted stem cells generally are placed into or near the target tissue and thus have little or no migrating to do in order to reach the target organ or tissue.

**UMBILICAL-CORD STEM-CELL AUGMENTATION**

In order to be clinically effective, stem cells often need to be introduced to the recipient’s body in large numbers. Many physicians who perform umbilical-cord stem-cell therapy advocate the use of anywhere from 1 million to 10 million stem cells per treatment. Since a single umbilical cord contains 80 to 220 milliliters of blood and only about 100,000 to 300,000 stem cells, it is necessary to separate the stem cells and then expand their numbers. This is done quite readily in the laboratory by the use of growth factors (substances produced by the body that control the growth, division, and maturation of cells and tissues) and compounds such as retinoic acid (a derivative of vitamin A), mak-
ing it possible to multiply the 300,000 stem cells in one umbilical cord to more than 10 million cells. This, in turn, can be administered to a patient all at once or in increments, depending on the condition or injury being treated.

Interestingly, a subset of these stem cells bear a unique biological signature, CD133, which has been shown to give rise to white matter, or glial cells, in the laboratory. These stem cells can be separated from other types of stem cells and then used to help the body heal or restore damage or disease in the brain and/or spinal cord. Other subsets that are being utilized clinically abroad include CD44−, which can be coaxed into becoming neurons, including astrocytes and oligodentrocytes, and CD45−, which are deemed “intrinsically pluripotent,” meaning they can become many tissue types. (However, researchers do not know yet whether these CD45− hUCSCs will retain this ability once in the human body. Patients have been treated in Mexico with these “intrinsically pluripotent” hUCSCs and their progress is being tracked and analyzed by experts at Steenblock Research Institute.)

Korean scientists recently reported finding that CD34−/45+ could be readily converted into a wide variety of cell types. All these cell subsets are being utilized by the physicians in Mexico mentioned elsewhere in this book to treat neurological diseases and a host of other conditions.

WHAT HAPPENS AFTER A STEM-CELL TREATMENT?

In studies of animals, it has been observed that when stem cells fitted with radioactive tags are introduced into the body and are tracked using radiation-detection devices, the stem cells tend to fan out and show up in various organs, including the brain. This may also be true in humans, as patient responses following stem-cell therapy are consistent with what one would expect to see of stem-cell-facilitated repair or regeneration. Indeed, many people have reported beneficial changes in their conditions during the first few weeks following treatment.

In some cases, improvements after stem-cell therapy begin to
The Safety Record of Umbilical-Cord Blood

Umbilical-cord blood was approved by the FDA for use in certain diseases in the late 1980s. Umbilical-cord blood transfusions, which include a very primitive (and thus biologically versatile) stem cell designated CD34+, have been used in more than 1,000 children and adults since 1986 in the United States. Many of these treatments were administered to cancer patients who subsequently showed significant improvement. Remember, the stem cells in the cord blood are the “active” components used to repair bone marrow and the immune system of patients treated with chemotherapy and radiation. In addition, stem-cell-rich umbilical-cord blood has a seventeen-year track record of being used to treat cancer without causing much in the way of secondary diseases or cancers. It also produces significantly fewer instances of graft versus host disease (GVHD) than bone marrow stem cells and is also easier to obtain.

Cord Blood Stem Cells Deemed Safe

Extract from “Korean Scientists Succeed in Stem Cell Therapy” by Kim Tae-gyu, Staff Reporter, The Korea Times, November 26, 2004

“Embryonic stem cells are omni-potent in that they can divide into any thing even including a tumor cell. But cord blood stem cells are developed enough not to cause such troubles while retaining as powerful a differentiation capacity at the same time,” he [Professor Kang Kyung-Sun] claimed.

Another upside of cord blood stem cells is that they can adapt to the injected bodies without triggering a big negative inner reaction, which are common in other transplantations, according to Han, Ph.D., of the SCB [Dr. Han Hoon of the Seoul Cord Blood Bank].

“We don’t need a strict match between cord blood stem cell type and the immune system of a patient because the latter accepts the former pretty well thanks to its immaturity,” Han said.

Source: http://times.hankooki.com/lpage/200411/kt2004112617575710440.htm
appear within a day of treatment; however, by and large, it takes two to three weeks to see improvements, with most patients seeing results from the end of the first month through the third month. This corresponds to the period of time it generally takes for the stem cells to bring about healthy changes in the recipient's body through the action of various compounds and growth factors and/or to engraft, or take hold, and bring about beneficial changes in tissues. While some people report experiencing benefits from three to six months or more following stem-cell therapy, most of the improvements appear to plateau and taper off after three to four months.

For those with conditions, such as cerebral palsy, which do not progress by nature, the number of improvements peak at three to four months and fewer gains are seen thereafter. These improvements have not been observed to be eroded or lost, though, because cerebral palsy is not progressive. For people with progressive diseases or conditions like multiple sclerosis or amyotrophic lateral sclerosis (ALS; also called Lou Gehrig's disease), the number and degree of improvements peak at three to four months and few are seen thereafter; however, some (and sometimes all) of these gains are lost or otherwise compromised as the disease progresses.

**Stem-Cell Successes**

The authors and others at the Steenblock Research Institute in San Clemente, California, have been following the cases of patients treated with hUCSCs, as well as tabulating results from pilot studies performed abroad involving stem-cell therapy for specific conditions such as cerebral palsy in children and stroke in adults. The following are but a few of the many responses documented as of the date of publication. (More detailed case histories are included in Chapter 4.)

- A sixty-five-year-old man with progressive multiple sclerosis was treated with umbilical-cord stem cells in July 2003. Prior to this treatment, he could not swallow water normally. Within a week of receiving hUCSCs, he was able to do so without a problem. He sub-
sequently made noticeable gains in his ability to get around and could communicate more clearly. The condition of his skin also improved. Moreover, as verified by his urologist, a nodule detected on his prostate prior to stem-cell therapy disappeared in the first three months following his treatment. (A more detailed account of this person’s experiences can be found on pages 41–44.)

• The Ramirez human umbilical-cord stem-cell therapy program in Mexico has treated more than forty children with cerebral palsy since

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**Gene-Enhanced hUCSCs for Cancer**

In 2005, a line of human umbilical-cord stem cells, into which laboratory scientists inserted two genes, was specifically created for treating cancer. One gene turns the stem cells into tiny factories that churn out interleukin-2, and the other gene, gamma-interferon. (Both of these substances rally the immune system against cancer.) In September 2005, doctors in Mexico began treating terminally ill, end-stage cancer patients with these cells.

Approximately fifteen patients with a variety of cancer types that have spread all through their bodies—for example, breast, melanoma, lung, prostate, and others—have been treated as this book goes to press. Virtually all these people have reported very significant reductions in pain and a greatly increased quality of life. Preliminary tests including body scans and biopsies indicate that this approach is bringing about impressive tumor shrinkage and solid tumor die-off. At least some of those treated appear to be headed toward complete remission.

The original idea for this novel approach was made by coauthor Dr. David Steenblock and was subsequently turned into reality by a group of medical school scientists who provide hUCSCs to researchers and research-oriented physicians such as Fernando Ramirez, M.D., and Frank Morales, M.D. (see the Resources section).
March 2003. Eighty-five percent of these children have experienced significant improvements in motor skills and cognitive functions. In one case, a four-year-old boy was cortically blind (a lack of visual functioning despite structurally intact eyes), could not speak well, and could not get around well prior to therapy with hUCSCs. Within seven months of therapy, however, he was able to track objects with his eyes, was beginning to speak, and could move around more ably.

• Jordan Logan, a four-year-old girl, with a terminal genetically based neurological disease called “metachromatic leukodystrophy” (MLD) was treated with 1.5 million hUCSCs. MLD is caused partly by a genetic defect in which a gene critical to the production of an enzyme called “arylsulfatase A” (ARS-A) is missing or not functioning properly. This enzyme makes it possible for a person’s body to deal with toxic molecules that we all generate called “sulfatides.” Children and adults who do not produce ARS-A or very little experience declines in their neurological function that culminate in disability and death. In children with advanced cases of MLD, improvements in neurological function are never seen and death typically occurs by age five. Prior to the treatment, the girl was cortically blind, her body was limp, and she was on a host of medications. Within two months of her hUCSC injection, however, she could track objects with her eyes and lift her arms and legs high in the air. Eventually, two of the three medications she was on were discontinued.

In late August 2005, the Logan’s two-story home in Pass Christian, Mississippi, was flooded and severely damaged by the passage of Hurricane Katrina, a category 4 hurricane. Fortunately, Jordan and her mother, Charlotte, had evacuated to a relative’s house in Alabama well before the hurricane hit their community. While all this was going on scientists at a medical school lab had succeeded in inserting a human gene for the ARS-A enzyme into hUCSCs and by doing so had turned them into little factors that produce and excrete the ARS-A enzyme. This approach was first suggested by coauthor Dr. Payne to the medical school researchers who produce hUCSCs that are utilized by Drs. Fernando Ramirez and Frank Morales in
Mexico. These scientists then went on to create a ARS-A trans-vected cell line using the highest quality control testing standards followed by careful experimentation involving lab animals. This phase was pretty much complete by late September 2005.

On October 4, 2005, Jordan Logan and her mother were flown to Brownsville, Texas, in a private jet whose use had been donated by a kindhearted, generous businessman named Jim Tatum of Fairhope, Alabama. The following day the Logan’s and their pilot made their way to Dr. Frank Morales’s clinic in Matamoras, Mexico, where Jordan received 1.5 million of the ARS-A producing hUCSCs. (The cells and Dr. Morales’s clinical services were all donated as well.) In the weeks since that historic treatment, Jordan has displayed physical energy and neurological responses not seen since she was an infant. For one thing, she is now turning her head toward people who call out her name. According to Charlotte, this is actually something Jordan has not ever done. She is also now off all medications. And as this book goes to press, tests are to be done shortly that will verify whether the ARS-A enzyme is now showing up in Jordan’s blood. Prior tests have shown 0 percent of the enzyme.

Jordan’s story has appeared in numerous regional and national newspapers, and has also been the focus of TV coverage in Mississippi. Charlotte is now getting almost daily phone calls from parents of MLD-stricken children residing not only in the United States, but also in many foreign countries such as Canada, England, and Spain. If Jordan Logan continues to improve, virtually all of them plan on going to Mexico to have their ailing children treated with hUCSCs bearing the ARS-A gene.
In a Nutshell: Umbilical-Cord Blood-Derived Stem Cells

• Since the stem cells are isolated from the umbilical-cord blood, there are no blood cells present, thereby virtually eliminating the need for blood typing or HLA matching. (As you may recall, HLAs are specialized proteins that exist on the surface of cells, marking the cells and tissues they make up as unique to the individual.)

• Cord blood-derived stem cells are safer than whole cord blood because there are virtually no instances of graft versus host disease (GVHD) or rejection issues.

• There are stem-cell subsets, such as CD45–, that are regarded by researchers as “intrinsically pluripotent,” which means they have the potential to become a wide range of cell or tissue types. Whether these cells retain this degree of plasticity in the human body is unknown.

• Cord blood-derived stem cells sport a good track record: Cord blood was used therapeutically for the first time in 1988. Since then, a host of laboratory and human-use studies have been carried out that point to the fact that cord-blood therapy is of merit in treating various blood diseases, autoimmune conditions, viral conditions, and neurodegenerative diseases.

• In the last decade or so, pure cord-blood stem cells have been utilized by physicians to treat a multitude of intractable diseases such as progressive multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), macular degeneration, retinitis pigmentosa, stroke, diabetes, and various forms of heart disease. This body of patient responses indicates that umbilical-cord stem-cell therapy does produce clinically significant improvements in many instances.

• While certainly no cure-all, umbilical-cord stem-cell therapy appears to be amassing a respectable track record in terms of both safety and clinical utility.