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Allo-HSCT: Placental Stem Cells and Cord Blood Key to Success (June 2017)

-Engraftment more rapid, and GVHD incidence lower

*ASCO Reading Room 05.31.2017
by Alec O'Neil, Contributing Writer*

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an essential component of modern care for children and young adults with hematologic malignancies who are at high risk for relapse following chemotherapy.

Donor sources can include bone marrow, peripheral blood stem cells, human placental-derived stem cells (PDSCs), and umbilical cord blood from related and unrelated donors. Cord blood in particular offers special advantages, including expansion of the pool of potential donors, rapid availability, decreased risk of viral and decreased transmission from donor to recipient, noted Mitchell Cairo, MD, chief of Pediatric Hematology, Oncology and Stem Cell Transplantation at Westchester Medical Center in Hawthorne, NY, and colleagues.

In addition, cord blood is enriched in hematopoietic progenitors compared with peripheral blood stem cells or marrow. Cord blood transfusions are associated with decreased severity of acute graft-versus-host disease (GVHD) and a reduced incidence of chronic GVHD.

Drawbacks to cord blood, however, include limited cell doses, prolonged immune reconstitution time, delays in hematopoietic recovery, and a higher incidence of graft failure compared with other sources.

At the 2017 meeting of the Pediatric Blood and Marrow Transplant Consortium (PBMT) and the American Society of Pediatric Hematology/Oncology in Montreal, Cairo and colleagues presented early data from an ongoing study aimed at optimizing immune reconstitution following allo-HSCT with a combination of umbilical cord blood and PDSCs in children with malignant conditions, including B-cell and T-cell leukemias and lymphoma, as well as non-malignant conditions.

To view the full article, please click on this link:

https://www.medpagetoday.com/reading-room/asco/hematologic-malignancies/65686?xid=NL_ASCORR_2017-06-08&eun=g8404572d39r&pos=1111

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Hepatitis C Has Been Eradicated in 20 Patients Who Received Infected Kidney Transplants (June 2017)

The gamble paid off.

Peter Dockrill 1 May 2017

For the patients, it was a gamble: if they took part in a new study, they'd be off the waiting list, and would receive a new kidney from an organ donor – but the organ they'd be getting would be one infected with the hepatitis C virus.

Those were the terms of two bold clinical studies conducted last year in the US, but for the patients who took part, the gamble paid off. Doctors this week [announced](#) that all 20 patients who received donated organs – and subsequently contracted hepatitis C – were able to beat the infection thanks to an antiviral treatment after the transplant. The approach carries an amount of risk, as there's a chance the patients receiving the organs might never be cured of hepatitis C.

But the early success of the two trials run separately by the University of Pennsylvania and Johns Hopkins University could provide new hope for the hundreds of thousands of patients on organ donation lists around the world.

In the US alone, more than 100,000 people are waiting to receive kidney transplants, but despite the level of need, organ donations from people with hepatitis C haven't been possible - with viable kidneys even being thrown out due to the infection.

To view the full article, please click on this link:

<http://www.sciencealert.com/scientists-have-eradicated-hepatitis-c-in-patients-who-received-infected-kidney-transplants>

The preliminary results of the University of Pennsylvania trial are published in The New England Journal of Medicine.

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After 2 lung transplants, 1 brain tumor and 15 years of hardship, Seattle U student earns a degree (June 2017)

Originally published June 11, 2017 at 7:00 am Updated June 11, 2017 at 5:58 pm

Steven Jenkins spent 15 years trying to earn his bachelor's degree at Seattle University, dogged by health problems so severe they nearly killed him.

Born with cystic fibrosis, he survived a double-lung transplant. Then he developed a brain tumor. Strong chemo and radiation put the tumor in remission, but life-threatening cases of swine flu and pneumonia caused his body to reject his lungs, leading to a second transplant.

Yet Jenkins also played for Seattle U's soccer team, where he was such an inspiration that coach Peter Fewing credits him with helping the team win the national championship in 2004.

On Sunday, Jenkins will don a cap and gown and accept a bachelor's degree in criminal justice. It will be an emotional moment for many at the Jesuit school.

"I don't know anybody in my 25 years at this school who's gone through as much as he's gone through to get this degree," said J.B. Helfgott, professor and chair of criminal justice. "I have never seen anything like it in my life."

Seattle U President Stephen Sundborg, who gave Jenkins a full-ride soccer scholarship despite his diseased lungs, called it an amazing story.

"The number of times through the years he almost didn't make it, the way the other players responded to him — the family is heroic, and so is Stevie, for just persevering through it all," Sundborg said.

To view the full article, please click on this link:

<http://www.seattletimes.com/seattle-news/education/after-two-lung-transplants-one-brain-tumor-and-15-years-seattle-u-student-earns-his-degree/>

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Advanced heart failure patients have superior outcomes with HeartMate 3 device (May 2017)

Apr 07, 2017 | Tim Casey

At six months, patients with advanced heart failure who were implanted with the HeartMate 3 left ventricular assist system were less likely to have hemocompatibility-related clinical adverse events (HRAEs) compared with those who received the HeartMate II device, according to a randomized trial.

The researchers defined HRAEs as clinical adverse events attributable to left ventricular assist system-related bleeding or thrombosis abnormalities.

Lead researcher Nir Uriel, MD, of the University of Chicago, and colleagues published their results online in *Circulation* on April 6. The findings were also presented at the International Society for Heart and Lung Transplantation annual meeting in San Diego.

For this secondary analysis, the researchers evaluated the MOMENTUM 3 trial, a prospective, multicenter, randomized, non-blinded, pivotal study comparing the HeartMate 3 and HeartMate II in patients with advanced-stage heart failure

Abbott, which manufactures the HeartMate 3 and HeartMate II, funded the study. The FDA has approved the HeartMate II, but it has not approved the HeartMate 3, which is a continuous-flow centrifugal pump.

The researchers considered the following as HRAEs: nonsurgical bleeding more than 30 days after implant; stroke or other neurological events at anytime; and suspected or confirmed pump thrombosis or arterial thromboembolism with or without organ involvement at any time.

At six months, 69 percent of patients in the HeartMate 3 group and 55 percent of patients in the HeartMate II group had survived and were free of any HRAE. For patients who were 65 years old or younger, the rates were 76 percent and 58 percent, respectively. For patients who were older than 65, the rates were 61 percent and 47 percent, respectively.

Patients in the HeartMate 3 group mostly had bleeding events, while bleeding and thromboembolic events were equally distributed in the HeartMate II group. The HeartMate 3 patients also had a 6.3 percent reduction in days spent in the hospital because of readmission.

To view the full article, please click on this link:

http://www.cardiovascularbusiness.com/topics/heart-failure/advanced-heart-failure-patients-have-superior-outcomes-heartmate-3-device?utm_source=CVHF&utm_medium=2d743d5f7b&utm_content=article&utm_campaign=newsletter_referral

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The Cutting Edge

Experimental Implant Returns Hand Movement to Quadriplegic (May 2017)

Spring 2017

UCLA doctors have implanted a spinal stimulator that is showing early promise in returning hand strength and movement to a California man, who broke his neck in a dirt-biking accident five years ago. Brian Gomez became one of the world's first patients to undergo surgery for the experimental device in June 2016 at Ronald Reagan UCLA Medical Center. UCLA scientists positioned the 32-electrode stimulator below the site of Gomez's spinal-cord injury, near the C-5 vertebra in the middle of his neck. That's the area most commonly associated with quadriplegia — the loss of function and feeling in all four limbs.

"The spinal cord contains alternate pathways that it can use to bypass the injury and get messages from the brain to the limbs," says Daniel Chia-Hsing Lu, MD, PhD, director of the UCLA Neuroplasticity and Repair Laboratory and the UCLA Neuromotor Recovery and Rehabilitation Center. "Electrical stimulation trains the spinal cord to find and use these pathways."

While other devices have shown promise in treating paralysis, these approaches involved animals or relied on robotic arms. This approach is unique because the device is implanted in the spine instead of the brain and is designed to boost patients' abilities to move their own hands. Dr. Lu likened the approach to a commute on a busy freeway. "If there is an accident on the freeway, traffic comes to a standstill, but there are any number of side streets you can use to detour the accident and get where you are going," he says. "It's the same with the spinal cord."

To view the full article, please click on this link:

http://magazine.uclahealth.org/body.cfm?id=6&action=detail&ref=1443&utm_source=U+Magazine+-+Resp+-+Spring+2017&utm_campaign=UMag_Spring_2017_Respn&utm_medium=email

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Novel Treatment Regimens Improve Survival Rate in Multiple Myeloma (May 2017)

April 2017

Multiple myeloma, a malignancy of antibody-secreting plasma cells, is characterized by cancer cell infiltration of bone marrow and widespread skeletal destruction, resulting in hypercalcemia, renal insufficiency, anemia, bone pain, and fractures. The disease constitutes 1.8% of all cancers and slightly more than 15% of hematologic malignancies in the United States. The annual incidence is about 3.3 per 100,000 population, and 30,330 new cases and 12,650 deaths were attributed to the condition in 2016. New cases have risen by about 0.8% per year, with death rates falling at about same rate from 2004 through 2013.

Advances in drug development and large randomized clinical trials, many with the participation of University of Minnesota, have significantly changed treatment options in the last decade. Findings from these trials have helped establish the current standard of care for patients with newly diagnosed multiple myeloma, a standard that includes induction therapy with multiagent chemotherapy regimens, consolidation therapy with autologous hematopoietic cell transplantation (autoHCT), and single-drug maintenance therapy.

University of Minnesota Health hematologist/oncologists who serve as medical researchers at Masonic Cancer Center, University of Minnesota have been active in the efforts to improve treatments and patient outcomes. They were key members of a national multicenter study that demonstrated the efficacy of the multiple myeloma maintenance therapy lenalidomide in delaying relapse and prolonging survival (Lenalidomide in Treating Patients with Multiple Myeloma Undergoing Autologous Stem Cell Transplant). Data from this randomized, phase III study, which assigned patients to receive maintenance therapy with either lenalidomide or placebo after autoHCT, changed treatment practice. Now, with 10 years of follow-up, a recent reanalysis comparing maintenance therapy outcomes to those of patients treated with placebo continues to confirm substantially improved survival rates for patients given lenalidomide.

To view the full article, please click on this link:

http://consult.mhealth.org/4-6-2017/novel-treatment-regimens-improve-survival-rate-in-multiple-myeloma?utm_source=m_health_consult_newsletter&utm_medium=email&utm_campaign=hematologic_malignancies_april_2017&utm_source=M+Health+Consult+Newsletter&utm_campaign=7b1a2bf492-EMAIL_CAMPAIGN_2017_04_10&utm_medium=email&utm_term=0_458d22411d-7b1a2bf492-331578581

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CAR T-Cell Therapy Drives Toward Market in 2017 (May 2017)

Fuerst, Mark L.

Oncology Times: 10 February 2017 – Volume 39 – Issue 3 – p 34

doi: 10.1097/01.COT.0000513044.18354.df

News

SAN DIEGO—The success of the first global pediatric trial of chimeric antigen receptor (CAR) T-cell therapy may lead to the availability of a commercial product as soon as next year.

At the American Society of Hematology annual meeting, researchers presented findings from the phase II ELIANA clinical trial evaluating the efficacy and safety of CTL019, an investigational CAR T-cell therapy in relapsed/refractory pediatric and young adult patients with B-cell acute lymphoblastic leukemia (ALL). They found that 82 percent of infused patients achieved complete remission (CR) or complete remission with incomplete blood count recovery (CRi) at 3 months post CTL019 infusion (Abstract 221).

For all patients with complete remission, no minimal residual disease was detected. In addition, the estimated relapse-free rate among responders was 60 percent 6 months after infusion with CTL019.

“These global multicenter trial data build on earlier encouraging research conducted at a single trial site, and advance the case for CTL019 as a potential treatment for children and young adults with relapsed or refractory B-cell ALL,” said lead author Stephan Grupp, MD, PhD, Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania and Director of the Cancer Immunotherapy Frontier Program at the Children's Hospital of Philadelphia.

The results set the stage for filing CTL019 with the FDA in early 2017 for pediatric and young adult patients with relapsed/refractory B-cell ALL.

To view the full article, please click on this link:

http://journals.lww.com/oncology-times/Fulltext/2017/02100/CAR_T_Cell_Therapy_Drives_Toward_Market_in_2017.12.aspx

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House Call: Types of Immunotherapy for Cancer (May 2017)

April 2017

B. Tutt

OncoLog, April 2017, Volume 62, Issue 4

You've probably seen news articles about breakthroughs in immunotherapy for cancer patients. But the word "immunotherapy" can be used to describe many different kinds of treatment. Some immunotherapy drugs help a specific part of the body's immune system—often white blood cells such as T cells, B cells, or natural killer (NK) cells—to attack a specific type of cancer cell; other treatments promote a more general immune response.

Below we describe some common types of immunotherapy. Please note that these are general descriptions only, and the side effects of these treatments are not discussed. If you have questions about a particular drug, please talk to your doctor.

Monoclonal antibodies

Antibodies, a natural part of the immune system, are proteins that bind to other proteins called antigens that are found on the surface of some cancer cells or pathogens (invading agents such as bacteria or viruses). Monoclonal antibodies are drugs created to work like natural antibodies.

Most monoclonal antibodies used in cancer treatment bind to specific antigens on cancer cells. This binding either neutralizes the cancer cells to prevent the cancer from spreading or signals the immune system to find and kill the cancer cells. For example, the monoclonal antibody rituximab binds to certain types of leukemia and lymphoma cells to help the body's NK cells destroy them.

Immune checkpoint inhibitors

A special type of monoclonal antibody is the new class of drugs called immune checkpoint inhibitors. These drugs block the action of immune checkpoint proteins, which are found on the surface of many T cells. The purpose of immune checkpoints is to stop T cells from attacking healthy cells in the body. But some types of cancer can activate these immune checkpoints to protect themselves from T cells.

To view the full article, please click on this link:

https://www.mdanderson.org/publications/oncolog/april-2017/house-call--types-of-immunotherapy-for-cancer.html?utm_source=Bronto+at+MD+Anderson&utm_medium=email&utm_term=House+Call:+Types+of+Immunotherapy+for+Cancer&utm_content=jthies@lifetracnetwork.com&utm_campaign=OncoLog:+April+2017

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Double hand transplant patient: 'I wrote a thank-you letter to my surgeon' (April 2017)

Tess de la Mare and agencies

Thursday 6 April 2017 14.16 EDT

The first person in the UK to undergo a double hand transplant has said writing a letter to thank his surgeon has been one of the highlights of his first nine months since the operation – that, and being able to applaud his favourite rugby league team.

Chris King, 57, described how he had got his life back since the surgery last July, when he became the second person to have a hand transplant at the UK's specialist centre for the operation at Leeds General Infirmary (LGI) and the first to have both hands replaced.

King, from Rossington near Doncaster, said he can now do a range of tasks, including writing, making tea and gardening, as he progresses faster than his surgeon anticipated. He said he was improving every week and that his next aims were to tie his shoelaces and button up his shirt (he has already cracked undoing them).

Looking at his hands, King said: "They are my boys, they really are. It's been going fantastically. I can make a fist, I can hold a pen, I can do more or less the same functions as I could with my original hands. There are still limitations, but I'm getting back to the full Chris again."

King has also discovered that he is now ambidextrous. "When I picked a pen up first time, it was with my right hand," he said. "The next time I picked it up, it was left. I might be able to write with both hands now." He said: "I think it will be the icing on the cake when I can do my laces, and I don't think that's far off."

To view the full article, please click on this link:

<https://www.theguardian.com/society/2017/apr/06/uks-first-double-hand-transplant-patient-delights-in-writing-letter-to-thank-surgeon>

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Stem Cell Transplants Lead to Cure for Some Type 1 Diabetes Patients (April 2017)

March 1, 2017 | by Katie Neith

A recent clinical trial monitored by City of Hope's Bart Roep, Ph.D., showed promising results for a possible cure of type 1 diabetes (T1D). Although the study involved risky stem cell transplant procedures, it identified new paths for personalized therapies of T1D.

The trial, which was conducted in Brazil, enrolled 21 T1D patients who had received autologous hematopoietic stem cell transplantation (AHSCT), which involves the use of a person's own stem cells.

Participants were monitored and assessed every six months. Most patients became insulin free for an average of 3.5 years after transplantation. C-peptide levels — which show how much insulin is being made by the pancreas — remained higher than initial values for at least four years post-AHSCT, indicating temporary immunological balance and preservation of insulin-secreting beta cells. Loss of beta cells is what causes T1D and the symptoms associated with the disease.

"This means we can cure type 1 diabetes, be it with a risky therapy — although one that is also very successful in cancer, and one for which City of Hope is a world-renowned expert, with more than 14,000 patients having received similar treatment for blood cancers," said Roep, the Chan Soon-Shiong Shapiro Distinguished Chair in Diabetes and professor and founding chair of the Department of Diabetes Immunology.

To view the full article, please click on this link:

https://www.cityofhope.org/stem-cell-transplants-a-cure-for-some-type-1-diabetes-patients?utm_source=Convio&utm_medium=email&utm_content=20170404&utm_campaign=eHop

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Kidney Waitlist Management: The Readiness Model of Predicting Transplants Under Kidney Allocation System (April 2017)

N. Elias, B. Kimball, L. Walsh, D. Wojciechowski, J. Markmann, E. Heher.

Transplant Center, Massachusetts General Hospital, Boston, MA

Meeting: 2017 American Transplant Congress

Abstract number: D289

Based on the Organ Procurement and Transplantation Network data, between 2001 and 2016 the national kidney wait-list has grown from 51,271 to 100,791 (97%). At the Massachusetts General Hospital (MGH) our kidney wait-list has grown by 257% over the same period. Also evident by 1 and 2 year transplant percentage figures, national waiting times have increased significantly with Region 1 (New England) showing an even greater increase. Over the same 15 year period, this resulted in a 97% rise in waiting list removals due to death or being too sick for transplant nationally, compared to 153% rise at MGH.

Pre-transplant associated charges are the sum of initial evaluation and waitlist maintenance charges. To minimize those, we developed a prediction model using methodology based on the newly implemented Kidney Allocation System (KAS), specifically its classifications and allocation points. We also factored in patients with shorter waiting time, e.g. eligible for Hepatitis C positive donor kidneys. With a growing waiting list of >750 patients, and annual transplant volume of only 125, the model predicted with 85% accuracy patients who received a deceased donor kidney transplant within one year. The majority of the 15% unpredicted transplants were 0-ABDR mismatch kidneys which could not be accounted for. Our model included a collaboration system which enabled the performance of required additional testing at the time of admission for transplant.

To view the full article, please click on this link:

<http://atcmeetingabstracts.com/abstract/kidney-waitlist-management-the-readiness-model-of-predicting-transplants-under-the-kidney-allocation-system/>

To cite this abstract in AMA style:

Elias N, Kimball B, Walsh L, Wojciechowski D, Markmann J, Heher E. Kidney Waitlist Management: The Readiness Model of Predicting Transplants Under the Kidney Allocation System. [abstract]. Am J Transplant. 2017; 17 (suppl 3). <http://atcmeetingabstracts.com/abstract/kidney-waitlist-management-the-readiness-model-of-predicting-transplants-under-the-kidney-allocation-system/>. Accessed April 11, 2017.

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Vascularized Composite Allograft Preservation: Ubi Sumus (April 2017)

Gorantla, Vijay S. MD, PhD, FRCS; Davis, Michael R. MD

*Transplantation: March 2017 – Volume 101 – Issue 3 – p 469-470
doi: 10.1097/TP.0000000000001599*

Autologous reconstruction of devastating injuries is often fraught with insuperable impediments. Life-changing esthetic and functional restoration of massive tissue defects is a reality today with vascularized composite allotransplantation (VCA). Since 1998, over 115 upper extremities and 35 craniomaxillofacial VCA have been performed worldwide. Per latest United Network of Organ Sharing data, there are 59 approved VCA programs located at 26 centers (including civilian, military or veterans affairs–affiliated institutions) across the nation.¹

Despite its clinical promise, the risks of lifelong immunosuppression, demands of functional nerve regeneration, and specter of chronic rejection continue to curb the potential impact of VCA as a paradigm shift for reconstructive surgery.

In addition to pioneering the art of vascular anastomoses, Alexis Carrell coined (with Charles Lindbergh), techniques for ex vivo organ perfusion with oxygenated solutions at body temperature.² These century-old groundbreaking achievements were seminal to the inception and progress of not only solid organ transplantation (SOT) and reconstructive surgery, but also of VCA.

Yet, the ideal organ preservation technology remains an elusive target.

The logistic simplicity and presumed effectiveness of static cold storage (SCS) preservation (at 4°C) drives its widespread use in SOT and VCA.³ SCS leads to anaerobic metabolism with loss of cell membrane integrity, reduced interstitial osmotic pressure (causing tissue edema and acidosis), and mitochondrial injury with cell death. Importantly, SCS also causes perivascular, intramuscular and intramyelinic edema, and axonal vacuolization.

Unique from any other solid organ, VCA outcomes depend on functional neuroregeneration and target muscle reinnervation. As in SCS, both muscular (beyond 4 hours) and neural (beyond 6 hours) tissues experience irreversible deterioration after warm ischemia. Ischemia-reperfusion injury (IRI) has a profound proinflammatory impact on the graft, through formation of reactive oxygen species and activation of innate, adaptive, and complement pathways, compounding the deleterious effects of SCS and warm ischemia and increasing risks of acute and chronic rejection.⁴

To view the full article, please click on this link:

http://journals.lww.com/transplantjournal/Fulltext/2017/03000/Vascularized_Composite_Allograft_Preservation_.9.aspx

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