MedicalXpress

The life-saving treatment that's being thrown in the trash

March 28 2017, by Bryn Nelson

A few hours before beginning chemotherapy, a man named Chris faces his cellphone camera with a mischievous smile and describes a perfectly absurd milestone at 1.37pm on a Wednesday. "There is no more beautiful moment in a man's life…" he says with puckish glee. Because how can you not laugh when you've been invited to bank your sperm in advance of being "Godzilla-ed" with chemotherapy and radiation, all just four days after being diagnosed with acute myeloid leukaemia at the age of 43 and given a 5 to 15 per cent chance of survival?

Oh, and the fertility clinic forgot to send someone over with a specimen kit and they're closing in little more than 20 minutes so you have to fire up your iPad for some quick visual stimulation to help you fill a sterile tube. Just try to ignore the legal consent paperwork all around you and the catheter that's been surgically inserted into your jugular vein.

And because there are no couriers available, your sister – who has been running half-marathons to get in shape – gamely volunteers to tuck the freshly filled tube in her sports bra to keep it at body temperature before dashing the mile to the clinic. You imagine her arriving as the window is closing, lurching towards the counter and shouting "Nooooo!" in the slow-mo way they do in action movies. She hands over her precious cargo in the nick of time and triumphantly exclaims, "This is my brother's!"

Nothing is normal about leukaemia or its aftermath, and Chris Lihosit has chosen to cope by learning everything he can about the disease and poking fun at its many indignities and absurdities. While some people

with cancer are reluctant to share because they see it as a sign of weakness, he knows that humour and openness have a way of breaking the ice and maintaining visibility.

On the last day of 2015, Chris received one of the estimated 40,000 umbilical cord blood transplants performed around the world to date. Cord blood contains what are known as stem cells and progenitor cells, which can give rise to oxygen-carrying red blood cells, infection-fighting white blood cells and clot-forming platelets.

Transplanted cord blood can be used to treat or cure more than 80 conditions, from leukaemia to sickle-cell disease. Based on current research exploring autism, brain injury, cerebral palsy, type 1 diabetes and cardiovascular disease, among others, the list of potential applications is likely to grow. Emerging strategies are even transforming cord blood left over after birth into a potent potion that might provide lifesaving treatments for victims of a nuclear disaster.

Stem and progenitor cells are also found in the spongy marrow within some bones and in the blood that circulates around our bodies. But cord blood, once dismissed as medical waste, is particularly rich in these cells. As researchers are discovering, it may carry other significant advantages too.

While a cord blood transplant might save your life, though, going through the process and then starting anew – your survival down to an anonymous baby – is far from easy.

1. Before

The first cases of leukaemia were documented some 200 years ago. The earliest known reports, by Scottish surgeon Peter Cullen in 1811 and French surgeon Alfred Velpeau in 1827, chronicled a baffling ailment

marked by an enlarged spleen. Cullen described the mysterious transformation of his patient's blood serum from a clear pale yellow to a "milky" liquid. Velpeau was just as astonished by what he likened to a thick gruel, leading him to conclude that his dead patient's blood was full of pus.

As we now know, bone marrow produces cells called "blasts", which take time to grow into infection-fighting white blood cells. But leukaemia sends production into overdrive, filling the blood with blasts that don't develop as they should. This army of immature cells crowds out the useful ones, leaving the host highly vulnerable to internal bleeding or foreign invaders.

Although the risk factors for leukaemia are only partly understood, scientists have linked it to genetic disorders such as Fanconi anaemia and Down syndrome, and to exposure to radiation or toxins like benzene. The out-of-control growth of abnormal white blood cells, though, has provided an opening for drug and radiation therapies that selectively cull the body's fastest-growing cells. As a last resort, doctors may deliberately kill off all leukaemia-riddled blood and bone marrow cells and attempt a full reset with someone else's blood-forming stem cells.

August to September 2015

In early August 2015, Chris Lihosit fell ill with an exhausting, dehydrating and pyjama-soaking fever that mysteriously disappeared two days later. During a check-up, on his 43rd birthday, his doctor named summertime flu the most likely culprit.

Then the same thing happened again, and it settled into a disturbing pattern: midweek chills and an escalating fever that would break on Sunday. By Monday, Chris would feel fine, only to have the sequence repeat itself. He joked about it with colleagues at T-Mobile, where he

works in software development, "Well, I hope it's not cancer!"

On alternating weekends from May to October, Chris would volunteer as a backcountry ranger for the US Forest Service – a physically demanding role that involves patrolling Washington's Cascade Mountain forests and hiking along high-altitude trails with a backpack that can weigh up to 32 kilograms. But now, even at sea level, he was getting winded just walking his two dogs around the block. What the hell was going on?

A medical appointment revealed a heart murmur and suspicions of endocarditis, an infection of the heart's inner lining. The scare triggered another series of tests that led Chris and his husband, Bill Sechter, to Emergency Room 4 at the University of Washington Medical Center.

A whiteboard checklist documented his Saturday morning: insertion of a large-bore IV as a potential conduit for antibiotics, a round of blood draws, and discussions with the ER doctor. Then the phone rang and the nurse answered, listened and responded to multiple questions in quick succession: "Yes. Yes. Oh, OK. OK. Yeah." He excused himself from the room and soon returned in a "full hazmat suit", as Chris describes it. Yellow.

"And that's when we were like, 'Oh shit, it's on. Something is seriously bad.'"

Chris learned that his level of infection-fighting neutrophil cells, normally churned out by the bone marrow, had fallen so low that his defences were in tatters. He was also severely anaemic, with roughly half the normal amount of red blood cells in his blood.

It wasn't endocarditis. And when one of his doctors performed a blood smear, she saw something on the microscope slide that shouldn't be

there: blasts. These leukaemic cells, stuck in adolescence, were the harbingers of the coming horde that had so astonished 19th-century surgeons.

The doctor apologetically broke the news and Chris and his sister dissolved into tears. In an emotional Facebook post later that day, he attached a picture of himself in a hospital gown and pink facemask and wrote: "this avowed agnostic could actually go for your good juju / positive thoughts or even your (gasp) prayers."

More tests, including a bone marrow biopsy of his pelvic bone, painted an increasingly disturbing picture. He had acute myeloid leukaemia, a fast-progressing cancer. The biopsy suggested that an astonishing 80 per cent of his bone marrow cells were cancerous. Strike one.

Other results suggested that chemotherapy wouldn't be as effective on his form of leukaemia. Strike two.

And genetic tests put him in the unfavourable risk category by revealing that his cancer cells carried only one copy of chromosome 21, a rare anomaly associated with "dismal" outcomes, according to recent studies. Strike three.

Chris needed to start chemotherapy immediately. But first, he had his sperm banked. Then, with family and a close friend at his side, he celebrated his impending treatment with prime rib and cheap champagne smuggled into his hospital room.

Over three days, he received multiple doses of the anticancer drugs cladribine, cytarabine and mitoxantrone, the last a dark blue concoction often dubbed "Blue Thunder". The drug turned his urine a shade he describes as "Seahawks green" in honour of Seattle's football team. Other patients have had the whites of their eyes temporarily turn blue.

On the third night of his drug infusion, a sudden back pain grew into an intense pressure in his chest that felt like he was being stabbed. A heart attack? An emergency CAT scan instead revealed two newly formed blood clots: one in his right leg and another in his right lung – not uncommon consequences of chemotherapy.

Over the next six months, Chris would need transfusions of blood-clotting platelets whenever his level of them dipped too low, and daily injections of a blood-thinning drug whenever it rose too high. Thirteen days after being admitted into the hospital, he posted a more hopeful Facebook entry: "And I'm finally going home! Now the real adventure begins."

2. During

In 1988, French doctor Eliane Gluckman saved a five-year-old boy from North Carolina by treating him with what was then deemed medical waste. The boy, Matthew Farrow, had been diagnosed with Fanconi anaemia, a rare genetic disorder that wipes out the bone marrow's ability to form new blood cells. At the Hôpital Saint-Louis in Paris, Gluckman used blood from the umbilical cord of Matthew's younger sister for an experimental transplant. It worked. Matthew survived, and now has a boy of his own.

Scientists had learned that, like bone marrow, cord blood is unusually rich in hematopoietic stem cells – which can give rise to every type of blood cell – and their more developed descendants, progenitor cells, which are more limited in what they can become.

But, unlike bone marrow, cord blood can be collected in advance and stored for decades in liquid nitrogen – a critical asset that opened the door in 1992 to the world's first public cord blood bank, in New York City.

Umbilical cord blood also doesn't require an invasive collection procedure. "One of the advantages of a cord blood graft is it's the only circumstance where you collect cells without touching the donor," says Mary Laughlin, medical director of the Cleveland Cord Blood Center in Ohio. When parents are celebrating a new life and asked about giving up cells that would otherwise go into the trash, she says, "That's a different donation."

In 1995, Laughlin and colleagues performed the world's first cord blood transplant on an adult, a woman in her early 20s who, like Chris, had been diagnosed with acute myeloid leukaemia. The team resorted to cord blood after failing to find a bone marrow donor who matched the woman's cells' highly uncommon identification tags.

To help the immune system distinguish friend from foe, nearly every cell in the body has protein tags on its surface, marking it as "self". We inherit half of these ID tags from each parent, meaning that any two biological siblings have a one in four chance that all their tags will align. But these proteins – known as human leukocyte antigens or HLAs – can vary enormously between two unrelated people.

For bone marrow and other transplanted tissue, the chance of finding an HLA match beyond immediate relatives can fall precipitously among people with more genetically diverse ancestries. In the US, the National Marrow Donor Program runs its Be The Match registry, which searches a global database of more than 29 million possible adult donors. A 2014 study suggested that white patients of European descent had a roughly three-in-four chance of finding an optimal match through the registry, while the likelihood dropped to less than one in five for blacks of African American, African, Caribbean, and South or Central American descent. Because Laughlin's patient was half-Native American and half-African American, she couldn't find any suitable matches at all.

Laughlin and her colleagues, however, correctly predicted that a cord blood transplant might work, thanks in part to a quirk of newborns' immune systems called neonatal immune tolerance. In telling self from other, cord blood cells are far more forgiving than adult bone marrow cells. The ability to use cord blood has significantly expanded patients' options, and black adults in the US now have at least a four-in-five chance of finding a suitable donor.

One of the biggest limitations of cord blood transplants, however, may come down to volume: doctors can extract roughly ten times more blood-forming stem cells and precursor cells from one bone marrow donation than from a detached umbilical cord.

Studies began suggesting that a cord blood transplant may be insufficient to rebuild the bone marrow in an adult, or take longer for it to become functional, leaving the recipient dangerously exposed to opportunistic infections or bleeding in the interim. "The fewer cells you gave, the higher the risk of death," says John Wagner, director of the Blood and Marrow Transplantation Program at the University of Minnesota.

Wagner and other researchers soon realised that cord blood transplantation would be pointless unless they could keep their patients alive long enough to see the benefits.

September to December 2015

Based on his leukaemia classification, Chris was braced for multiple rounds of chemotherapy. He and his husband were overjoyed when a second bone marrow biopsy suggested that the leukaemia had become undetectable after only a single round. Because of his high-risk classification, however, Chris's doctors said that the cancer was likely to return without a bone marrow transplant.

But, like Laughlin's patient, Chris discovered that he had inherited an extremely rare set of HLA cell-identifying tags. Only one bone marrow donor on the worldwide registry matched his genetic tags, and that person was unable to donate. A cord blood transplant, Chris and his doctors agreed, was his best hope.

First, he would need to spend another five days in the hospital for a standard follow-up round of chemotherapy to pick off any hidden cancer cells. Chris marked the occasion with a Facebook post of himself in a grey felt Viking helmet and attached braids. "Round 2… And FIGHT!" This time, the chemo went off without a hitch.

He was a familiar face at the medical centre, though, with three additional hospitalisations: twice for bacteraemia, a bacterial blood infection marked by high fevers, and once so doctors could tame an allergic reaction to a transfusion of platelets, which always reminded Chris of chicken broth.

He had to steel himself again on Christmas Eve for the arrival of the "big guns": two days of conditioning chemotherapy, headlined by a derivative of mustard gas. Its name is cyclophosphamide, and it works by sabotaging the machinery that copies DNA in rapidly dividing cells. As it does this, it breaks down to form toxic chemicals, including a pungent one called acrolein, which can destroy the lining of the bladder. To neutralise its effects, patients must take another drug, called mesna, and drink plenty of water.

After a day of rest, Chris began a radiation therapy regimen so intense that it would have killed him if delivered in a single dose. Instead, his radiologists used a particle accelerator to fire X-rays at him in multiple bursts during morning and evening sessions over four days.

"You basically get into a tanning booth made out of clear Plexiglas," he

says. Wearing nothing but a paper gown, Chris had to stay completely still behind two metal shielding blocks, each the size of a brick, positioned to protect his lungs from irreversible radiation-induced scarring. He did get a mild tan, he says, along with damaged skin that still resembles crepe paper. Another absurdity still makes him laugh: while he requested punk rock for one of the sessions, he was instead blasted with the tune of Prince's 'Erotic City'.

When he finished the final round of total body irradiation on 30 December, the radiology team gathered for a final tribute and let Chris hit a small ceremonial gong.

§

Cord blood transplants in adults, still an option of last resort in the early 2000s, nearly slammed to a halt over the quandary of how to keep patients alive until their new bone marrow cells could kick in. Some researchers reasoned that they could boost the transplant volume by giving adults two cord blood units instead of one. Wagner and colleagues at the University of Minnesota performed the first double transplant in 2000, using cells from two infant donors.

The tactic dramatically reduced the rate of graft failure, in which the recipient's body rejects the new cells. But it barely changed the time needed to regenerate the bone marrow, and some critics have questioned whether a double cord blood transplant offers any significant benefits. Wagner says his research suggested that transplanting enough blood-forming cells was necessary – but likely not sufficient – for better results. Improved patient survival, in fact, seemed to depend more upon a revised roster of drugs given pre-transplant.

To their surprise, researchers also discovered that the donors in a double cord blood transplant seem to battle for dominance, a curious "graft-

versus-graft" phenomenon that almost always results in the victor dominating the recipient's new bone marrow and blood cells. Filippo Milano, associate director of the Cord Blood Program at the Fred Hutchinson Cancer Research Center in Seattle, compares it to a pivotal scene in the 1986 movie Highlander, when the antagonist exclaims, "There can be only one!"

On a sunny morning nearly a year after Chris's transplant, he and I meet the Italian-born doctor in his lab so he can greet one of his star patients and explain the science behind the therapy that saved Chris's life. Milano is passionate about coaching soccer and cooking. On the side, he jokes, he conducts research on cord blood transplants. Upon his arrival to "The Hutch" in 2009, Milano teamed up with Colleen Delaney, founder and director of the Cord Blood Program, to test and refine a treatment strategy that may yet prove a better option than a bone marrow transplant for people with leukaemia who are at high risk of relapsing.

Based on collaborations and discussions with other experts in the field, Delaney pioneered a method to minimise the risk of infection and bleeding after a cord blood transplant by reducing the time needed for the new blood cells to kick in. The strategy relies on what she and Milano call an "expanded" blood unit. Starting with an extra batch of cord blood, they separate out the minuscule fraction of blood-forming stem cells and their early descendants and expand that population in the lab. The hundreds of millions – even billions – of resulting stem and progenitor cells can jumpstart the generation of protective blood cells in the recipient. When infused along with a more traditional transplant, they can act like a temporary bridge until the replacement bone marrow takes over. "The net gain was that you didn't have those very prolonged periods of recovery," Wagner says.

One crucial component, Delaney discovered, is a protein called Notch ligand. When added to the blood-forming stem cells, Notch ligand lets

them divide quickly in the lab but temporarily pauses their development by preventing them from maturing into the normal range of cell types. Critically, they never give rise to T or B immune cells, which would seek out and destroy any perceived threats lacking the proper "self" ID tags.

Putting a donor's T cells into an unmatched recipient, Delaney says, would trigger fatal graft-versus-host disease. "That's the key: we get rid of all those bad parts of the immune system that need to be matched or they can kill you."

The "bridge of recovery" lasts only so long before the full contingents of other donor cells begin attacking and dismantling it. But, with no cells checking IDs initially, the early flood of blood-forming stem cells need not be matched to the recipient at all, meaning that the "expanded" cord blood unit could be created well ahead of time and used whenever needed as a universal donor.

Other researchers are working on strategies toward the same end, and Mary Laughlin describes the overall progress as "very exciting". Delaney's work, she says, "is very important, saving lives and improving the tolerability of these transplants and the success of these transplants."

December 2015

It's the morning of New Year's Eve, and Chris writes on Facebook, "I'm as nervous as an expectant father!" An hour and a half later, he marks the delivery of his "zero birthday" with a small chocolate cake and a decorative "0" candle: the day when his own bone marrow cells, erased by radiation and chemotherapy, will be replaced by roughly four tablespoons of a life-granting elixir from the cord blood of two baby girls.

Chris and Bill have nicknamed the donors Amelia and Olivia based on

their blood types, A-negative and O-positive. In a later post, Chris marvels at the new arrivals reseeding his bone marrow: "I use more vanilla flavoring creamer in my coffee than the volume of cells that are rebuilding my entire blood and immune system."

Four hours after the initial infusions, he will receive his protective bridge of blood-forming stem cells, collected and expanded from the cord blood of a third baby, a boy he and Bill have nicknamed Eddie. In a celebratory video, they cue up Kay Starr's version of the 1946 Peggy Lee classic, 'It's a Good Day':

I woke up this morning, hated to get out of bed

But I called up the weatherman and this is what he said,

"It's gonna be a good day, a fine day"

Yes, it's a good day for singing a song and it's a good day for moving along.

3. After

Preliminary results suggested that Delaney and Milano's strategy of adding temporary bridges like Eddie's to cord blood transplants could significantly shorten the time needed to reboot the recipient's population of neutrophils, the microbe-digesting white blood cells.

Based on their early success, the researchers have launched a larger randomised trial of 160 patients. Eighty are receiving one or two units of intact cord blood. The other 80, including Chris, are also receiving the experimental expansion unit of blood-forming stem cells. When Milano recruited Chris for the study, he punctuated his pitch with a simple message: "The only thing I want you to think is that cord blood is not

trash."

Chris became patient 69, a detail that still makes him giggle. In his body, the researchers believe, Eddie's cells provided the critical early support for his bone marrow until Amelia's or Olivia's cells could take over.

Even before the new strategy, a review of double cord blood transplants by John Wagner and colleagues suggested that recipients carried a significantly lower risk of relapse than people who received bone marrow transplants. The benefit seemed particularly apparent for people whose leukaemic cells hadn't been completely eradicated by chemotherapy and radiation.

Delaney, Milano, Wagner and others have since raised a question that was previously anathema among doctors: what if cord blood's unexpected cancer-killing prowess is actually linked to there being a partial mismatch between donor and recipient?

Milano explains the rationale: "Something that's different will fight," he says. It's also why an identical twin is a poor donor choice: if the replacement bone marrow is too similar to the flawed original, Delaney says, it will do nothing new to prevent the cancer from returning. "Your cells are like, 'Hey, I haven't seen you in a while. Come on in, let's have a party!'" she says. For high-risk patients, in fact, several transplant centres now advocate the opposite of the once-intuitive strategy: using deliberately mismatched cord blood to minimise the risk of recurrence.

Although the clinical trial likely won't be completed and analysed for another year or two, Milano says Chris has done exceptionally well, even among those given expanded cord blood units. The researcher jokes that Chris received the Tesla 2.0 model of transplants, though the variable outcomes also raise the question of whether some donor units simply work better than others.

Bill joins us on our tour and gives Milano a hug. They discuss plans for a highly anticipated get-together; at a recent fundraiser for the cancer centre, Chris and Bill successfully bid on a dinner that Milano will cook.

We head to the basement and peer into the window of a rigorously controlled cell-processing room, where technicians are clad in disposable caps, masks, gowns, gloves, leggings and booties to prevent contamination of stem cells destined for clinical use. The technicians then grow the cells for roughly two weeks with the Notch ligand that directs their fate. After a separate lab tests each culture to weed out any contaminated batches, the individual units of expanded cells from Eddie and other donors could potentially be stored indefinitely.

January to July 2016

Even with some of the best help that medicine can offer, transplant recipients face a daunting few weeks without functional bone marrow when nearly anything can kill them.

Chris's third feverish bout of bacteraemia arrived on the fourth day after his transplant. Each infection, blamed on varying strains of E. coli bacteria that had somehow made their way from his gut to his bloodstream, kept finding new ways to evade the potent antibiotics his doctors threw at it. His conditioned worsened over four days and culminated in a fever dream that he describes as a dystopian mix between the movies Blade Runner and Speed Racer, with an African American Goth as his guardian angel. When he eventually awoke, his fever was gone.

After the infection scare, Chris was confined to his room to minimise the risk of passing along the drug-resistant bacteraemia to other patients. On the inside, though, Amelia and Olivia were vying to become his internal guardian angel and soon left Eddie in the dust.

Recipients pass the first big post-transplant milestone – engraftment – when their new blood precursor cells begin growing rapidly and developing into the proper components within their bone marrow. Daily blood tests can chart the progress of the new recruits: white blood cells such as neutrophils recover first, followed by red blood cells and platelets.

Less than three weeks after the transplant, Chris's neutrophils had fully engrafted and genetic tests suggested that Amelia had decisively won the fight to form his new blood and bone marrow. He progressed so rapidly, in fact, that he had to stay in the hospital for two days after he was fit to leave, so that Bill could finish preparing the apartment.

28 January: discharge day. As his family packed up his hospital room, Chris was taking a shower when a wall of exhaustion hit him. He could no longer stand or even dry himself off and sat dripping on the shower bench until Bill heard his calls for help.

He had survived, but life had fundamentally changed.

At home, every surface had to be disinfected daily with a bleach solution. At first, Chris couldn't walk 100 feet down the apartment hallway without leaning on his brother. Until he hit the 100-day milestone after his transplant, the end of the most vulnerable period for recipients, he returned to the Seattle Cancer Care Alliance every other day for blood tests and checkups.

On the 97th day, Chris and his family celebrated a hard-fought victory when he was officially declared cancer-free: a leukaemia survivor.

His "never-ending kick line of drugs" required parties of a different sort every Sunday to apportion close to 60 daily pills into time-stamped plastic bags. His once-photographic memory also failed him frequently –

one lingering side-effect of chemotherapy known as chemo brain. And he commonly felt the cold and tingly or warm and prickly sensation of neuropathy in his hands and arms. Combined with tremors in his hands, this meant he often struggled to hold a pen or spoon steady. This eventually subsided, although the prickliness still returns for occasional night-time cameos in his feet.

Chris had two reactivations of a painful viral infection that homed in on his kidneys and urinary tract and tended to announce its presence dramatically, through large blood clots in his urine. As he discovered, the pain-relieving remedy stains anything it touches – including bodily fluids – a bright orange.

A keen member of the Seattle Men's Chorus, Chris was warned by one nurse not to sing or hum for months until his platelets rebounded, lest he permanently damage his vocal cords. Nor should he have sex or masturbate until his body could recover, to avoid the excruciating pain and risk of tearing the lining of his urethra, breaking a blood vessel and causing "bruising in places that are awkward and weird", as Chris puts it. The threat of another E. coli infection also interfered with his sex life (anal sex could increase his risk of bacteraemia), as did his faltering self-image. "You just don't really feel comfortable in your skin, which kills your confidence a bit," he says.

Chris isn't alone. A recent Danish study of nine patients found that many were still struggling to regain their sexuality a full year after a bone marrow or cord blood transplant, because of negative body image, physiological limitations and other concerns. One 49-year-old described his fear of passing out or keeling over during an unexpectedly strenuous session:

"And in that very moment, you believed you were going to die because the air simply… you wanted to finish even though you were fighting for

breath; because it is unfair to the other person to stop, so I thought, 'If I pass out, then that is just what I will do', because you push yourself to the limit, and then you have to lie still for 10–15 minutes afterwards."

Even with all this, Chris reminded himself, things could be far worse.

4. Now

Despite dozens of studies documenting its curative powers, cord blood is saved after only 5 per cent of all US births. The rest is simply thrown away. Michael Boo, chief strategy officer for the National Marrow Donor Program, estimates that only one in ten of those retained units passes the required screening tests and has enough volume to merit long-term storage.

Cord blood is also notoriously expensive, ranging from $22,000 to $45,000 per unit. Due to the relatively low demand from doctors, Boo says, public banks – at least in the US – are collecting as much as they can afford to keep. Beyond persuading new parents to donate, then, lowering the cost of cord blood transplants may depend upon persuading more doctors to use the cells and more insurers to cover them.

Units that never make it into long-term storage often go to research labs like Milano's or to Delaney's new cancer centre spinoff, Nohla Therapeutics. The startup, with Delaney as chief medical officer, hopes to develop an off-the-shelf blood precursor product – essentially a biological drug – that doesn't require any matching of the HLA tags that distinguish self from other (hence the name, from "no HLA"). If the company can craft a universal donor out of stem cells from cord blood, public health agencies could theoretically pool and stockpile the units.

One potential use has attracted the avid interest of the Biomedical Advanced Research and Development Authority, part of the US

Department of Health and Human Services. As part of Project BioShield, the federal agency has been on the lookout for medical interventions that could treat acute radiation syndrome after a dirty bomb or nuclear disaster.

Not unlike the radiation therapy that killed off Chris's bone marrow prior to his transplant, nuclear radiation can wreak havoc on healthy marrow. And just as Eddie provided the initial defences until Amelia could take over, a timely dose of blood-forming stem cells could offer a critical window of protection for people exposed to radiation until their own bone marrow recovers.

"We have stem cells that are incredibly hardy and so it may take two months but most people, if they can live that long, will finally start making their own blood cells again," Delaney says.

Not everyone's on board, though, with some critics questioning the intervention's practicality and applicability in the wake of a disaster. The same temporary product, however, could be given to any at-risk patient with low red blood cells, white blood cells or platelets, Delaney says. "Are you septic? Did you just get chemotherapy? Are you getting a transplant? Did a nuclear bomb go off?"

A pared-down batch of blood-forming stem cells also might help usher in a cheaper version of what Milano dubs the Tesla 3.0 strategy: if doctors could achieve the same transplant results or better with just one full cord blood unit plus an off-the-shelf expanded unit, they could cut costs significantly.

In her new Seattle lab, with its meeting rooms named after past patients, Delaney uses a small thawing device to demonstrate the simplicity she believes could greatly expand her end product's utility and accessibility to others in the future. A nurse could pop a small syringe of frozen cells

into a bedside device, push a button to thaw the solution, and inject it into the patient. "It can't be more complicated," Delaney says, "because otherwise not everyone can get it."

July 2016 and beyond

This is Chris's new normal, at least for now: his once stick-straight hair is slightly curly, softer and darker (no more grey!). His blood type was previously A-positive, now it's A-negative: Amelia's blood. With her blood and immune cells, he's technically a chimera.

Cord blood transplants can ramp up the incidence of acute graft-versus-host disease, in which the incoming cells attack their new neighbours. Chris has had to fend off occasional assaults on his own cells, including a lacy rash that has covered his back and shoulders. He documented another bout that affected his gut in a post in August 2016: "Uncool Amelia, uncool!"

Compared with bone marrow transplants, though, chronic graft-versus-host disease may stop occurring sooner after cord blood transplants; a few cord blood recipients have been able to discontinue all immune-suppressing drugs after only a year.

So far, Amelia's cord blood hasn't brought other unwanted genetic baggage, though a few other transplant recipients have actually acquired new genetic conditions, raising the ethical question of whether doctors should inform the donor's parents of such findings as well.

Chris always travels with a thermometer, and had to start his childhood vaccinations all over again in February 2017, with eight boosters combined into six painful injections. He and his family have received flu shots as well, but he remains vigilant about avoiding anyone with the sniffles. He loves kids, but they now make him nervous, and people who

don't have their children immunised are a very real threat.

His hay fever and allergies to pine pollen and oily dogs have disappeared, although they may be replaced with others. To ward off what he can, he is slowly reintroducing potential allergens like peanut butter.

His food options have contracted to the point where several friends took cooking classes for immune-suppressed people to learn how to prepare meals for him. Everything must be kept frozen or piping hot. Most seafood and salads are out, as are raw vegetables and nuts. So are any fruits that he can't peel or scrub, runny eggs, many dairy products and undercooked steak. "Who in their right mind wants to have a well-done steak?" says Chris.

For the remaining items, his sense of taste skewed so dramatically from the after-effects of radiation that he began keeping a list of spices and flavours that he could discern. Pepper upset his stomach. And more than a few former favourites became all but inedible. Chocolate – chocolate! – tasted like flour paste. Ketchup was suddenly disgusting.

His body has changed in other ways. He's still dealing with radiation damage to his skin, the lenses of his eyes and other body tissues. His doctor told him he will need cataract surgery within ten years. And because sunburn could trigger a severe graft-versus-host reaction, the sun is now his enemy.

The forced inaction and side-effects of chemotherapy and other drugs wasted away an alarming amount of lean muscle. When Chris started working out with a trainer, he couldn't manage a single push-up.

§

At a cost of $1.25 million so far – covered by insurance except for an annual deductible – Chris has been reborn. But who is he now? Sometimes he wonders, and he had to battle through an existential crisis when he realised that an essential part of him – his lifeblood – was gone for ever.

A recent survey of more than 400 adult survivors of another blood cancer, lymphoma, found that many were still grappling with grief, guilt and existential concerns years after the initial diagnosis. More than half had lost a sense of security, while roughly one in four had lost a sense of their own identity. Those who had undergone a stem cell transplant were the most likely to express discomfort over their identity and security. For Chris, the emotional calculus has meant learning to accept a new co-existence with a stranger's cells. Whenever he has his blood drawn now, Amelia is there.

But she also exists independently, a toddler starting her own life somewhere else in the world. On New Year's Eve, Chris thanked her for his rebirth, wherever she might be. And on 26 July – the date on the cord blood unit – Chris and his family acknowledged her with a card. "Somewhere in America a three year old had her birthday, never knowing she actually has two lives to celebrate," he wrote on a post accompanying a card from his mom that read, "Thank you for saving Chris. You are one very special 3 year old & we love you!"

Chris has rejoined his beloved community chorus, no longer gasps for breath when taking his two Havanese dogs for a walk, and has begun contemplating more ambitious travel plans with Bill and a return to his forest ranger duties. To his relief, he's also begun thinking of geeky projects he wants to do, like grinding a telescope lens or designing a mini-satellite. "Physically and mentally, I knew I was going to be OK when I started becoming interested in hobbies again," he says.

After his sister's heroic run with his sperm sample, the fertility clinic gave Chris one more thing to think about: his potential to be a father through IVF if he and Bill are so inclined. Chris is pleased that the option remains open, despite the uncertainties of his recovery, his husband's busy career and his other worries about the future.

If it ever comes to pass, he has the names already picked out. If it's a boy, Adam, and if it's a girl, Amelia – he's always liked that name.

This article first appeared on Mosaic and is republished here under a Creative Commons licence.

Provided by Mosaic