Increased use of cord blood to treat CGD and other immune disorders

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The 2006 pan-European based survey shows cord blood transplants for all blood and immune conditions rose from 86 in 1997 to 544 in 2006 and accounted for 15% of all transplants for immune disorders. The data show marked differences in cord blood use between European countries with the UK showing one of highest rates of cord stem cell use. To date, more than 70 different diseases, including CGD have been treated with cord blood transplants.

So what are cord stem cells? Cord stem cells come from umbilical cord blood. After a baby is born, the umbilical cord is cut, and some blood remains in the blood vessels of the placenta and the portion of the umbilical cord that remains attached to it. After birth, the baby no longer needs this extra blood. This blood is called placental blood or umbilical cord blood: "cord blood" for short. It contains all the normal elements of blood - red blood cells, white blood cells, platelets and plasma. But just like bone marrow it is also rich in haematopoietic (blood-forming) stem cells, that are capable of generating all the cellular elements in the blood and immune system.

What is the importance for CGD? Transplant centres may recommend cord blood collection and storage for babies born into a family that has an older child with a CGD who could be treated by stem cell transplantation. In this case, the transplantation centre would raise this as a possibility with the family and the obstetrician and would offer support and advice on the collection of the sample. Your clinician will be able to arrange for cord blood to be collected and stored in the NHS cord blood bank for future use by your family. Experience on the use of cord blood to treat CGD comes from the team at Newcastle General Hospital. Dr Andy Gennery, Consultant in Paediatric Immunology and Bone Marrow Transplants in Newcastle comments: "Families who have children with CGD may be interested in storing cord blood from future pregnancies to potentially use for haematopoietic stem cell transplantation as an alternative to bone marrow. In order to use cord blood haematopoietic stem cells successfully, the newborn child would have to not be affected with CGD, and also have an identical tissue type (a 1 in 4 chance for children of the same parents). Because the volume of cord blood that can be collected is usually quite small, there is usually not enough to treat an older brother or sister weighing more than 15 kg. However, it could be used to treat a subsequent child born in the family, providing the tissue type match is satisfactory."

Why is cord blood collection important for the general population? Cord blood is becoming a really important source of stem for transplantation if no related donor is available. It is a particularly important source of stem cells transplant for ethnic minorities who have a much lower chance of finding a bone marrow donor than Caucasian patients because they express tissue types not present in established bone marrow donor registries.

What are the advantages of cord blood? Fortunately, a cord blood transplant does not have to be quite such a perfect match to the patient. Adult bone marrow contains immune cells (so-called T-lymphocytes or T-cells) that are fully mature. When transplanted, these T-cells may attack the patient's own cells, causing a condition called graft vs. host disease (GvHD), which can be severe and even lethal. T-cells in cord blood do not appear to be as "immunologically mature" as those in bone marrow. As a result, cord blood transplants are less likely than bone marrow to cause GvHD and, when it does occur, it may be less severe. Because cord blood transplants cause less GvHD, the match to the patient does not need to be perfect. This means that patients who cannot find a perfectly matched bone marrow donor may have a chance to find a suitable cord blood transplant. Patients with rare tissue types and members of other minority groups, therefore, benefit especially from this stem cell resource. “Cord blood haematopoietic stem cells do have certain advantages over marrow cells”, says Dr Gennery. “In particular, when there is a lot of inflammation e.g from colitis, treatment with cord blood cells can be more ‘gentle’ lessening the risk of graft versus host disease, a potential complication of haematopoietic stem cell transplantation. The success rates using cord blood haematopoietic stem cells in this setting is equal to using bone marrow.”

Other advantages are that cord blood can be frozen and stored for years so it is more readily available and there are fewer delays with a cord blood transplant. Delays are inevitable in the case of bone marrow transplants because of the need to search registers, contact would-be donors and the bone marrow retrieval procedure itself.

What are the disadvantages of cord blood? A cord blood transplant may not be possible. There may not be enough cells from one cord for a transplant, especially to an adult as the volume collected is relatively small. Therefore, the number of stem cells available for transplantation is low compared to the number of cells that can be collected in a bone marrow or peripheral blood stem cell harvest. The average total nucleated cell dose (number per kilogram of the patient's weight) in a cord blood graft, for example, is about 1/10th that of the average bone marrow graft. As a consequence, engraftment (the return of nucleated blood cells, red blood cells and platelets) can be slower with cord blood than with bone marrow transplants. To over come the problem with cell numbers cord blood stem cells from multiple donors are pooled to increase cell numbers.

Receiving cord blood transplants from unrelated donors does carry a small risk of passing on another genetic condition to the recipient. This risk has been estimated at less than 1 in 10,000. Families who donate cord blood are asked about their ethnic background and family history of genetic diseases. Cord blood is tested for common genetic diseases such as sickle cell anaemia. However at present, it also is not possible to test for all rare diseases. Thus, there is a chance that a cord blood transplant will give a patient a rare serious genetic disease that was not recognized beforehand but this risk is very small.

Cord blood banking, the NHS Public Cord Blood Bank and private cord banks. Cord blood banking is when cord blood is collected and stored for treating a disease or illness. Mothers can donate their umbilical cord blood to the NHS Cord Blood Bank with the aim of helping others although is only currently possible at certain UK hospitals. It is a gesture of good will. This provides another source of hope for patients who have no matching donor in their own family, no unrelated donor in bone marrow donor registries that is a suitable match or no time to find a donor. Currently most hospitals in the UK do not have the facilities to routinely store cord blood from newborn babies. There are presently four hospitals in the south east of England where if you give birth, you can donate cord blood to a public bank such as the NHS cord blood bank. There is also a small NHS public bank in Belfast in Northern Ireland. Donation is voluntary and collection and storage is free of charge. There are plans for more hospitals to have this facility. A public bank stores cord blood for use by anyone anywhere in the world, thus ensuring fair access for all patients requiring stem cell transplantation. It is an alternative to a volunteer bone marrow donor registry. Earlier this month it was announced by the Human Tissue Authority that all facilities which collect umbilical cord blood cells should have a licence to do so. The potential licensee will have to demonstrate they have fully trained specialist staff to collect the cells using best practice to ensure the third stage of labour will not be jeopardised. Centres will also have to show that any cells collected for future use can be traced for identification and monitoring purposes. Dr Gennery comments on this new legislation ‘Unfortunately, the new regulations issued by the Human Tissue Authority could make the collection of cord blood difficult for families with CGD patients. The regulations are intended to make procedures for collecting cord blood safer, which is to be commended. It does mean, however, that it may be more difficult to have cord blood collected locally. Many institutions are currently working to maintain access to cord blood collection whilst working within the new legal framework."

There are now many private commercial companies that offer personal cord banking services for fees of around £1, 500. There is no need to do this for families with a high risk of a genetic disorder because this will be recommended by the treating physicians and will be done for free. People store cord blood with a private bank in the hope that, in the future, cord stem cells may be useful, should a member of their own family develop a

disease treatable by stem cell therapy. In the general population the chances of a child ever needing to use his or her own cord blood are extremely small (1/20,000 – 1/37,000), so it is very unlikely that the cord blood will ever be needed. There is still much debate about the use of private cord blood banks but the Royal College of Obstetricians and Gynaecologists remains unconvinced about the benefit of storing cord blood with a private bank for families who have no known medical reason to do so. However 'directed cord collections', when a child in the family already has a disease treatable by transplant, are considered very worthwhile.

Further information

The UK's HTA to regulate the collection of cord blood stem cells.
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NHS Cord Blood Bank http://nhscordblood.co.uk/

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