



Australian Government

National Health and Medical Research Council

Stem Cell Treatments – A Quick Guide for Medical Practitioners

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A limited review of this resource has been undertaken to take account of changes to the regulation of autologous human cell and tissue products, commonly referred to as 'stem cells', that came into force on 1 July 2019. It was updated in December 2019 to reflect the impact of those amendments. Medical practitioners should note that the resource has not undergone a full review, and up-to-date information about the regulation of autologous human cells and tissues products can be found via <https://www.tga.gov.au/autologous-human-cells-and-tissues-products-regulation>.

The science of stem cells is a field with great potential for treating injury and disease. Reports in the media suggest that stem cell treatments are close to being available to patients to treat a wide range of diseases, and these reports influence public perception. However, further research is required to create safe and effective treatments. The reality is that other than the use of haematopoietic stem cell transplantation for blood and certain immune related disorders, the majority of stem cell treatments are still in the early stages of research and development.

How does this document help you and your patient?

This document has been adapted from existing patient handbooks^{1,2} and aims to provide practitioners with information to assist in discussing stem cell treatments with patients.

It is supported by a *Frequently Asked Questions* document which provides information for patients about stem cell treatments.

What are stem cells and why are they important?

Stem cells are precursor cells that can divide to produce either more identical stem cells, or many other different cell types in the body. This capability has stimulated enormous interest in the potential of stem cells to replace defective or damaged cells that cause disease. Stem cells can be derived from embryonic, fetal or some adult tissues and have different properties depending on their origin.

A glossary of stem cell-related terms is presented at the end of this document.

Further information on stem cells can be found on the International Society for Stem Cell Research (ISSCR) website at: <http://www.closerlookatstemcells.org>

What stem cell treatments are available, and are they safe and effective?

Stem cells offer promise and have the potential to treat a number of conditions. However, the only stem cell treatment that has been scientifically proven is haematopoietic stem cell transplantation. Haematopoietic stem cell transplantation has been available in Australia for several decades and is an established effective therapy for haematopoietic reconstitution. Haematopoietic stem cell transplantation is standard treatment for disorders of the blood and immune system such as leukemia and lymphoma, and is also used as supportive treatment in therapy of other cancers.

All other medical stem cell treatments are currently unproven and have not yet been established as safe and effective. An increasing number of people are travelling overseas for stem cell treatments that are unproven (often referred to as ‘stem cell tourism’). Unproven treatments using a mixture of the patient’s own (autologous) cells are also being offered by private clinics in Australia.

Some stem cell clinics offer unproven treatments directly to consumers, often advertised via the internet. Treatments are offered for a wide range of diseases, such as multiple sclerosis, spinal cord injury, osteoarthritis, rheumatoid arthritis, heart disease, autoimmune diseases, cerebral palsy and autism. Often the same treatments are promoted for several diseases, raising doubts about their credibility. Furthermore, many treatments being offered as stem cell therapies may not actually involve stem cells, but rather an ill-defined and heterogeneous mixture of different cell types.

Can stem cell treatments be advertised in Australia?

Advertising of stem cell treatments to customers in Australia is prohibited by the Therapeutic Goods Administration (TGA). Concerns about supply and advertising should be reported to TGA.^a

^a <https://compliance.tga.gov.au/advertising-complaint/> and <https://www.tga.gov.au/hubs/compliance-and-enforcement/report-breach>

How are stem cell treatments regulated in Australia?

The regulation of human cells and tissues in Australia is complex. It is important to be aware that not all stem cell treatments available in Australia have been tested for safety and effectiveness.

In Australia, the importation, manufacture and supply of biological therapeutics is regulated by the TGA. Stem cells intended for therapeutic use must be included on the Australian Register of Therapeutic Goods (ARTG) or otherwise excluded or exempt, approved or authorised.

The TGA’s remit is the regulation of therapeutic goods – it does not regulate medical practice.

All providers of stem cells for therapeutic use who operate outside of hospitals will be subject to some level of regulation by TGA. Providers who fail to meet the requirements may face criminal penalties.

Stem cell treatments that are offered in hospitals by registered medical and dental practitioners are excluded from TGA regulations. It is up to the hospital to decide the suitability and safety of the stem cell treatments offered.

The Medical Board of Australia, supported by the Australian Health Practitioner Regulation Agency (AHPRA), regulates medical practice through the development of standards, codes and guidelines for the medical profession.

Some medical practitioners in Australia are offering autologous stem cell treatments that may not have been demonstrated to be effective. Concerns about a practitioner’s professional conduct can be directed to AHPRA or to the health complaints entity in the relevant state or territory. Concerns may arise under the Australian Consumer Law where consumers are misled or deceived into believing that certain treatments are safe or effective when that is not the case. Where practitioners make claims about their treatments, they should be able to substantiate them. Concerns about such claims can be raised with state or territory fair trading agencies or the Australian Competition and Consumer Commission.

What are the risks to your patients of undergoing unproven stem cell treatments?

Participation in unproven stem cell treatments may pose serious risk to the health and well-being of patients. Serious adverse events have been reported as a result of stem cell treatments, including the development of tumors^{4,5,8} and abnormal bone growth⁶ as a result of stem cell injections. Infection, allergic reaction and immune system rejection are also side effects reported as a result of stem cell therapies.

In addition to the health and safety risks, there are other significant risks associated with unproven stem cell therapies. Clinics offering these treatments often raise hopes about the treatability of a disease or condition, where the safety and efficacy of the treatment has not been established. Pursuing unproven stem cell therapies can divert patients from more conventional treatments that, even if not curative, have demonstrable beneficial or palliative effects and are based on sound scientific evidence. Undergoing such treatments may also disqualify patients from future participation in a registered clinical trial. In addition to these opportunity costs, unproven stem cell treatments come with significant financial costs, including costs associated with travel such as accommodation, airfares, meals and carer's expenses.

Internationally, stem cell clinics can be located in countries with different standards of medical care (including poor hygiene practices and inadequate infection control procedures). These countries may also accept different standards in the qualifications and insurance coverage required to practice as a medical practitioner. In addition, the regulation of medical practitioners (e.g. by government authorities or medical boards) may not be as rigorous as in Australia, and restrictions on who can perform stem cell treatments (e.g. whether a medical qualification is required) may be limited or not enforced. Further, in some countries where stem cell treatments are offered, there are no accessible legal pathways in the event of negligence or malpractice.

In these ways, unproven stem cell therapies have the potential to harm patients, even if they do not directly cause adverse health effects.

What advice can medical practitioners give to their patients?

One of the main challenges in discussing stem cell treatments is dealing with the patient's expectations after he or she has read advertisements and self-promotion material by clinics offering unproven stem cell treatments.^b

Whilst it is ultimately the patient's decision whether he or she decides to undertake unproven stem cell treatments in Australia or abroad, medical practitioners have a responsibility to ensure their patient makes a well informed decision and has a thorough understanding of the potential risks outlined above.

When investigating stem cell treatments in Australia or abroad, you may wish to encourage your patients to consider whether any approved clinical trials exist for their condition. In Australia, clinical trials must be approved by a Human Research Ethics Committee that is registered with the National Health and Medical Research Council. While the experimental treatments offered to participants in an approved clinical trial may not yet be established therapies, they have usually undergone preliminary tests for safety and efficacy (e.g. in animal models or in small human trials). Patients will also be fully informed about the possible outcomes and risks involved in participation and provided with a high standard of expert medical care and regular monitoring throughout the trial.

The Australian Clinical Trials website (www.australianclinicaltrials.gov.au) provides more information about clinical trials. The website includes links to registers of clinical trials to assist patients to identify any clinical trials for their particular disease or condition.

The accompanying Frequently Asked Questions resource can be provided to your patients. The document provides background information about stem cells, clinical trials and general points to consider before embarking on unproven stem cell treatments.

^b Advertising of stem cells treatments to customers in Australia is now prohibited by the TGA.

QUICK TIPS FOR MEDICAL PRACTITIONERS

- Ask your patients whether they have considered using an alternative therapy for their disease. This may help initiate the conversation about stem cells.
- Encourage your patients to make well informed decisions about their healthcare, emphasising the importance of considering scientific evidence when making these decisions.
- Encourage your patient to research the treatment, and consider the following:
 - ▷ What is the status of the treatment? (i.e. is it proven, such as haematopoietic stem cell transplantation, part of an approved clinical trial, or unproven?)
 - ▷ Is there published evidence on the effectiveness and safety of the treatment? Is there a scientific rationale for how the treatment works?
 - ▷ What types of stem cells are being used (e.g. patient's own cells from bone marrow or fat, umbilical cord blood, fetal tissue or embryos)? Are the cells being administered mixed or are they pure stem cells?
 - ▷ What are the costs involved with the entire process? Are these clearly explained? Are there substantial upfront fees?
 - ▷ What are the risks and potential complications?
 - ▷ Is the person who performs the stem cell treatment a specialist? Are their credentials specific to your condition, or do they claim to be an expert in treating multiple diseases or conditions?
 - ▷ Will you have access to follow up care? What will this entail?
- Encourage your patients to think twice about statements describing the therapy as a 'quick fix', 'scientific breakthrough', 'miracle cure', or similar. It may help to suggest to patients that if it sounds too good to be true – such as a claims that a therapy can cure a disease or treat a variety of conditions – it usually is.
- Offer to help interpret and discuss any information that the patient uncovers in their research, or that the stem cell centre provides to the patient.
- Ask the patient whether they have considered participating in any stem cell clinical trials that may be available for their condition.
- For further information, direct patients to the following resources:
 - ▷ *The Australian Stem Cell Handbook* available at:
https://www.stemcellfoundation.net.au/educational_resources
 - ▷ International Society for Stem Cell Research (ISSCR) patient website available at:
<http://www.closerlookatstemcells.org/>
 - ▷ ISSCR patient handbook available at:
<https://www.closerlookatstemcells.org/patient-resources/>
 - ▷ Stem Cells Australia website available at:
<http://www.stemcellsaustralia.edu.au>

Glossary

The following is a glossary of common terms relating to stem cells and stem cell treatments.^{c,7}

Adult stem cells: Stem cells found in different tissues of the developed, adult organism that remain in an undifferentiated, or unspecialised, state. These stem cells can give rise to specialised cell types of the tissue from which they came (i.e. a heart stem cell can give rise to a functional heart muscle cell, but it is still unclear whether they can give rise to all different cell types of the body).

Allogeneic transplantation: Cell, tissue or organ transplant from one member of a species to a genetically different member of the same species.

Autologous transplantation: Cell, tissue or organ transplants from one individual back to the same individual. Such transplants do not induce an immune response and are not rejected.

Differentiation: The process of development with an increase in the level of organisation or complexity of a cell or tissue, accompanied with a more specialised function.

Embryonic stem cell (ES cell): Cells derived from the inner cell mass of developing blastocysts. An ES cell is self-renewing (can replicate itself), pluripotent (can form all cell types found in the body) and theoretically is immortal.

Haematopoietic stem cells: The precursors of mature blood cells that are defined by their ability to replace the bone marrow system following its obliteration (e.g. by γ -irradiation) and can continue to produce mature blood cells.

Haematopoietic stem cell transplantation: The transplantation of haematopoietic stem cells with blood-forming potential. Haematopoietic stem cells provide rapid and sustained reconstitution of blood formation and are found in adult bone marrow, umbilical cord blood, peripheral blood and in the fetal liver.

Histocompatible: A tissue or organ from a donor (the person giving the organ or tissue) that will not be rejected by the recipient (the patient in whom the tissue or organ is transplanted). Rejection is caused because the immune system of the recipient sees the transplanted organ or tissue as foreign and tries to destroy it. Tissues from most people are not histocompatible with other people. In siblings, the probability of histocompatibility is higher, while identical twins are almost always histocompatible.

Mesenchymal stem cell (bone marrow stromal cells): Rare cells, mainly found in the bone marrow, that can give rise to a large number of tissue types such as bone, cartilage (the lining of joints), fat tissue, and connective tissue (tissue that is in between organs and structures in the body).

Multipotent stem cells: Stem cells whose progeny are of multiple differentiated cell types, but all within a particular tissue, organ, or physiological system. For example, blood-forming (haematopoietic) stem cells are single multipotent cells that can produce all cell types that are normal components of the blood.

Neural stem cell: A type of stem cell that resides in the brain, which can make new nerve cells (called neurons) and other cells that support nerve cells (called glia). In adults, neural stem cells can be found in very specific and very small areas of the brain where replacement of nerve cells is seen.

Oligopotent progenitor cells: Progenitor cells that can produce more than one type of mature cell. An example is the myeloid progenitor cell which can give rise to mature blood cells, including blood granulocytes, monocytes, red blood cells, platelets, basophils, eosinophils and dendritic cells, but not T lymphocytes, B lymphocytes, or natural killer cells.

Pluripotent stem cells: Stem cells that can become all the cell types that are found in an implanted embryo, fetus, or developed organism, but not embryonic components of the trophoblast and placenta (these are usually called extraembryonic).

^c Adapted from the ISSCR Glossary of stem cell-related terms. For a more comprehensive list of terms, visit <https://www.closerlookatstemcells.org/patient-resources/resources-from-isscr/stem-cell-glossary/>

Progenitor cell: an early descendant of a stem cell that can only differentiate (divide and with each cell division evolve more and more into different types of cells). Unlike a stem cell, a progenitor cell cannot renew itself (make more stem cells by cell division). A progenitor cell is often more limited in the kinds of cells it can become than a stem cell. In scientific terms, it is said that progenitor cells are more differentiated than stem cells.

Regenerative medicine: Medical interventions that aim to repair damaged organs, most often by using stem cells to replace cells and tissues damaged by ageing and by disease.

Stem cells: Cells that have both the capacity to self-renew (make more stem cells by cell division) as well as to differentiate into mature, specialized cells.

Totipotent stem cells: Stem cells that can give rise to all cell types that are found in an embryo, fetus, or developed organism, including the embryonic components of the trophoblast and placenta required to support development and birth. The zygote and the cells at the very early stages following fertilisation (i.e., the 2-cell stage) are considered totipotent.

Umbilical cord stem cells: Haematopoietic stem cells are present in the blood of the umbilical cord during and shortly after delivery. These stem cells are in the blood at the time of delivery, because they move from the liver, where blood-formation takes place during fetal life, to the bone marrow, where blood is made after birth. Umbilical cord stem cells are similar to stem cells that reside in bone marrow, and can be used for the treatment of leukemia and other diseases of the blood. Efforts are now being undertaken to collect these cells and store them in freezers for later use. However, one problem is that there may not be enough umbilical cord stem cells in any one sample to transplant into an adult.

Unipotent stem cells: Stem cells that self-renew as well as give rise to a single mature cell type; e.g. spermatogenic stem cells.

References

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