



Transplantation and Alternatives to Treat Autoimmune Diseases

Pravin Shende, Bernice Rodrigues, and R.S. Gaud

Abstract

Transplantation is considered as one of the methods for the treatment of autoimmune diseases. There are different sorts of transplantation which improved the situation for the cure of different kinds of autoimmune diseases. Cord blood transplantation is favored over other transplant techniques. The propelled treatments incorporate interferon administrative elements and mesenchymal stromal cells for the management of immune system issue particularly in the treatment of rheumatoid joint inflammation. According to the studies conducted, it was proven that cord blood/UC mesenchymal cells along with DMARDs, without consistent organization expanded the level of administrative regulatory T-cells of the peripheral blood which might be a protected and huge technique for the treatment of patients experiencing rheumatoid joint inflammation. This review article focusses on different organ transplantation and alternative methods to treat autoimmune condition like rheumatoid arthritis. Using 3D printing and artificial intelligence are some of the recent trends that may be used for the management of autoimmune diseases.

P. Shende (✉), B. Rodrigues, and R. S. Gaud
Shobhaben Pratapbhai Patel School of Pharmacy and
Technology Management, SVKM'S NMIMS, Mumbai,
India
e-mail: shendepravin94@gmail.com

Keywords

Stem cells · Mesenchymal stromal cells ·
Rheumatoid arthritis · Transplantation

Abbreviations

DMARDs	Disease-Modifying Antirheumatic Drugs
UC	Umbilical Cord
MSCs	Mesenchymal Stromal Cells
RA	Rheumatoid Arthritis
SCs	Stem Cells
HSCs	Hematopoietic Stem Cells
GVHD	Graft Versus Host Disease
RBCs	Red Blood Cells
IRFs	Interferon Regulatory Factors
HLA	Human Leukocyte Antigen
FLSs	Fibroblast-like synoviocytes
TH1	T helper 1
IL-18BP	Inter-leukin18 Binding Protein
TNF α -NF κ B	Tumor Necrosis Factor alpha Nuclear Factor kappa-light-chain-enhancer of activated B cells
cJUN	c-Jun N-terminal kinase
ACPAs	Anticitrullinated protein antibodies
EULAR	European Group Against Ailment
DAS	Disease Activity Scores
UC-MSC	Umbilical Cord-derived MSC
NOTA	National Organ Transplant Act

OPTN	Organ Procurement and Transplantation Network
PSDA	Patient Self-Determination Act
SGB V	Sozialgesetzbuch Fünftes Buch
TPG	German Transplantation Law
ZTCC	Zonal Transplant Coordination Center
ANNs	Artificial Neural Network
ESCs	Embryonic Stem Cells
siRNA	small interfering Ribonucleic Acid
NOC	No Objection Certificate
NGO	Non-Governmental Organization
3D	3 Dimensional

1 Introduction

Transplantation is an act of surgical transfer of healthy organ, tissue or cell from one place to another or from one organism to another. Transplantation is obligatory for patients who have an organ failure or the organs have been damaged due to some accident, injury or disease or no alternative conventional treatment available. In conventional treatment, the disease is controlled to refrain the immune system with immunosuppressant like DMARDs, cytotoxic drugs, azathioprine. These medicines reduce few signs of the illness but cause side effects like weakness, melancholy, prone to infection and may even cause cancer. In autoimmune diseases the response to immunosuppression is observed 60–70% primarily because of either disease progression or non-response to the drug used. The autoimmune diseases, in some cases, may show clinical remission to relapse (Chandrashekar 2012; Kooij et al. 2007). Presently, use of site-targeted drugs explores to reduce the toxicity of immunosuppressant drugs and also offers more robust immunosuppression effect (Feldmann and Steinman 2005). Such targeted immunosuppressive treatments do not escalate the remission rate considerably inclusive of rheumatoid arthritis (Böhm et al. 2006). Due to associated side effects of conventional drugs and treatment options,

transplantation is an alternative for the treatment and survival for human being.

The body parts like kidney, heart, lungs, liver, pancreas, intestines, stomach and testis can be transplanted and are shown in Fig. 1. The tissues, cells and fluids that can be transplanted like hand, cornea, face skin and face transplant, an islet of Langerhans, bone marrow or SC, blood cells and blood parts transfusion, blood vessels, heart valve and bone.

1.1 History

During the 500 BCE- 600 CE, the rebirth of the Lord Ganesha by cephalic transplant as depicted in Hindu scriptures (Nanda et al. 2016) is the first example of xenotransplantation on the earth as shown in Fig. 2. In 1743, William Hunter (1718–1783) stated that “ulcerated cartilage is a troublesome disease which when destroyed, it is not recovered from Hippocrates down to the present age” (Hunter et al. 1743). Since onward the efforts were made by orthopedics to develop reliable methods to restore the cartilage (Hunter 1744). Henri Judet first reported the implantation of osteochondral grafts in animals (Judet 1908) but the clinical use of allograft joint transplants was first introduced by Lexer in 1908 (Nikalaou and Giannoudis 2017; Langer and Gross 1974). A patient in 1838 underwent the first corneal xenotransplantation (from a pig), whereas transplantation of the first corneal allograft (human-to-human) was carried out in 1905 (Cooper 2012). Hara and Cooper reviewed the field of corneal xenotransplantation (Hara and Cooper 2010, 2011). By 1925, Lexer had documented 34 hemi or whole knee allogenic implants in humans and reported a 50% success rate (Lexer 1925). By the 1960s, Keith Reemtsma said that kidney transplant other than that of human might function in human recipients and thus be a successful treatment for renal failure. Earlier transplantation of kidney from a deceased person to a patient with a kidney failure was less as the numbers of deaths were less. So he performed a research wherein he

Fig. 1 Major organs used for transplantation

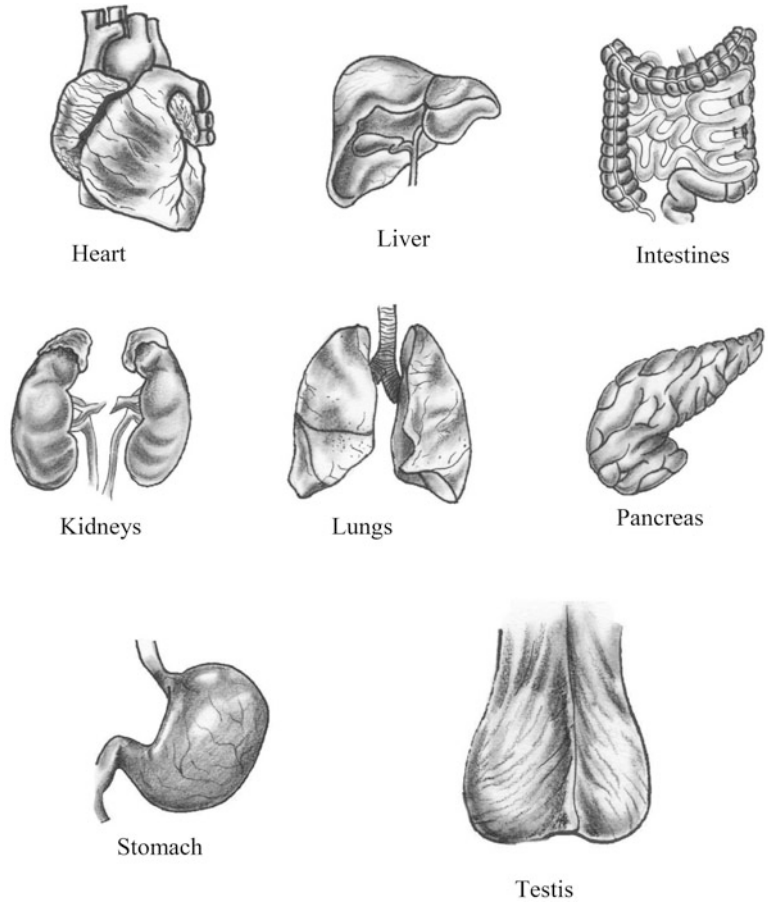
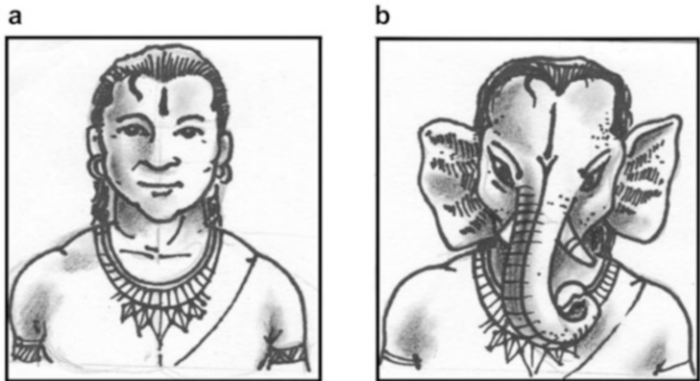


Fig. 2 Picture of Lord Ganesha (a) before and (b) after transplantation



said he could give life to a patient by providing him with a kidney from a non-human primate. In this case, kidney of a chimpanzee was used to transplant it into the patient (Reemtsma et al. 1964) but most of the patients died within few weeks. Fortunately, one patient survived for few months and then expired. After autopsy, it was found out that no signs of acute or chronic rejection appeared in the chimpanzee kidneys. The patient had suffered from electrolyte imbalance because the transplant was from a non-human primate. In 1967, Barnard and his colleagues established the procedure of cardiac allotransplantation (Barnard 1967), two cardiac xenotransplants were also carried out by them (Barnard et al. 1977). In 1983, Leonard Bailey performed a surgical procedure which involved the transplantation of a baboon heart known as Baby Face into an infant girl. It was technically successful but the patient died in 20 days later as the graft underwent acute rejection (Starzl et al. 1966). It was concluded that the rejection was caused due to the blood type 'O' which is primarily not found in baboon. Tom Starzl, performed liver transplants from a nonhuman primate to a human which was unsuccessful in the 1960s (Starzl 1969; Starzl et al. 1974; Giles et al. 1970). He performed two liver transplants in the 1990s but failed again as the patient lasted for just a few days (Starzl et al. 1993). In 1993, a Swedish group first attempted to transplant a pig islet in patients with diabetes was carried out. The group was headed by Carl Groth (Groth et al. 1994; Alexander BR P OFM 2008). The timeline of successful transplants started from 1905 and is illustrated in Fig. 3.

1.2 Advantages

Societal Duty Everyone has a societal duty to contribute for the betterment of the community. The donation of organs to the patients in need and help them to endure is a noble cause which can serve the society.

Supports the Family of the Deceased For a healthy and a productive life of a person who is in need of an organ transplant.

Imparts a New Hope for Normal Life Organ transplant gives a new hope to the recipients.

Recovers Life In the case of kidney dysfunction, the patients depend on dialysis due to kidney failure for their entire life but when a kidney transplant is done they get a new life.

1.3 Disadvantages

Complications During and After Surgery The complications include severe hemorrhage, blood clot formation or development of infection at the site where the surgical procedure was performed. In some cases the doctor can control such complication but in exceptional cases such complications may be fatal to the donor.

The Overall Health in the Long Term Individual may face some adverse reactions depending on the organ of live donor. For example, hypertension or kidney failure may be caused if a healthy person donates one kidney.

Financial Problems High cost in surgery in transplantation.

Trade of Human Vital Organs The prohibited and immoral trade of organs in *illicit business* is the most negative impact that has affected the society.

Transplantation is classified on basis of organs or tissues to be transplanted and the anatomical site and is depicted in Fig. 4.

Organ transplantation is a major task due to lack of organ donors and large number of recipients. In order to overcome such problems, various alternatives are used for treating autoimmune diseases without organ transplantation include bone marrow replacement therapy, SC

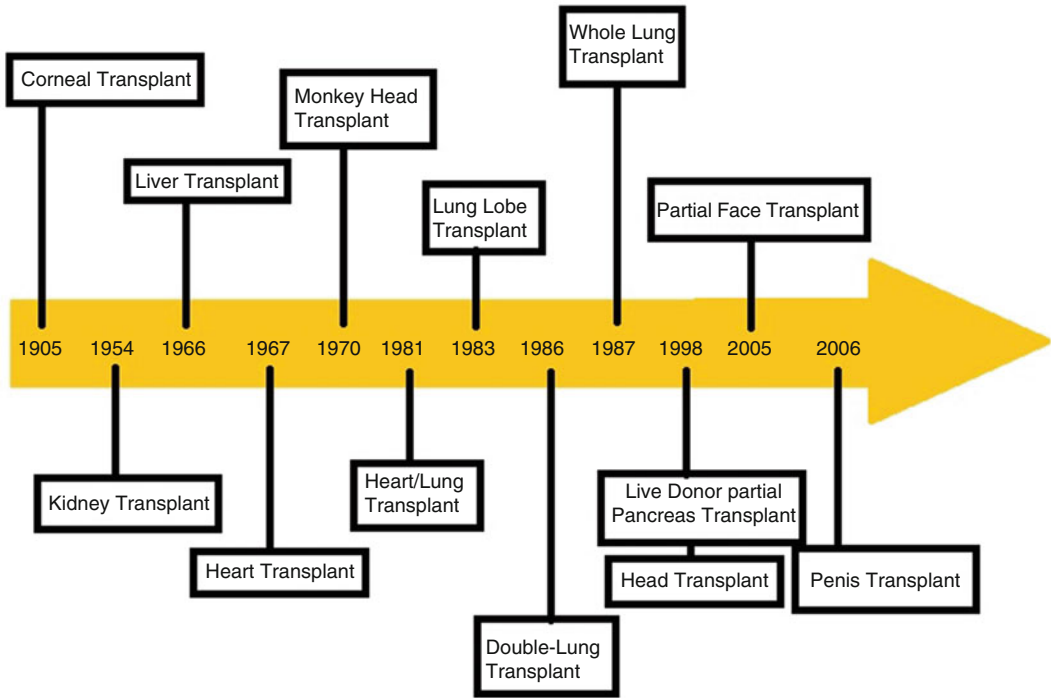


Fig. 3 The time-line of successful transplants

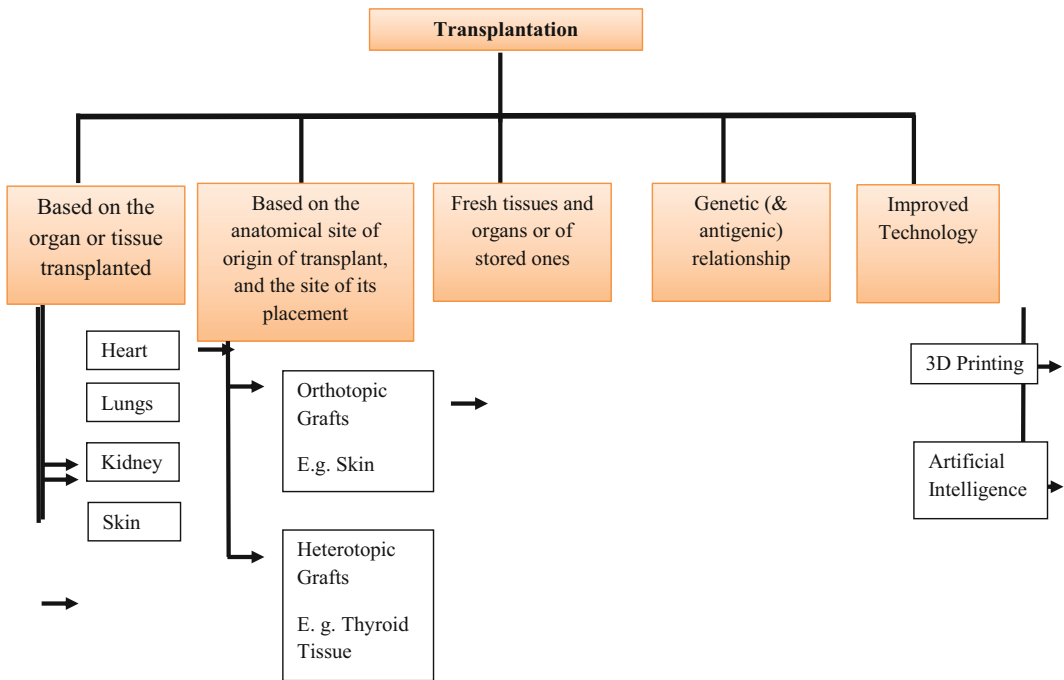


Fig. 4 Classification of transplantation

transplantation, cord blood cells some medical devices, and medicines like immunosuppressant.

2 Bone Marrow Transplantation

A fatty tissue and spongy structure that is present inside bones which contains immature cells known as SCs is called the bone marrow. The bone marrow produces red platelets which are utilized to transport oxygen, white platelets which act against disease and platelets which are in charge of the arrangement of clumps. The structure of bone marrow incorporates juvenile blood-framing undifferentiated cells known as hematopoietic foundational microorganisms, or HSCs which can possibly duplicate through cell division and either remain immature microorganisms or separate and develop into a wide range of blood cells. A bone marrow is a methodology to supplant a man's flawed or harmed foundational microorganisms with solid cells. The beneficiary gets solid foundational microorganisms either from a sound donor or they can originate from a similar individual's body. Ailments like leukemia, serious blood sicknesses, for example, thalassemia, aplastic iron deficiency and sickle cell weakness including various myeloma and certain resistant lack diseases. There are various types of bone marrow transplants which include autologous transplant that use its own SCs, allogenic transplants (cells from a donor and/or UC blood transplant where right after birth the SCs from a newborn UC are removed). The SC procedure is usually performed after completion of chemotherapy and radiation therapy. The delivery of SCs into the bloodstream is carried out using central venous catheter. The SCs flow through the blood to the bone marrow and no surgery is required. The way a donor cell is collected can be classified in two ways as shown in the Table 1.

Bone marrow procedure is performed in the cases of certain cancers like leukemia, diseases that affect the production of bone marrow cells

like aplastic anemia, severe immune system illnesses like sickle cell anemia and if chemotherapy has destroyed the bone marrow. Chest pain, hypotension, taste disturbances, shortness of breath etc. may be some risks that are involved in bone marrow transplantation. The complications of bone marrow therapy may depend on the treatment of the disease, whether chemotherapy or radiation is conducted before the bone marrow transplant and the dosages of such treatments, the match with the donor and the type of bone marrow transplant received etc. Delayed growth in children who receive a bone marrow transplant, GVHD, infections, which can be very serious, stomach problems, early menopause are few of the complications that may occur due to bone marrow transplant.

The various terminologies of bone marrow transplant are shown in the Fig. 5.

2.1 UC Transplantation/Cord Blood Cells

The UC is being cut after a baby is born. The placenta contains some amount of blood vessels and also the part of the UC that is in contact of the baby contains these blood vessels. After birth, this extra blood is not needed by the baby. This blood is called placental blood or UC blood "cord blood". This is the motivation for line blood can be utilized for transplantation as a contrasting option to bone marrow. This system has been utilized as another option to bone marrow transplant. Cord Blood transplants have mostly been used for patients suffering from blood and immune system diseases (Ballen 2005; Lubin and Shearer 2007; Meyer et al. 2005).

2.1.1 The Advantage to Patients

Availability The prescreening and testing of selected cord blood and was frozen for the future use.

Table 1 Differentiation in collecting donor cell

Bone marrow harvest	Leukapheresis
Minor surgery where the donor is given general anesthesia and is mostly a pain-free technique.	The blood is withdrawn from the donor through the IV line.
The region at the back and of both the hips is considered as a site for bone marrow removal and the amount of bone marrow removal depends on the weight of the recipient.	The SCs are given to the recipient prior to which they are separated from the part of white blood cells by a machine. The RBCs are then returned back to the donor.

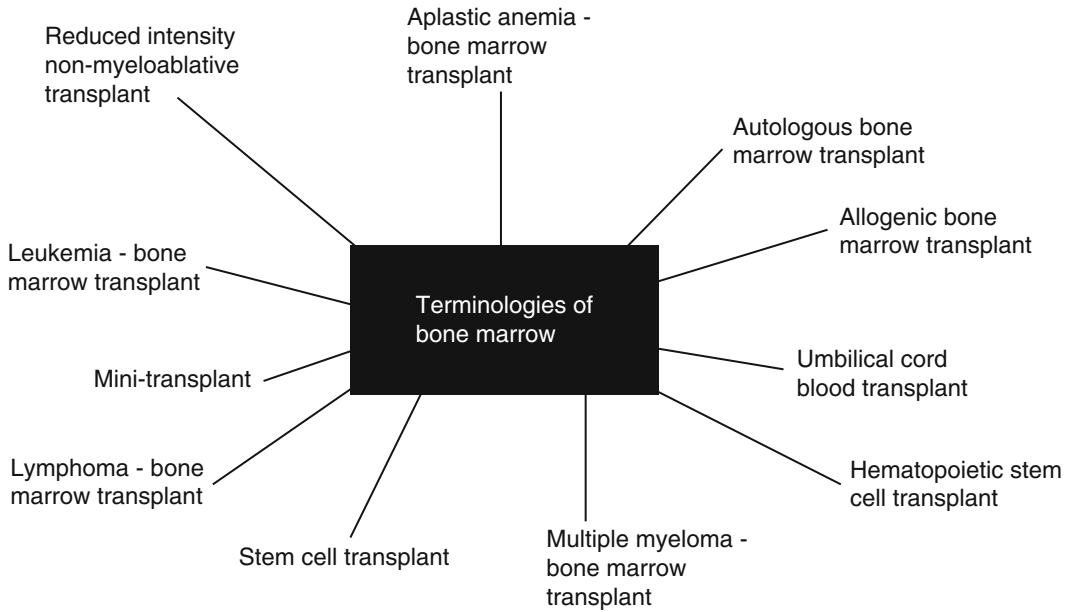


Fig. 5 Terminologies used for bone marrow transplant

GVHD Lesser people are suffering from this disease.

Infectious Disease Transmission Transplantation with the cord blood SC limits the diseases caused by blood-blood transfusion.

HLA Matching Transplants are subjected to the level of HLA coordinating among the transplant beneficiary and the contributor string blood. HLA coordinating assumes an essential part of effective engraftment, the seriousness of GVHD and general survival. A patient’s result after transplantation can be by enhancing a nearby match amongst the individual and the cord blood unit.

2.1.2 Disadvantage

Storage The effectiveness of storage of cord blood can be frozen or stored is not known. The successful transplantation of cord blood samples that have been preserved for 10 years have been reported.

Engraftment Individual’s weight, age and illness status decides the quantity of cells required for transplant in a patient. Due to the presence, fewer undeveloped cells in the cord blood unit the engraftment of cord blood SC is better from bone marrow or peripheral blood. Until the point that

engraftment happens, patients are in danger of creating hazardous diseases. Cord blood transplant may make beneficiaries be defenseless against diseases for a normal of 1–2 months which is more than marrow and fringe blood undeveloped cell beneficiaries.

Clinical Data Transplantation is carried out to a patient via donor cord blood SCs, even if the genetic diseases present in the individual that are not evident at the time of birth, hence routine checkup must be conducted.

3 Advanced Therapy

3.1 IRFs

These were first identified as regulators of virus-induced type I interferon (IFN A and B) gene expression (Ning 2014; Matta et al. 2017). Several findings stated that IRFs play a major role in regulating both innate and adaptive immune responses, and are also involved in the activation and differentiation of distinct immune cell populations (Tamura et al. 2008; Battistini 2009). Currently, 10 IRFs have been discovered in vertebrates of which some are inactive in humans and in mice. (Nehyba et al. 2009).

3.1.1 RA

RA is a systemic autoimmune diseases that is caused by expansion of synovial tissue, chronic inflammation and progressive damage of a joint. Several immune cell subsets such as macrophages, monocytes, neutrophils, dendritic cells, natural killer cells, T-cells, and B-cells perform an important part in RA pathogenesis. The major pro-inflammatory cytokines that show a prominent function in RA development are TNF α , IL1b and IL6. The major constituents of synovial hyperplasia are FLSs and FLS-dependent effector molecules are known as important mediators of RA. FLS show critical part to occupy cartilage and bone tissue (Ganesan and Rasool 2017). IL18, a cytokine for RA

pathogenesis, (Gracie et al. 1999) promotes T-cells to produce TH1 type cytokines and helps in the differentiation of TH1 cells. The biologic activity of IL18 is controlled by IL-18BP, which has an IRF1 binding site in the IL-18BP promoter (Hurgin et al. 2002). During joint replacement or synovectomy, the fibroblasts were isolated from synovium of RA patients and an *in vitro* knock-down system was utilized to analyze the effect of TNF α -induced IRF1 nuclear translocation and regulate IL-18BP expression when NF κ B or JNK2 signaling pathway was blocked, IRF1 nuclear translocation was reduced. Further, it was shown that IRF1 forms a complex with NF κ B and cJUN in the nucleus (Marotte et al. 2011). ACPAs found to persuade IRF4 and IRF5 protein expression. IRF5 siRNA weakened ACPA movement fundamentally while ACPAs prompted IRF5 action and prompted M1 macrophage polarization. (Zhu et al. 2015).

3.2 MSC Treatment for Autoimmune Disease

The first effective therapeutic use of MSCs was stated in year 2000 for bone marrow graft enhancement in humans (Koc et al. 2000). There are various factors like diverse and multiple are responsible for the practical biological effects of MSC. The first *in vivo* model showed a positive effect of MSC on a murine skin graft model similar positive reports have been seen in many autoimmune diseases like RA, multiple sclerosis (Bartholomew et al. 2002; Tyndall and Uccelli 2009). Besides pharmacological advantages, it has been used in cosmetic surgery in the treatment of burns.

3.2.1 RA

Four patients suffering from RA accepting allogeneic or bone marrow-determined MSC IVI was basically negative, however no adverse condition was observed. Two of the three had a EULAR direct reaction at a half-year yet encountered backslide at 7 and 23 months, separately. Two patients had no EULAR reaction to MSC

transplant. No patient accomplished the DAS-28-characterized abatement in the follow-up period (Liang et al. 2012; Djouad et al. 2005). Not with standing, a moment bigger, non-randomized relative trial in 172 RA patients with dynamic RA who had deficient reactions to conventional prescription was distributed in which 136 patients received 40 x10⁶ allogeneic UC-MSD and 36 patients received just the cell-dissolvable without the cells. The two treatment choices were: DMARDs in addition to medium without UC-MSD, or DMARDs in addition to UC-MSD gather through intravenous infusion. No genuine unfriendly impacts were seen amid or after imbuement. The helpful impacts kept up for 3–6 months without consistent organization, associating with the expanded level of administrative WBCs in fringe blood. Conversely, there were no such advantages saw in the control gathering of DMARDs in addition to medium without UC-MSD. No patients demonstrated intense genuine reactions either amid or after UC-MSD imbuement, and 4% indicated mellow unfriendly impacts amid the mixture, for example, chill and additionally fever (< 38.5 8C), which vanished inside 2 h with no treatment. No major strange discoveries in hematologic or serum science profiles were found in the investigation. It was reasoned that treatment with DMARDs in addition to UC-MSD may give sheltered, noteworthy, and industrious clinical advantages for patients with dynamic RA (Wang et al. 2013; Ra et al. 2011).

3.3 Dendritic Cells-Derived Exosomes

Resemblance to biology of the cell from which they are derived, dendritic cells have gained importance in the treatment of autoimmune diseases and tumor (Sousa et al. 2017). They overcome barriers like synovial membrane and the blood-brain. These molecules can interfere with different pathways; they are likely to possess more target and long-lasting therapeutic effect due to hyper branched structure (Aryani and Denecke 2016).

4 Worldwide Regulatory Aspects

4.1 USA

In 1968, the Uniform Anatomical Gift Act was enacted to solve the problems of different rules of transplantation in states and provided an outline of even laws in the United States related to organ and tissue transplantation. The Uniform “Organ Contributor Card” was authorized in 1972 which was an authoritative report in every one of the 50 states under the Uniform Anatomical Blessing Act. This engaged any individual matured 18 years or more to lawfully make a promise to give his organs upon death. The OPTN in 1984 by the NOTA expressed that the purchasing and offering of organs are precluded. Also, the installment of “the costs of movement, lodging, and lost wages brought about by the (living) contributor” is allowed in segment 301(Arthur 2008). The various acts along with their roles are shown in Table 2.

4.2 South Africa

On 2nd May 2005, the National Wellbeing Act 61 of 2003 (South Africa, 2003) became effective. In 1983, the Human Tissue Act 65 states that any person of 16 years or more should make a will or a record with his/her marks and 2 witnesses demonstrating the desire for organ gift. (Slabbert and Mnyongani 2011).

4.3 Europe

The Mandate 2010/45/EU on the norms of value and security of human organs required for transplantation was received on seventh July 2010. The point was to absorb the gauges of value and security and grow more proficient transplantation frameworks. The European Parliament presented the Activity Anticipate Organ Gift and Transplantation (2009–2015) notwithstanding the order. In Article 19 et. Seq. the Gathering of Europe made extraordinary standards on organ expulsion.

Table 2 Various Acts and their roles

Year	Act	Role
1987	Uniform anatomical gift act (amended)	Expressed to encourage a helpful and uniform lawful condition of organ gift all through the nation
1991	PSDA	Engages and advances the utilization of propelling mandates, for example, living wills and sturdy forces of the lawyer for human services.
1999	Organ donor leave act	Leave of 7 days for bone marrow gift and 30 days for strong organ gift is accommodated an organ benefactor who is the government workers.
1999	Organ procurement and transplantation network final rule	The reason for the last govern is to help accomplish the most evenhanded and therapeutically compelling use of human organs that are given in trust for transplantation
2000	Children's health act	The law tends to the uncommon need of youngsters who are beneath the age of 18 years.
2004	Organ donation and recovery improvement act	Gives subsidizing to the states, in the accompanying cases: Bolster organ gift programs so that there are more organ benefactors. Give money related help to living contributors which includes travel allowances and other benefits Accidental non-restorative costs.

4.4 Germany

On 5th November 1997 the Act was passed by the German Bundestag which came into force on 1st December 1997; on 4th September 2007 and on 1st August 2012, an amended version of the act was published wherein the later stated that all health insurance members who are 16 years or older will be asked frequently if they are willing to donate their organs.

4.4.1 Law for Post-Mortal Organ Donation under the TPG

The law stated that if the individual give prior permission for organ donation after his/ her death only then the organs will be transplanted.

4.4.2 Law for Living Donation under the TPG

Once a living donation is carried out, the recipient has to be ensured that he/ to no expected hazard past that of the operation. Organs that make them recharge properties can be given to obscure people, the gift of non-regenerative organs (e.g. kidney, parts of the liver) is allowable to transplant to relatives or with whom the donor has a very close personal relationship. The code of SGB V state expresses that a living donor has an expansive case against the health care coverage of the organ recipient, for example,

therapeutic treatment, recovery, travel costs, ailment pay. On the other hand, the organ recipient can guarantee for repayment of wages in the event that he can't work.

Guidelines and opinions of the German Medical Association.

The German Medical Association (Bundesärztekammer) establishes Guidelines for specific areas of transplantation medicine. The "Permanent Committee for Organ Transplants of the German Medical Association" (Ständige Kommission Organ transplantation der Bundesärztekammer) elaborates these guidelines and keep it updated at regular intervals.

4.5 Regulatory Aspects in India

In 1994, the transplantation of Human Organs Act was passed. The aim was to regulate the removal, storage and transplantation of human organs for therapeutic purposes and also to prevent the commercial dealings of human organs. The 3 states Maharashtra, Himachal Pradesh and Goa initiated the act (who therefore adopted it by default) and which was subsequently adopted by all states except Jammu and Kashmir and Andhra Pradesh. In 2009 the states Goa, Himachal Pradesh and West Bengal proposed an amendment to address inadequacies in the efficacy,

Table 3 Amendments of 2009 and 2013

Transplantation of human organs (Amendment) Bill, 2009	Transplantation of human organs (Amendment) Bill, 2013
This amendment bill offers regulation of the transplantation of human tissue along with organ transplant	A composite set of guidelines for dealing with deceitful practices and for countering illegal organ transplant
It was necessary that every organ donation case should go to the authorization committee first.	Along with an authorization committee, there will be a 'verification committee' to check the details provided by the donor and recipient.

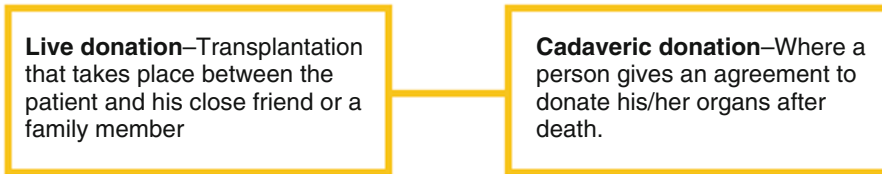


Fig. 6 Types of donation

relevance and impact of the Act. In 2011, the amendment to the Act was passed by the parliament, and in 2014 the rules were notified.

The various amendments done in the act are shown in Table 3.

4.6 Types of Donations

The types of donation are live donation and cadaveric donation. It is shown in Fig. 6.

4.6.1 Steps Involved in Organ Donation

The steps for organ transplant is shown in the Table 4.

4.6.2 Requirements for Recipient

- Get an NOC by registering yourself with the ZTCC for cadaveric donations.
- Your physician can assist or guide you through the process of registering.
- Cross-matching is a must for every organ transplant

5 Future Perspective

5.1 Artificial Intelligence

Studies demonstrated that computerized reasoning can be utilized as an apparatus to distinguish donor beneficiary by utilizing ANNs for benefactor coordinating in liver transplantation (Briceño et al. 2014).

5.2 3D Printing

This innovation has been utilized to make blood manufactured vessels. Chen and his group created advanced 3D microstructures that copy the perplexing plans and elements of organic tissues. The veins that were embedded were not yet equipped for different capacities like transporting supplements and waste. In any case, researchers say that it can be enhanced sooner rather than later. (Zhu et al. 2017).

A biotechnology organization, in particular, Sichuan Revotek situated in Chengdu, China, has effectively embedded a printed segment of the vein into a monkey. Organovo, a firm in San

Table 4 Steps for organ donation

Donating to your own family member	In case of cadaver donation
Individual needs an NOC from the government if he/she wants to donate an organ	An organ donation card will be arranged for an individual after registration with any NGO, if you want to donate an organ.
Individual has to undergo a complete health check-up along with a blood cross matching test before the operation.	Your family must be informed about your willingness so that after the death of the individual doctor may go for organ harvesting.
	The body has to be covered properly after transplantation and returned to the family members in an aesthetic manner
	After being declared brain dead or after death the organs of an individual are tested for their usability.

Diego, declared that it had transplanted printed human-liver tissue into mice and that this tissue had survived and worked. Johnson and Johnson, L'Oréal, Proctor and Gamble, and BASF are chipping away at printing human skin. They propose to utilize it to test their items for unfavorable responses.

5.3 Nuclear Transplantation, ESCs and the Potential for Cell Therapy

Nuclear transplantation is also known as nuclear cloning or nuclear transfer. It alludes to a procedure where a cloned fetus is created by the presentation of a core from a grown-up benefactor cell into an enucleated oocyte. The incipient organism show in the female uterus has the ability to develop into a newborn child which would be a clone of the grown-up contributor cells. This developing life produces embryonic foundational microorganisms that can possibly turn out to be any sort of cells shown in the grown-up body. As embryonic undifferentiated organisms are inferred by atomic exchange they are hereditarily indistinguishable to the contributor and are along these lines valuable for some remedial applications, this procedure is called "nuclear transplantation therapy" or "therapeutic cloning." Restorative cloning may be utilized to enhance the treatment of blood issue, neurodegenerative sicknesses or diabetes. (Hochedlinge and Jaenisch 2003).

6 Conclusions

Autoimmune disease is a condition wherein body's own cells attack individual's own cells and disrupt the immune system. Various techniques of transplantation like bone marrow transplantation and cord blood cells have been employed for the treatment of autoimmune diseases. Cord blood method along with the use of DMARDs is most effective technique used in the management of rheumatoid arthritis. Newer approaches like IRFs and mesenchymal stromal cells have been used in the treatment of autoimmune diseases. The combination of MSCs with DMARDs is considered to be therapeutically effective as compared to the individual technique.

References

- Alexander BR P OFM (2008) Organ transplantation (Catholic-Ethical-Appraisal)
- Arthur C (2008) Regulation of organ transplants: a comparison between the systems in the United States and Singapore
- Aryani A, Denecke B (2016) Exosomes as a nanodelivery system: a key to the future of neuromedicine. *Mol Neurobiol* 53:818–834
- Ballen KK (2005) New trends in umbilical cord blood transplantation. *Blood* 105:3786–3792
- Barnard CN (1967) A human cardiac transplant: an interim report of a successful operation performed at Groote Schuur hospital, Cape Town. *S Afr Med J* 41 (48):1271–1274
- Barnard CN, Wolpowitz A, Losman JG (1977) Heterotopic cardiac transplantation with a xenograft for assistance of the left heart in cardiogenic shock after

- cardiopulmonary bypass. *S Afr Med J* 52 (26):1035–1038
- Bartholomew A, Sturgeon C, Siatskas M, Ferrer K, McIntosh K, Patil S, Hardy W, Devine S, Ucker D, Deans R, Moseley A, Hoffman R (2002) Mesenchymal stem cells suppress lymphocyte proliferation in vitro and prolong skin graft survival in vivo. *Exp Hematol* 30:42–48
- Battistini A (2009) Interferon regulatory factors in hematopoietic cell differentiation and immune regulation. *J Interf Cytokine Res* 29(12):765–780
- Böhm M, Luger TA, Schneider M, Schwarz T, Kuhn A (2006) New insight into immunosuppression and treatment of autoimmune diseases. *Clin Exp Rheumatol* 24 (1 Suppl 40):S67–S71
- Briceño J, Cruz-Ramírez M, Prieto M, Navasa M, Ortiz de Urbina J, Orti R, Gómez-Bravo MÁ, Otero A, Varo E, Tomé S, Clemente G, Bañares R, Bárcena R, Cuervas-Mons V, Solórzano G, Vinaixa C, Rubín A, Colmenero J, Valdivieso A, Ciria R, Hervás-Martínez C, de la Mata M (2014) Use of artificial intelligence as an innovative donor-recipient matching model for liver transplantation: results from a multicenter Spanish study. *J Hepatol* 61(5):1020–1028
- Chandrashekhara S (2012) The treatment strategies of autoimmune disease may need a different approach from conventional. *Indian J Pharm* 44(6):665–671
- Cooper DKC (2012) A brief history of cross-species organ. *Transplantation* 25(1):49–57
- Djouad F, Fritz V, Apparailly F, Louis-Pence P, Bony C, Sany J, Jorgensen C, Noël D (2005) Reversal of the immunosuppressive properties of mesenchymal stem cells by tumor necrosis factor alpha in collagen-induced arthritis. *Arthritis Rheum* 52(5):1595–1603
- Feldmann M, Steinman L (2005) Design of effective immunotherapy for human autoimmunity. *Nature* 435:612–619
- Ganesan R, Rasool M (2017) Fibroblast-like synoviocytes-dependent effector molecules as a critical mediator for rheumatoid arthritis: current status and future directions. *Int Rev Immunol* 36(1):20–30
- Giles GR, Boehmig HJ, Amemiya H, Halgrimson CG, Starzl TE (1970) Clinical heterotransplantation of the liver. *Transplant Proc* 2(4):506–512
- Gracie JA, Forsey RJ, Chan WL, Gilmour A, Leung BP, Greer MR, Kennedy K, Carter R, Wei XQ, Xu D, Field M, Foulis A, Liew FY, McInnes IB (1999) A proinflammatory role for IL-18 in rheumatoid arthritis. *J Clin Invest* 104(10):1393–1401
- Groth CG, Korsgren O, Tibell A, Tollemar J, Moller E, Bolinder J, Ostman J, Reinholt FP, Hellerstrom C, Andersson A (1994) Transplantation of porcine fetal pancreas to diabetic patients. *Lancet* 344 (8934):1402–1404
- Hara H, Cooper DKC (2010) The immunology of corneal xenotransplantation: a review of the literature. *Xenotransplantation* 17(5):338–349
- Hara H, Cooper DKC (2011) Xenotransplantation—the future of corneal transplantation? *Cornea* 30 (4):371–378
- Hochedling K, Jaenisch R (2003) Nuclear transplantation, embryonic stem cells, and the potential for cell therapy. *N Engl J Med* 349:275–286
- Hunter W (1743) Of the structure and disease of articulating cartilages. *Clin Orthop Relat Res* 1995:3–6
- Hunter W (1744) Of the structure and diseases of articular cartilages. *Phil Trans* 1744:514–521
- Hurgin V, Novick D, Rubinstein M (2002) The promoter of IL-18 binding protein: activation by an IFN-gamma-induced complex of IFN regulatory factor 1 and CCAAT/enhancer binding protein beta. *Proc Natl Acad Sci USA* 99(26):16957–16962
- Judet H (1908) Essai sur La greffe des tissus articulaires. *C R Acad Sci* 193–196:600–603
- Koc ON, Gerson SL, Cooper BW, Dyhouse SM, Haynesworth SE, Caplan AI, Lazarus HM (2000) Rapid hematopoietic recovery after co-infusion of autologous-blood stem cells and culture-expanded marrow mesenchymal stem cells in advanced breast cancer patients receiving high-dose chemotherapy. *J Clin Oncol* 18:307–316
- Langer F, Gross AE (1974) Immunogenicity of allograft articular cartilage. *J Bone Joint Surg Am* 56:297–304
- Lexer E (1925) Joint transplantation and arthroplasty. *Surg Gynecol* 40:782–789
- Liang J, Li X, Zhang H, Wang D, Feng X, Wang H, Hua B, Liu B, Sun L (2012) Allogeneic mesenchymal stem cells transplantation in patients with refractory RA. *Clin Rheumatol* 31:157–161
- Lubin BH, Shearer WT (2007) Cord blood banking for potential future transplantation. *Pediatrics* 119:165–170
- Marotte H, Tsou PS, Rabquer BJ, Pinney AJ, Fedorova T, Lalwani N, Koch AE (2011) Blocking of interferon regulatory factor 1 reduces tumor necrosis factor alpha-induced interleukin-18 bioactivity in rheumatoid arthritis synovial fibroblasts by induction of interleukin-18 binding protein a: role of the nuclear interferon regulatory factor 1-NF-kappaB-c-jun complex. *Arthritis Rheum* 63(11):3253–3262
- Matta B, Uthoff-Hachenberg C, Waisman A (2017) Interferon regulatory factor signaling in autoimmune disease. *Cytokine* 98:15–26
- Meyer EA, Hanna K, Gebbie K (2005) Cord blood: establishing a national hematopoietic stem cell bank program. The National Academies Press, Washington, DC
- Nanda A, Filis A, Kalakoti P (2016) Mythological and pre-historical origins of neurosurgery. *World Neurosurg* 89:568–573
- Nehyba J, Hrdlickova R, Bose HR (2009) Dynamic evolution of immune system regulators: the history of the

- interferon regulatory factor family. *Mol Biol Evol* 26 (11):2539–2550
- Nikalaou VS, Giannoudis PV (2017) History of osteochondral allograft transplantation injury. *Int J Care Injured* 48(7):1283–1286
- Ning S (2014) Interferon regulatory factors and autoimmune diseases, HSOA. *J Med Genom Biomarkers* 1:001
- Salloum WD, Pan HF, Xu Y, Ye DQ (2013) Interferon regulatory factor 5 and autoimmune lupus. *Expert Rev Mol Med* 15:e6
- Ra JC, Kang SK, Shin IS, Park HG, Joo SA, Kim JG, Kang BC, Lee YS, Nakama K, Piao M, Sohl B, Kurtz A (2011) Stem cell treatment for patients with autoimmune disease by systemic infusion of culture-expanded autologous adipose tissue derived mesenchymal stem cells. *J Transl Med* 9:181
- Reemtsma K, Mccracken BH, Schlegel JU, Pearl MA, Pearce CW, Dewitt CW, Smith PE, Hewitt RL, Flinger RL, Creech O Jr (1964) Renal heterotransplantation in man. *Ann Surg* 160:384–410
- Slabbert M, Mnyongani FD (2011) Law, religion and organ transplants. *Koers* 76(2):261–282
- Sousa C, Pereira I, Santos AC, Carbone C, Kovačević AB, Silva AM, Souto EB (2017) Targeting dendritic cells for the treatment of autoimmune diseases. *Colloids Surf B Biointerfaces* 158:237–248
- Starzl TE (1969) Orthotopic heterotransplantation. In: Starzl TE (ed) *Experience in hepatic transplantation*. WB Saunders, Philadelphia, p 408
- Starzl TE, Marchioro TL, Faris TD, McCardle RJ, Iwaski Y (1966) Avenues of future research in homotransplantation of the liver with particular reference to hepatic supportive procedures, antilymphocyte serum, and tissue typing. *Am J Surg* 112(3):391–400
- Starzl TE, Ishikawa M, Putnam CW, Porter KA, Picache R, Husberg BS, Halgrimson CG, Schroter G (1974) Progress in and deterrents to orthotopic liver transplantation, with special reference to survival, resistance to hyperacute rejection, and biliary duct reconstruction. *Transplant Proc* 6(4 Suppl1):129–139
- Starzl TE, Fung J, Tzakis A, Todo S, Demetris AJ, Marino IR, Doyle H, Zeevi A, Warty V, Michaels M, Kusne S, Rudert WA, Trucco M (1993) Baboon-to-human liver transplantation. *Lancet* 341(8837):65–71
- Tamura T, Yanai H, Savitsky D, Taniguchi T (2008) The IRF family transcription factors in immunity and oncogenesis. *Annu Rev Immunol* 26:535–584
- Tyndall A, Uccelli A (2009) Multipotent mesenchymal stromal cells for autoimmune diseases: teaching new dogs old tricks. *Bone Marrow Transplant* 43:821–828
- Van der Kooij SM, de Vries- Bouwstra JK, Goekoop-Ruiterman YP, van Zeben D, Kerstens PJ, Gerards AH, de Vries-Bouwstra JK, Güler-Yüksel M, Zwinderman AH, Kerstens PJSM, van der Lubbe PAHM, de Beus WM, Grillet BAM, Ronday HK, Huizinga TWJ, Breedveld FC, Dijkmans BAC, Allaart CF (2007) Limited efficacy of conventional DMARDs after initial methotrexate failure in patients with recent onset rheumatoid arthritis treated according to the disease activity score. *Ann Rheum Dis* 66:1356–1362
- Wang L, Cong X, Liu G, Zhou J, Bai B, Li Y, Bai W, Li M, Ji H, Zhu D, Wu M, Liu Y (2013) Human umbilical cord mesenchymal stem cell therapy for patients with active rheumatoid arthritis: safety and efficacy. *Stem Cells Develop* 22(24):3192–3202
- Zhu W, Li X, Fang S, Zhang X, Wang Y, Zhang T, Li Z, Xu Y, Qu S, Liu C, Gao F, Pan H, Wang G, Li H, Sun B (2015) Anti-citrullinated protein antibodies induce macrophage subset disequilibrium in RA patients. *Inflammation* 38(6):2067–2075
- Zhu W, Qu X, Zhu J, Ma X, Patel S, Liu J, Chen S (2017) Direct 3D bioprinting of prevascularized tissue constructs with complex microarchitecture. *Biomaterials* 124:106–115