Allogeneic blood stem cell transplantation

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The development of haematopoietic blood stem cell transplantation after World War II was stimulated by the concept of having an efficient treatment against irradiation damage after the military use of nuclear weapons and after accidents in nuclear plants. In 1956, Barnes and colleagues reported the successful transplantation of bone marrow in a mouse model after irradiation [1]. The first transplantation of bone marrow after supralethal irradiation in man was reported by Thomas and colleagues in 1957 [2]. However, the transplantation was only successful in patients receiving the marrow of an identical twin [3].

In the following years, it was recognised that immunoreactive cells of donors are able to induce a disease in the recipient, which was described as "wasting syndrome" [4]; later on, the term Graft-versus-Host disease (GvHD) was introduced [5,6]. One of the most important scientific achievements in the field of transplantation was the discovery of the underlying genetic factors in the human leukocyte antigen system (HLA) by Dausset and van Rood [7,8]. By applying this knowledge, the early catastrophic results were improved [9].

Serologic test methods for human leukocyte antigen (HLA) typing were introduced in the early 1970s. From then on, individual patients with otherwise fatal diseases could be cured by bone marrow transplants [10–12]. In 1968 and 1969, three children suffering from immune deficiency syndromes were successfully transplanted and the Seattle team reported, in 1972, successful transplants in patients with severe aplastic anaemias [13].

The period between 1976 and 1985 was characterised by a rapid increase of transplants and the establishment of transplant centres in many countries. The supportive care procedures improved. The procedure was applied in many malignant and non malignant diseases. The first report about transplants in patients with acute myeloid leukaemias in first complete remission was published in 1979 [14].

E.D. Thomas received the Nobel Prize in medicine in 1990. He described the milestones of blood stem cell transplantation to be: (i) cytomegalovirus (CMV) treatment, (ii) conditioning protocols with chemotherapy only, (iii) donors lymphocytes infusions, (iv) peripheral blood stem cells and cord blood stem cell, (v) molecular typing strategies, and (vi) a worldwide network of unrelated blood stem cell volunteers [15]. His review was updated by F. Appelbaum more recently [16].

Stem cell sources

Bone marrow

Bone marrow is aspirated after multiple punctures from the posterior iliac crest under general anaesthesia.

Peripheral blood stem cells

After 4–5 days pretreatment with **granulocyte colony-stimulating factor** (GCSF) a large volume cytapheresis is performed. If the target yield can not be achieved, a second apheresis is done on the following day [17–20].

Cord blood

A harvest of the remaining cord blood, preparation and freezing procedures are critical steps to receive sufficient numbers of haematopoietic stem cells [21–23].

The transplantation of cord blood is now also regarded as a safe procedure in adults [24,25].

Transplant engineering

To reduce the morbidity and mortality from GvHD, *in vitro* depletion methods were developed and the administration of monoclonal antibodies *in vivo* after transfusion of unmanipulated was also explored [26, 27]. The incidence of GvDH could be lowered but the overall survival could not be improved because of prolonged immunorecovery, transplant failures and an increase in relapse rates.

The transplantation from a donor with a match in only one HLA haplotype has been increasingly applied using CD34+ selected blood stem cells or more selective depletion methods that do not decrease the NK-population [28].

Perspectives in the field of oncology

A graft versus tumour effect was reported in several cancer types. The high treatment related mortality and the discovery of targeted therapies, however, had limited the broader use. The graft engineering technologies of today would now allow us to further investigate cellular therapies (e.g. NK cells) in certain diseases.

Conflict of interest statement

None declared.

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