The skin is a tissue which is the most exposed to external factors. It is formed by numerous specialized cells and performs mainly protective functions. Due to its special properties such as: resistance, elasticity and semi-permeability, it protects our body from mechanical injuries, infections, loss of physiological fluids as well as harmful radiation (1, 2).

The human skin is formed of multi-layer squamous epithelium; epidermis and dermis. It is the largest organ in our body in terms of the occupied space. Patients who lose a large percentage of their skin’s surface as a result of thermal traumas face life threatening complications particularly connected with infections and loss of body fluids (3). Extensive and frequently very deep wounds resulting from burning require specialist treatment. The primary method of choice in the management of full-thickness burn traumas (third degree burns) is skin grafting with the use of the patient’s own skin (autologous split-thickness skin graft) (4, 5, 32). The first attempts to close wounds using the skin as a biological dressing date back to the beginning of the 19th century. At first, these were experiments which were not successful, but which gave rise to the search for effective treatment methods of burns and chronic wounds. In 1871, Pollock performed the first autograft of his own skin mixed with the skin of the patient. Finally, in 1881, Girdner dressed a large wound with the skin obtained from a cadaver and described graft rejection (6).

Autologous split-thickness skin graft constitutes a treatment method which presents certain constraints. The main limitation of this technique is insufficient amount of healthy, uninjured skin – donor site deficit, in patients with severe burns (4, 7). Donor sites are areas from which the split-thickness skin is removed and used to cover burn wounds. Unfortunately, in the case of massive and extensive burns encompassing numerous body areas, the lack of donor sites frequently renders the removal of the skin and, consequently, the autograft impossible. On other occasions, it may happen that the extent of burn wounds is so large that the amount of the skin removed from the donor sites is insufficient to cover the whole area of burning. The situations mentioned above prompt the search for other methods to treat burn wounds with the use of other available biological dressings.

After burn traumas, the human skin loses its protective properties. Therefore, the organism is at risk of infections and body fluid loss...
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A biological dressing (water, electrolytes and proteins), which may constitute a direct life hazard after the sustained trauma. Two purposes for using biological dressings may be distinguished. Biological dressings may be applied directly to the burn wound in order to reduce the portal of entry for pathogens (8, 9) and inhibit fluid loss. They are also frequently applied to the donor sites, which is particularly significant in the case of their deficits (9). What is more, the donor sites constitute an additional inconvenience for the patient – they cause pain and leave scars (33). The patients with burn traumas must undergo several or even a dozen or so surgeries. Therefore, efficient healing of the donor sites, from which the skin is obtained, is an essential condition for multiple skin removals from this area. Biological dressings – natural skin substitutes, may be divided into: autologous, allogeneic and xenogeneic.

AUTOLOGOUS DRESSINGS

The autologous split-thickness skin graft constitutes the main and primary method of burn wound treatment which has been successfully applied for many years. Its advantage is a practically instant accessibility and long-lasting wound covering. Its disadvantages, on the other hand, include: pain in the donor sites after skin removal and limited accessibility in patients with extensive burns (6). An alternative method, which enables lifesaving of the burned patients, is in vitro culture of autologous keratinocytes and subsequent application of the obtained suspension to the wound (32). The foundation for the human keratinocyte culture results from the work of Rheinwald and Green from 1975. The technique they described allows for increasing the number of human keratinocytes, which enables their further grafting. The method consisted in the separation of the epidermis from the dermis by the process of trypsinisation. The epidermis was then gently chopped and expressed through a sieve until keratinocyte suspension was obtained. The keratinocytes acquired this way were cultured on the feeder layer from irradiated mouse 3T3 fibroblasts in the serum which contained cholera toxin and EGF (34). Thereby, it is possible to obtain 100 sheets of 25 cm² from a slight sheet (circa 2 cm²). The entire process of obtaining the given number of sheets takes approximately 3 weeks. The Rheinwald and Green method allows for the creation of repeatable cultures. The theoretical basis put forward by these two scholars is used for in vitro culturing in the tissue banks worldwide (11, 12, 13, 34). The durable covering of a large area from a slight biopsy and acceptable aesthetic outcomes constitute the advantages of the cultured autologous keratinocytes. This technique effectively accelerates wound healing and the velocity of this process is largely dependent on the amount of the in vitro cultured keratinocytes applied to the wound (9). The disadvantages of this method encompass: long period of culturing (3 weeks), delicacy of the graft, high susceptibility to infections and mechanical damage as well as long period of dermis regeneration (10).
ALLOGENEIC DRESSINGS

The allogeneic skin grafting has been used in medicine since 1881 (Girdner). The material is most frequently obtained from cadavers (cadaver allograft) or living related donors. Such grafts constitute temporary dressings since they are rejected by the immune system of the recipient. The allogeneic skin is primarily used in critical situations in order to cover a large skin loss as quickly as possible when autograft is not possible. Advantages: immediate accessibility (from the Tissue Bank) and good adherence to the wound. Disadvantages: possibility to reject the graft and transfer an infection to the recipient (14, 15, 16, 35, 36).

Allogeneic dressings are retrieved from the deceased who, whilst living, did not express their objections in the Central Objection Register (Polish CRS – Centralny Rejestr Sprzeciwów). The donor is initially qualified by the Poltransplant (screening for HIV, HCV, HBV). The medical board, which states brain death of a patient, and a surgeon, who recovers the skin, qualify the donor on the basis of a post-mortem examination. During the process of retrieving the cadaver allograft, the employees of the Tissue Bank take part in all procedures. The skin is retrieved by means of a dermatome and subsequently, in the temperature of 4°C, it is transported to the Tissue Bank. In the Bank, further bacteriological and virological tests are conducted. The following tests are performed: anti-HIV, anti-HBc and anti-HCV antibody testing as well as Treponema Pallidum-specific test. The allogeneic skin is stored (in the Tissue Bank) in -80°C for 3 years or in -195°C for 5 years. The skin from related donors is obtained directly before transplantation. The cells from other organisms cultured for the purposes of grafting (allografts) were first used in 1983. At first, it was believed that allogeneic keratinocytes constitute a permanent graft. During culturing, Langerhans cells, which were considered critical for graft rejection, are removed. Initially, it was thought that their removal would ensure permanent immune tolerance.

Currently, it is known, however, that such grafts are not permanent and multiple genetic studies have revealed that allogeneic keratinocytes are replaced by the autologous ones in the process of healing. Thus, cultured allogeneic keratinocytes merely constitute a temporary dressing. Advantages: instant accessibility and acceleration of the healing process of superficial wounds. Disadvantages: graft rejection, possibility to transfer infections and lack of effectiveness in deep wound healing (6, 17, 18, 34). In the recent years, undifferentiated stem cells of various origins and various degree of plasticity have become highly promising. Cell regeneration and their therapeutic application constitute a great challenge for science. The sources of stem cells include placental tissues and umbilical blood. The only epithelial cells in this group come from the amniotic sac. They are frequently used as a biological dressing (19, 20). The amniotic fluid shows the expressiveness of the markers characteristic of embryonic stem cells (20). The amniotic membrane is a thin and semi-permeable tissue which constitutes the innermost aspect of the amniotic sac and is obtained during a caesarean section. It is composed of a thick basement membrane and avascular (without blood vessels) parenchymal layer.

Numerous authors suggest that these two features influence the success of the graft which intensely facilitates the epithelialisation and inhibits the process of fibrosis. The biological dressings containing allogeneic amnion have been used for several years in the treatment of eye conditions (including eye burns) (21). Using the amniotic membrane as a biological dressing of burn wounds has numerous advantages. It is very easy and relatively cheap (storing in the Tissue Bank). After covering the burn wound, the amniotic membrane protects the organism against water and body fluid loss as well as constitutes a barrier for all kinds of infections. The effects of burn wound treatment with amnions are highly satisfying. Such treatment is simple and may

Fig. 3. Division of allogeneic biological dressings
be used even in small hospitals that do not specialize in treating burn wounds (22).

XENOGENEIC DRESSINGS

Transplantology is a continuously developing field of science. Unfortunately, constant deficits of tissues and organs for transplant purposes still cause death of many people in the whole world. There are many reasons of this, among others, ethical issues. The improvement of this situation may be brought by tissue engineering (recovering stem cells from patients and inducing their transformation into desired tissues), bioengineering (e.g. artificial skin substitutes) and xenotransplantation. Xenotransplantation is the process of transferring (transplantation) and implantation of living cells (tissues and organs) which originate in other species to the human organism (xenografts). The first animal tissues were transplanted into a human being in 1682. This procedure consisted in filling in the loss in a human skull with a fragment of a dog’s skull. In treating burn wounds, in the 1960s, attempts were made to transplant frogs’ skin into people with severe burns (23, 26). The first attempts to use porcine skin as a biological dressing in the treatment of burn wounds date back to 1860s. (24). Porcine skin provides a good protection against bacterial infections from the external environment as well as secures the organism from body fluid loss.

Apart from these advantages, porcine skin xenograft is burdened with certain risks. Porcine xenografts may transmit viruses. There is a risk that infections will spread into a human organism. The viruses which may be transmitted by porcine xenografts include: PERV (Porcine Endogenous Retroviruses), PCMV (Porcine Cytomegalovirus) and PCV (Porcine Cirkovirus) (25, 26, 28, 29, 30). Moreover, porcine skin dressing is temporary. The immune barrier is too great and, in the end, the graft is always rejected. However, there is ongoing research concerning the porcine transgenic skin that aims at reducing the immune barrier of the recipient. Transgenic animals, whose immune systems are modified, may in the future become “tissue and organ banks” which will be successfully used for transplant purposes. Graft rejections are caused by genetic differences between the recipients and the donors. The antigens of the xenograft are recognized by the immune system of the recipient, which results in the immune reaction and, in consequence, leads to graft rejection. However, owing to the accomplishments of genetic engineering, porcine genome modification has become possible. Human genes that regulate the complement system are inserted by the method of DNA microinjection. The introduction of the gene of human fucosyltransferase into porcine genome may mask the epitope by decreasing the affinity for anti-Gal antibodies. Lower affinity for this antibody may decrease the inter-species barrier and minimise the risk of graft rejection (23, 26, 31).

CONCLUSIONS

Burns constitute frequent and serious traumas. Patients with severe burns are prone to infections and loss of body fluids (water, proteins and electrolytes). Serious burn wounds require specialist treatment and the fundamental condition for recovery is rapid replacement of a burn wound with a surgical one. The best method is autologous split-thickness skin graft. In this case, the greatest problem is posed by the extensiveness of burning and deficit of donor sites available for autologous skin grafting. This necessitates the search for alternative methods. However, finding an optimal biological substitute for the human skin is a demanding challenge. There is no ideal biological dressing that would successfully face all the hazards with which patients struggle in the first days following the thermal trauma. The most significant causative factor in the selection of dressing is the time available for obtaining and applying a given dressing so as to ensure that a severely burned patient man-

Fig. 4. Division of biological xenogeneic dressings used in burn wound management.
ages to survive until the alternative procedure is performed (e.g. cultured keratinocytes – about 21 days from the beginning of the culture). The allogeneic and xenogeneic dressings may be applied instantly.

One needs to bear in mind that cultivating keratinocytes constitute a long technological process and frequently, waiting is not possible. Allogeneic amnion has good effects. Xenotransplantations, on the other hand, are burdened with a high risk of graft rejection and transmission of a viral infection from farm animals. The latter aspect is not entirely known and requires creating accurate screening techniques for viruses. Nevertheless, the future will probably belong to tissue engineering and using xenogeneic-transgenic skin. The first attempts to apply treatment with the use of porcine skin are conducted by research groups from Poznań, Kraków and the Centre of Burn Treatment in Siemianowice Śląskie. This requires further studies and work on developing even better methods which will successfully interfere in the donor-recipient immune barrier and thus, decrease the number of rejections of such skin grafts.

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