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## Current possibilities of using materials for temporary closure of burn wound surface

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The **aim** of the work was a comparative analysis of clinical effectiveness of existing materials for temporary closure of burn wounds.

The advantages of biological wound dressings over gauze or synthetic materials are obvious today. However, the issue of comparing the clinical effectiveness of allo- and xenografts remains debatable. The latter provide rapid reepithelialization, analgesia, wound protection and, as a rule, a favorable treatment outcome. In terms of personal experience, over the past 20 years, with the transition to active surgical tactics for the treatment of patients with burns, enough evidence has been accumulated to confirm the high efficiency of using xenodermografts from domestic pigs to close postoperative wounds. Regarding the advantages of animal derived materials, we can highlight the safety, affordable price, unlimited raw materials for their manufacture, as well as the avoidance of various moral, ethical and legal restrictions.

Thus, closure of burn wounds is a major issue in the treatment of thermal injuries, which is especially critical for deep and extensive burns. Xenoderm grafts of our own design, which are widely used in clinical practice and significantly improve the course of burn disease are among the existing and most effective dressings in Ukraine.

No conflict of interests was declared by the authors.

**Keywords:** burns, biological dressings, differentiation, alloskin, porcine xenograft.

### Сучасні можливості використання матеріалів для тимчасового закриття ранової поверхні при опіках

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**Метою** роботи став порівняльний аналіз клінічної ефективності існуючих матеріалів для тимчасового закриття ран опікового генезу. Якщо на сьогодні переваги біологічних ранових покриттів над марлевими чи синтетичними матеріалами є очевидними, то питання порівняння клінічної ефективності ало- та ксенотрансплантатів залишається дискусійним. Останні забезпечують швидку реепітелізацію, знеболювання, захист рани та, як правило, хороший результат лікування. Що стосується власного досвіду, то за останні 20 років із переходом до активної хірургічної тактики лікування пацієнтів з опіками накопичено достатньо фактів, які підтверджують високу ефективність використання ксенодермоімплантатів вітчизняного виробництва зі шкіри свині для закриття післяопераційних ран. Щодо переваг матеріалів тваринного походження можна виділити безпечність, доступну ціну, необмежені сировинні ресурси для їх виготовлення, а також уникнення численних морально-етичних і законодавчих обмежень.

Отже, закриття опікових ран залишається важливим елементом лікування термічних уражень, особливо це стосується великих та поширених опіків. З існуючих покриттів в Україні одними з ефективних залишаються ксенодермотрансплантати власного виробництва, які широко використовуються в клінічній практиці і значно поліпшують перебіг опікової хвороби.

Автори заявляють про відсутність конфлікту інтересів.

**Ключові слова:** опіки, біологічні ранові покриття, порівняння, алодермотрансплантати, ксенодермоімплантати свині.

Despite rapid development of cell technology and active emergence of new wound dressings, the use of allogeneic (cadaveric) skin and xenodermografts, obtained mainly from pigs, remains an integral part of comprehensive treatment of patients with burns to temporarily close the wound surface [57]. Advantages of these materials over typical gauze or some hydrogel dressings have already been established and are not in dispute [50]. Nevertheless, conducting an objective comparative analysis of the effectiveness of allo- and xenodermografts is still challenging [27,36,53,55].

The *aim* of the work was a comparative analysis of clinical effectiveness of existing materials for temporary closure of burn wounds.

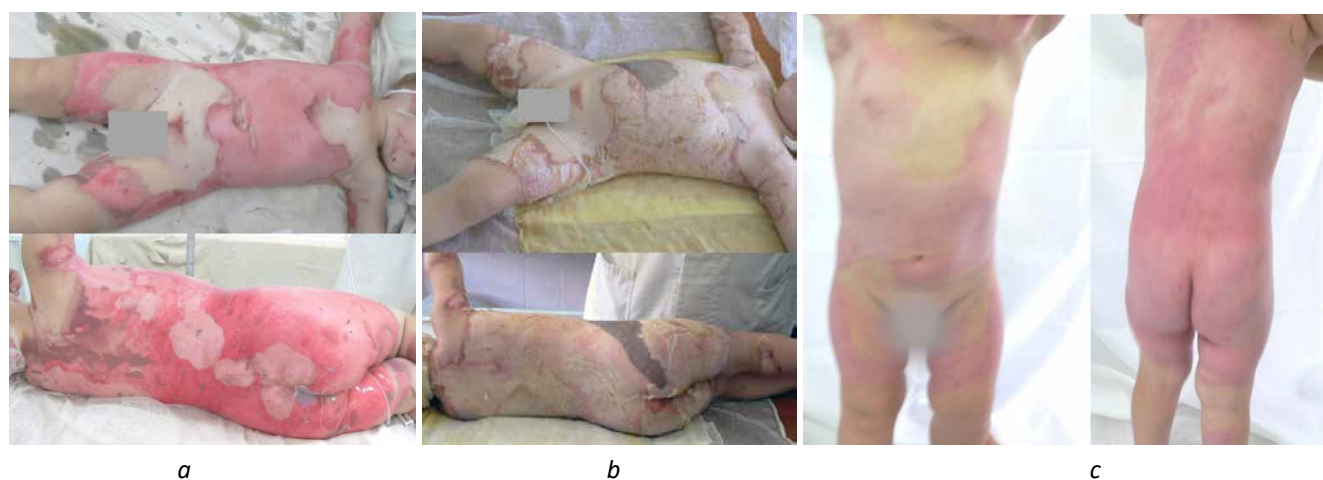
Allogeneic skin made of cadaveric material was for a long time considered the «gold standard» among temporary substitutes for skin of biological origin [39]. The first theoretical and practical successes occurred about 80 years ago under the leadership of a young biologist P. B. Medawar in response to the growing number of the wounded with severe burns received during World War II [45,48]. Since then, research in this direction has not ceased, but many problems remain far from being finally solved [25]. Even the transition to the use of cryopreserved or glycerol-preserved cadaveric skin is considered ineffective, as it does not fundamentally solve the problems of aggressive immune reactions caused by grafts, secondary infections, poor outcome of autologous skin grafts engraftment and increased risk of scarring [15]. Numerous moral, ethical and legal restrictions that are regulated by each country should also be borne in mind. But even if the latter are resolved, a number of other organizational and technological issues that must be overcome to ensure stable provision of medical institutions with such materials in the required amount, namely: high financial costs, complexity of material sampling, manufacturing, storage, transportation etc., should not be forgotten. For this purpose, biobanks or skin banks are created, the maintenance of which can be afforded mainly by countries with high level of well-being [35,51].

Appearance of acellular dermal matrix derived from cadaveric skin, the manufacturing of which involves the removal of all immune elements (keratinocytes, fibroblasts, vascular endothelium, smooth muscle elements), can be considered a solution to the above-mentioned

drawbacks [7]. Many of them remain in the clinical trial phase, but some have already passed all the necessary certification and are now available for clinical trial (AlloDerm® (LifeCell Laboratories, USA), GraftJacket® (Wright Medical UK Ltd, Hertfordshire, UK), SureDerm™ (Hans Biomed Corp, Korea) etc.). Despite the fact that scientists have not been able to completely eliminate antigenic components in these materials, their main drawback is the price, which can definitely be called «sky-high».

Realizing the lack of prospects in the complete removal of the restraints and shortcomings that are connected to allografts, scientists around the world have been studying xenografts since the 60s of the last century [30]. In the history of local treatment of burns, the use of skin of various animals is known: frogs, fish, pigeons, cats, dogs, sheep etc. [3,13,47]. Territorial and ethnic peculiarities of living served as a criterion for selection. With the beginning of full-scale research in this field, most scientists have focused on pigs, whose skin is available in different parts of the world and the histological structure of which is most similar to the human one [6]. There are also various technologies for its preparation and storage: «fresh» [9], frozen (with a retention period of up to 3 weeks [32], up to 30 days [42] or for a long time under cryopreservation [24]), after chemical glycerol dehydration or lyophilization (freeze drying) [11].

As for the clinical effectiveness of xenomaterials from porcine skin, from the standpoint of comparing them with the properties of allografts, most researchers consider these materials similar [42,44]. This can be explained by a small number of relevant studies, a limited sampling, which is mainly represented by a comparison of several clinical cases, low level of randomization of groups, personal unsubstantiated assumptions of individual authors. This is just an assumption, but based on our own experience gained on the basis of the Clinical Center for Thermal Injury and Plastic Surgery of the Municipal Non-Profit Enterprise «Vinnytsya Regional Pirogov Clinical Hospital of the Vinnytsya Regional Council» (Fig. 1) and authoritative results of other studies, it can be asserted that xenomaterials from porcine skin are able to create favorable conditions for healing burns or their rapid preparation for autologous skin grafting by reducing the level of pain in the wound with



**Fig. 1.** Appearance of *patient R.*, 2 years 4 months, the diagnosis «Burns with boiling water of II a, b degree with 60% of body surface area» on admission (the 1<sup>st</sup> day after the injury) (a), after surgery – early necrectomy, xenografting (the 3<sup>rd</sup> day after the injury) (b) and before discharge from the hospital on the background of complete wound healing (the 18<sup>th</sup> day after the injury) (c)

the possibility of rapid activation of the patient, reducing heat loss, fluid, protein, electrolytes in the injured surface, ensuring its protection from the harmful effects of the environment [1,2,5,8,10,19,22,28,29,37,38,41,46,52,56]. And most importantly it is an affordable price (the estimated cost of the product in the US market is about \$20 for xenograft coverage of 25 cm<sup>2</sup>, while the price from the Ukrainian manufacturer is even lower) and risk of infection, especially the viral one, is low [12,43].

There have been literature reports of the theoretical risk of transmission of zoonotic infections from the graft to the patient, including porcine endogenous retroviruses and *Clostridium difficile* [11,18,21]. However, there is no convincing evidence to support the fact of infection in this way in the available information sources [4,17]. No evidence of zoonotic origin of *Clostridium difficile*, which is occasionally detected in the wound contents of patients with burns, is also available [31]. Moreover, the use of special breeds of pigs kept in proper conditions, sampling and preparation of xenografts according to strictly regulated and controlled technologies in specialized conditions, radiation and ethylene oxide terminal sterilization not only reduces the risk of possible infection of the patient but also prevents the occurrence of immune responses.

Ethical and religious aspects that limit the widespread use of xenomaterials derived from certain animal species can also be found in the literature. In particular, some Muslim movements are mentioned, which strictly limit the use of xenomaterials derived from pigs [20]. Nevertheless, other Muslim movements allow the use of such materials, especially when there is no alternative, and their use directly affects the survival of the victim. For example, in Iran, xenografts

have been legalized at the state level and are actively used to help patients with burns [26,54].

Finally, there is a significant amount of research at various stages and focused on improving preparation technology, using genetic engineering technology, implementing alternative dosage forms, combinations with synthetic components, justifying the use of other animal tissues to close wounds (peritoneum, small intestine), etc. that confirm the prospects for the use of xenomaterials [11,16,23,33,39,49]. Results of the study of temporary skin substitutes obtained from fish, namely the Nile Tilapia (*Oreochromis niloticus*), are of particular interest [34]. Along with the convincing results of studying the effectiveness of such materials for the treatment of patients with burns in the experiment, their ability to significantly accelerate healing processes in comparison with materials obtained from porcine skin was established [49]. However, it should not be forgotten that the use of the above-mentioned materials of fish origin remains in the testing phase, and the practical possibilities of its use are limited by the habitat of this species of fish [14].

As for Ukraine, an enterprise was founded in Ternopil in 1993 on the initiative of Professor V. V. Bihunyak, which, after obtaining all necessary permits, began producing xenodermografts of porcine skin by cryogenic processing, lyophilization, sterilization, and it successfully continues its work to this day, ensuring the quantities requested for all national medical institutions. The enterprise, which in 2011 handed over a permit for the manufacture and registration of medical devices to LLC «Institute of Biomedical Technologies», was repeatedly awarded various awards. The sphere of activity of the institution includes not only constant monitoring of product quality, but also systematic research aimed at



improving its medicinal properties and expanding the range. For example, the production of silicone plates and kerat Xenografts has recently been established, and the study of the potential possibilities of medical use of other porcine tissue structures (peritoneum, pericardium, liver, spleen, pancreas) continues. The company did not stop functioning even during the height of the pandemic caused by the coronavirus (SARS-CoV-2). With the beginning of active military events on the territory of Ukraine and an increase in the number of patients with mine-blast wounds, which are often accompanied by thermal injury, fully functioning of the domestic production of temporary skin substitutes of biological origin is especially relevant and strategic in nature.

## Conclusions

1. Closure of burn wounds is a major issue in the treatment of thermal injuries, which is especially critical for deep and extensive burns.

2. A large number of different types of wound dressings require differentiated application.

3. Xenoderm grafts of our own design, which are widely used in clinical practice and significantly improve the course of burn disease are among the existing and most effective dressings in Ukraine.

## Prospects for further research

Against the background of the Ukrainian legislative regulation on the principles of manufacturing and use of skin allografts for the provision of medical care to patients with burns, we consider it promising to conduct our own experimental and clinical comparison of the effectiveness of similar materials obtained from cadaver donors and xenoderm grafts of animal origin.

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