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Experimental Models of Chronic Wounds

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ABSTRACT

Management of chronic, non-healing wounds is one of the pressing challenges in surgery. Demonstrating the effectiveness of novel drugs and medical devices is essential for their implementation in clinical practice. For this purpose, many animal models of wound healing have been developed, including in small rodents, which, however, have a specific skin structure and soft tissue regeneration. This review presents comparative characteristics of the main experimental wound models, including chronic ones, and describes their benefits and limitations.

Experimental studies most commonly involve mice, rats, and rabbits due to their relatively low cost and ease of maintenance. The most widely used wound modeling method is the creation of an excisional skin defect (with or without modifications) on the back of rodents. This model is technically simple and allows for partial reproduction of various pathological conditions. Although none of the models fully replicates the chronic wound healing process, modeling in small rodents (mice, rats) and rabbits remains the primary approach for studying regeneration and evaluating the efficacy of therapeutic interventions. Excisional and incisional wound models on the back of rodents are popular due to their simplicity and reproducibility. However, a significant limitation of these models is rapid wound closure by contraction, which is uncharacteristic of human healing. Chronic wound models (splinting, tail wounds in mice or ear wounds in rabbits, hyperglycemia, and others) more accurately reproduce the healing process and better reflect clinical situations. The choice of a specific model depends on the study aims and the species-specific features of laboratory animals. Moreover, the short healing period in animals often limits the ability to assess treatment efficacy. Improving and standardizing existing wound models, as well as developing novel experimental approaches, remain important tasks for regenerative medicine and surgery.

Keywords: chronic wounds; animal models; skin defects.

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Экспериментальные модели хронических ран

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АННОТАЦИЯ

Одной из актуальных задач хирургии является коррекция длительно незаживающих, хронических ран. Подтверждение эффективности разрабатываемых препаратов и медицинских изделий необходимо для их внедрения в практическую медицину. С этой целью разработано множество моделей раневого процесса на животных, в том числе на мелких грызунах, которые, однако, имеют особенности строения кожи и регенерации мягких тканей. В данном обзоре представлены сравнительные характеристики основных экспериментальных моделей ран, включая хронические, а также описаны их преимущества и недостатки.

В экспериментальных исследованиях чаще всего используют мышей, крыс и кроликов в связи с их относительно невысокой стоимостью и доступностью содержания. Наиболее распространённый вариант моделирования ран — формирование эксцизионного кожного дефекта (с модификациями и без) на спине у грызунов. Эта модель проста в выполнении и даёт возможность частично воспроизводить различные патологические состояния. Несмотря на то, что ни одна из моделей в полной мере не воспроизводит хронический процесс заживления ран, моделирование на мелких грызунах (мышах, крысах) и кроликах остаётся основным методом изучения регенерации и оценки эффективности разрабатываемого лечения. Эксцизионные и инцизионные модели ран на спине грызунов широко используются из-за простоты и воспроизводимости. Однако важным ограничением этих моделей является быстрое заживление путём контракции, что не характерно для человека. Модели хронических ран (шинирование, раны на хвосте мыши или ухе кролика, гипергликемия и другие) более точно воспроизводят процесс заживления и приближают его к клиническим ситуациям. Выбор конкретной модели зависит от целей исследования и особенностей вида лабораторных животных. Кроме того, короткий период заживления зачастую не позволяет оценить эффективность терапии. Совершенствование и унификация существующих моделей ран, а также разработка новых экспериментальных подходов остаются важными задачами для регенеративной медицины и хирургии.

Ключевые слова: хронические раны; модели на животных; кожные дефекты.

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慢性创伤的实验模型

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摘要

慢性创伤及其长期不愈合的矫治仍是外科领域中的重要研究课题。为使新开发的药物和医疗器械能够进入临床应用，必须确认其疗效。为此，已建立多种动物创伤模型，包括用于小型啮齿动物的模型，尽管这类动物在皮肤结构和软组织再生方面存在一定的物种特异性。本综述对主要实验性创伤模型，包括慢性创伤模型，进行了比较分析，并阐述了其优势与局限性。

在实验性研究中，最常使用小鼠、大鼠和家兔，这是由于其成本相对较低且易于饲养。最常见的创伤建模方式是在啮齿动物背部形成皮肤切除性缺损（可带改良，也可不带改良）。该模型操作简单，能够在一定程度上再现多种病理状态。尽管尚无模型可完全重现人类慢性创伤的愈合过程，但在小型啮齿动物（小鼠、大鼠）和家兔上建立模型，仍是研究再生机制和评估治疗效果的主要方法。啮齿动物背部的切除伤和切开伤模型因操作简便、结果可重复性强而被广泛应用。然而，这些模型的重要局限在于其通过组织收缩实现快速愈合，而这并不符合人类的创伤愈合特征。慢性创伤模型（如支架固定伤口模型、小鼠尾部创面、家兔耳部创面、高血糖等）能够更准确地再现创伤愈合过程，使其更接近临床情境。具体模型的选择应依据研究目的和所用动物种属的特点。此外，愈合时间过短往往使疗效评估变得困难。创伤模型的进一步完善与统一，以及新实验方法的开发，仍是再生医学与外科领域的重要任务。

关键词：慢性创伤；动物模型；皮肤缺损。

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INTRODUCTION

Chronic non-healing wounds, including trophic ulcers, extensive burns, and skin changes associated with diabetic foot syndrome, represent one of the major challenges in surgery and public health. According to epidemiological studies, the estimated prevalence of chronic wounds is 1%–2% of the global population [1]. Chronic wounds are associated with prolonged pain and may be complicated by sepsis. In diabetes mellitus, chronic defects of the skin and soft tissues of the foot (diabetic foot syndrome) often lead to lower limb amputation. Despite many therapeutic approaches proposed for the management of such wounds, the development of effective treatment strategies remains a pressing issue [2].

Mice, rats, and rabbits are most commonly used to model acute and chronic wounds in experimental settings. Several fundamentally different approaches to wound creation can be distinguished: excisional (removal of a tissue fragment), longitudinal incisional (surgical incision of tissues), burn models, adhesive tape methods, and exposure to X-irradiation. Other techniques are generally modifications of these basic approaches.

CHOICE OF EXPERIMENTAL ANIMALS

The choice of animal species is a crucial step in experimental design and should be based both on general aspects, including the anatomical and physiological characteristics of the species, and on practical considerations such as cost, availability, and housing requirements. The skin structure of rodents and rabbits differs considerably from that of humans (Table 1): their skin is thinner and more mobile relative to underlying layers; sweat glands are absent on the trunk, and wound healing occurs primarily through contraction due to the presence of the subcutaneous muscle *m. panniculus carnosus*. Additionally, animal skin is characterized by a high density of hair follicles, and some rodent species are capable of endogenous vitamin C synthesis, which promotes collagen formation [3–6]. Table 1 and Table 2 show comparative characteristics of selected experimental animals.

EXPERIMENTAL MODELS OF ACUTE WOUNDS

Various techniques are used to create experimental skin wounds, and their main characteristics are summarized in Table 3. The most common approach to evaluation of comparative healing dynamics is the excisional wound model on the dorsal surface of rodents [7–9]. Published experimental protocols are highly variable—they differ in wound size, number of wounds per animal, and methods of assessing wound healing [10, 11]. It is well established that the rate of healing is influenced by the stage of the hair growth cycle, because regenerative processes and hair growth are partially regulated by common intracellular signaling pathways, including fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), and transforming growth factor beta (TGF-β) [12]. For this reason, some authors recommend using animals in the late catagen or telogen phase [13].

Another approach to wound modeling involves creating a longitudinal (incisional) skin wound on the back of the animal with sharp instruments such as a scalpel or scissors [14, 15]. The healing process of such wounds may be classified as primary intention or secondary intention, depending on whether the wound edges are approximated. Primary healing, achieved by suturing wound margins, enables the evaluation of re-epithelialization, testing of surgical materials, and investigation of repair mechanisms, though to a lesser extent, because the volume of injured tissue is limited. Secondary healing occurs when the wound is left open and is used to study scar formation, including the development of hypertrophic scars [14].

Table 1. Skin structure in experimental animals and humans

Parameter	Human	Mouse	Rat	Rabbit (New Zealand breed)
Skin thickness, mm	2.0–3.0	0.4–1.0	1.0–2.0	1.8–2.0
Hair density, hairs/cm^2	20–50 (trunk) 500–1000 (scalp)	658	289	80
Presence of eccrine sweat glands	Yes	Yes (on plantar surfaces of forepaws and hind paws)	Yes (on palmar surfaces of forepaws and hind paws)	No
Mobility relative to underlying tissues	No (except cervical region)	Yes	Yes	Yes
Endogenous synthesis of vitamin C	No	Yes	Yes	Yes
Primary wound healing mechanism	Re-epithelialization	Contraction	Contraction	Contraction

Note: Scalp, hairy part of the head.

Table 2. Comparative characteristics of laboratory animals used for wound modeling

Experimental Animal	Advantages	Disadvantages
Mouse	Small size; convenient housing; numerous transgenic lines; wide availability of species-specific antibodies; tail wound model is considered a chronic wound [3]	Mouse skin differs from human skin; chronic non-healing wounds are not typical; wounds heal primarily by contraction; wound models require modification to prolong healing
Rat	Relatively inexpensive; convenient housing; larger than mice, which allows for larger wound areas; widely used	Same limitations as in mice
Rabbit	Readily available and widely used; large wound surface area can be created; wound healing in the ear pinna is similar to humans	More expensive than mice and rats; ischemic ear model is poorly reproducible; ischemia is reversible

Burn injuries induced by heated objects, hot water, or, less commonly, electricity are also widely applied as a method for creating acute wounds. Thermal injuries are well suited for assessing re-epithelialization, granulation tissue formation, neovascularization, and other processes of tissue regeneration. Depending on the experimental objectives and the intended observation period, the surface area of thermal injury can be adjusted, allowing for an extended window to evaluate the effects of experimental therapies [16–19].

The use of adhesive tape stripping to create wounds is the least common approach. This model induces partial skin injury limited to the stratum corneum of the epidermis and is primarily designed to study re-epithelialization in acute injury. It is also well adapted for assessing barrier function impairment. However, because this method does not involve deeper dermal injury, it is unsuitable for investigating the mechanisms of damage and regeneration in full-thickness wounds. Furthermore, the technical aspects of tape application complicate standardization [9].

EXPERIMENTAL MODELS OF CHRONIC WOUNDS

Unlike acute wounds, which are characterized by sequential healing phases (coagulation, inflammation, migration-proliferation, and remodeling) and relatively predictable time frames, chronic wounds lack such clear phase-dependent and temporal characteristics [20]. Delayed

Table 3. Experimental models of acute wounds

Model	Description	Advantages	Disadvantages
Excisional model	Creation of full-thickness skin wounds of various diameters on the dorsum, involving the *m. panniculus carnosus*	One of the primary models; technically simple; creating wounds of various sizes; multiple wounds induced in the same animal [7, 8, 9]	Healing occurs predominantly by contraction; does not reproduce chronic wound processes
Incisional model	Longitudinal full-thickness skin incision on the dorsum	One of the primary models; technically simple; high reproducibility; enables evaluation of scar formation and postoperative wound healing	Same as in the excisional model
Burn model	Burn injuries induced using: • heated metal rods; • hot water; • steam; • electricity	Technically simple	Rapid healing due to contraction; does not reproduce the pathophysiological processes of burn wound healing in humans
Adhesive tape model	Repeated attachment and removal of adhesive tapes on the dorsum of rodents	Technically simple; non-invasive; minimal pain for animals; reproduces the epithelialization stage in humans	Only superficial wounds can be created (stratum corneum defects); does not reproduce chronic wound processes; low reproducibility due to difficulty in standardizing adhesive strength, detachment speed, and angle

healing of chronic wounds is driven by both isolated and combined factors, including damage to components of the microcirculatory bed and innervation (as in diabetes mellitus), local tissue compression (edema), and persistent immune cell accumulation. One of the main limiting factors in modeling chronic wounds in rodents and rabbits is their inherent capacity for rapid healing. Therefore, investigators reproduce conditions that mimic pathological processes typical of humans so that the duration of skin regeneration is extended artificially.

The splinting technique involves the implantation of splints, most often silicone rings, into wound margins, physically preventing contraction of the panniculus carnosus. This approach shifts healing from contraction toward granulation tissue formation and re-epithelialization, thereby prolonging the regeneration period [21–23]. Another approach is the skin-fold chamber model, where a skin flap is clamped with a device that creates a defect. Originally intended for *in vivo* microcirculatory studies rather than wound healing *per se*, this model also enables visualization of small vessels during primary and secondary healing [24, 25].

Acute wound models supplemented by additional factors can partially reproduce pathological processes of chronic wound regeneration. One such factor is experimentally induced hyperglycemia [26–29]. Diabetic animal models can be generated using chemical or surgical interventions, as well as specialized diets. Furthermore, transgenic mouse strains such as db/db (type 2 diabetes) and ob/ob (obesity) are available [30]. Chemical induction with agents such as streptozotocin or alloxan is a rapid and accessible method, but it does not fully reproduce the natural course of disease. Transgenic strains avoid this limitation, but substantially increase research costs.

Limitations of diabetes models and transgenic lines prompted the development of alternative approaches to create skin defects with prolonged healing. One such model is the mouse tail skin excision wound, where an excision of 0.5 × 1.0 cm is made on the dorsal tail surface, 0.5–1.0 cm distal to the trunk [31]. Unlike standard dorsal excisional wounds in mice or rats, this model heals within 18–25 days, providing a sufficiently long observation period to evaluate therapeutic interventions. A similar technique involves creating wounds on the plantar surface of rodent paws [32, 33]. Rectangular wounds of approximately 2 × 5 mm are made on rat hindlimbs to study inflammation, contraction, and epithelialization; diabetic animals can also be included in such experiments.

Due to structural features of rabbit ear skin (firm attachment to underlying cartilage), auricular wounds predominantly heal by epithelialization and granulation, which corresponds to the late phases of human wound healing [34, 35]. Additional factors that impair skin restoration in this model include hyperglycemia, as well as ischemia and denervation following transection of neurovascular bundles [36]. Chemical or surgical denervation of other skin regions can also be used to investigate the role of the nervous system in cutaneous regeneration [37–40].

Infected wounds in humans often complicate chronic defects, thus requiring the development of new therapeutic strategies and corresponding animal models. To reproduce infected wounds, investigators combine acute injuries with inoculation of pathogenic microorganisms or insertion of foreign materials [41–43]. Suspensions of microorganisms such as *Staphylococcus aureus*, *Pseudomonas aeruginosa*, or *Candida albicans* are applied onto excisional wounds on the dorsal or ventral trunk, producing infectious, often purulent, complications. This model is widely used for evaluating the pharmacodynamics of antimicrobial drugs and medical devices.

Radiation therapy for cancer may cause skin injury with markedly delayed regeneration. This necessitated the development of radiation-induced wound models in animals, which are used both for studying complications of radiotherapy and for creating chronic wounds in general. In these models, skin on the dorsum or limbs of rodents is irradiated at various doses, followed by excision of a flap in the irradiated area [44–47]. High doses of radiation produce delayed healing but require specialized equipment, technical expertise, and shielding of the animal body to avoid lethal exposure.

The dead space model is created by subcutaneous or intramuscular implantation of foreign bodies, such as polypropylene tubes, producing cavities similar to those that develop in humans after soft-tissue excision and closure of postoperative defects. This model, usually performed in rabbits, is convenient for assessing implant responses. Multiple “dead spaces” can be created in a single animal; the defect size is clinically relevant, and outcomes can be evaluated by histological, laboratory, and instrumental methods [48].

Restoration of blood flow after ischemia due to prolonged compression is pathophysiologically similar to pressure ulcer development [49]. Implantation of magnets under the skin with periodic compression by an opposing magnet mimics this condition [50]. This model has been successfully applied in mice and rats. Magnetic compression markedly reduces skin perfusion, decreases trophic factor levels, and increases exudate formation. Depending on the study design, the degree of injury can be varied by altering compression duration and ischemia/reperfusion cycles [51–53]. Chronic ischemic ulcers may also be induced by sustained compression of a skin fold without magnet implantation.

CONCLUSION

At present, the published data describe numerous approaches to modeling wounds in animals, which, to varying degrees, reproduce the pathological processes observed in humans [54]. Mice, rats, and rabbits are most frequently used in such studies because of their relatively low cost and ease

of maintenance. The most common method is the creation of an excisional skin defect on the back of rodents, owing to its reproducibility and technical simplicity. In addition to the structural features of rodent skin, model selection should take into account the specific research objectives and the ability to create conditions that closely approximate clinical situations. The main limiting factor of all described models is still the duration of wound healing: first, it is not comparable with the actual timeframe of skin repair in humans; second, it is often insufficient for evaluating the pharmacodynamics of investigational drugs. In this regard, some approaches have been developed and validated. They allow modeling chronic wounds, including excisional skin defects on the mouse tail or rabbit ear, as well as the use of transgenic animal lines, such as diabetic mice [55].

CONCLUSION

Existing wound models do not fully reproduce clinical conditions characterized by chronic, protracted healing of skin defects. They only partially reflect the pathophysiological processes occurring in humans with diabetes mellitus, chronic limb ischemia, radiation injury, and other conditions. Moreover, outcomes obtained with the same models often vary among different investigators and are not always reproducible. Despite the active development of new wound therapies, including agents targeting chronic processes, there is still an urgent need to establish, validate, and implement standardized protocols for modeling both acute and chronic wounds. Such protocols should provide high reproducibility and maximum fidelity to the pathological processes specific to relevant clinical scenarios.

ADDITIONAL INFORMATION

Author contributions: E.D. Kopylov: sources review, formal analysis, writing—original draft; E.V. Presnyakov: sources analysis, writing—review & editing; M.V. Tolgsky: collection and analysis of sources, writing— review & editing; A.N. Andreeva: collection and analysis of sources, writing—original draft; N.A. Somov: collection and analysis of sources, writing—review & editing, visualization; M.V. Revkova: writing—review & editing, visualization, project administration; I.Ya. Bozo: supervision, writing—review & editing, project administration. All the authors approved the version of the manuscript to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Доступ к данным. Редакционная политика в отношении совместного использования данных к настоящей работе не применима, новые данные не собирали и не создавали.

Генеративный искусственный интеллект. При создании настоящей статьи технологии генеративного искусственного интеллекта не использовали.

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REFERENCES | СПИСОК ЛИТЕРАТУРЫ

1. Martinengo L, Olsson M, Bajpai R, et al. Prevalence of chronic wounds in the general population: systematic review and meta-analysis of observational studies. *Ann Epidemiol*. 2019;29:8–15. doi: 10.1016/j.annepidem.2018.10.005 EDN: OEYDZX

2. Kathawala MH, Ng WL, Liu D, et al. Healing of Chronic Wounds: An Update of Recent Developments and Future Possibilities. *Tissue Eng Part B Rev*. 2019;25(5):429–444. doi: 10.1089/ten.TEB.2019.0019

3. Grada A, Mervis J, Falanga V. Research techniques made simple: Animal models of wound healing. *J Invest Dermatol*. 2018;138(10):2095–2105.e1. doi: 10.1016/j.jid.2018.08.005

4. Mustoe TA, O'Shaughnessy K, Kloeters O. Chronic wound pathogenesis and current treatment strategies: a unifying hypothesis. *Plast Reconstr Surg*. 2006;117(7 Suppl):35S–41S. doi: 10.1097/01.prs.0000225431.63010.1b

5. Wang X, Ge J, Tredget EE, Wu Y. The mouse excisional wound splinting model, including applications for stem cell transplantation. *Nat Protoc*. 2013;8(2):302–309. doi: 10.1038/nprot.2013.002
6. Choudhary V, Choudhary M, Bollag WB. Exploring skin wound healing models and the impact of natural lipids on the healing process. *Int J Mol Sci*. 2024;25(7):3790. doi: 10.3390/ijms25073790 EDN: VSLJSZ
7. Rhea L, Dunnwald M. Murine Excisional Wound Healing Model and Histological Morphometric Wound Analysis. *J Vis Exp*. 2020;(162):10.3791/61616. doi: 10.3791/61616 EDN: WTKIEH
8. Cogan NG, Mellers AP, Patel BN, et al. A mathematical model for the determination of mouse excisional wound healing parameters from photographic data. *Wound Repair Regen*. 2018;26(2):136–143. doi: 10.1111/wrr.12634
9. Sami DG, Heiba HH, Abdellatif A. Wound healing models: A systematic review of animal and non-animal models. *Wound Medicine*. 2019;24(1):8–17. doi: 10.1016/j.wndm.2018.12.001
10. Lou D, Luo Y, Pang Q, et al. Gene-activated dermal equivalents to accelerate healing of diabetic chronic wounds by regulating inflammation and promoting angiogenesis. *Bioact Mater*. 2020;5(3):667–679. doi: 10.1016/j.bioactmat.2020.04.018 EDN: HNHUCN
11. Cogan NG, Mellers AP, Patel BN, et al. A mathematical model for the determination of mouse excisional wound healing parameters from photographic data. *Wound Repair Regen*. 2018;26(2):136–143. doi: 10.1111/wrr.12634
12. Shestakova VG. Stimulated angiogenesis and its role in reparative skin regeneration. *Journal of Anatomy and Histopathology*. 2018;7(3):117–124. (In Russ.) doi: 10.18499/2225-7357-2018-7-3-117-124 EDN: VCJVFR
13. Ansell DM, Kloepper JE, Thomason HA, et al. Exploring the "hair growth-wound healing connection": anagen phase promotes wound re-epithelialization. *J Invest Dermatol*. 2011;131(2):518–528. doi: 10.1038/jid.2010.291 EDN: OASNWH
14. Ansell DM, Campbell L, Thomason HA, et al. A statistical analysis of murine incisional and excisional acute wound models. *Wound Repair Regen*. 2014;22(2):281–287. doi: 10.1111/wrr.12148
15. Gamelli RL, He LK. Incisional wound healing. Model and analysis of wound breaking strength. *Methods Mol Med*. 2003;78:37–54. doi: 10.1385/1-59259-332-1:037
16. Blaise O, Duchesne C, Banzet S, et al. A murine model of a burn wound reconstructed with an allogeneic skin graft. *J Vis Exp*. 2020;(162):10.3791/61339. doi: 10.3791/61339 EDN: CXPOMY
17. Calum H, Høiby N, Moser C. Burn mouse models. *Methods Mol Biol*. 2014;1149:793–802. doi: 10.1007/978-1-4939-0473-0_60
18. Blaise O, Duchesne C, Banzet S, et al. A murine model of a burn wound reconstructed with an allogeneic skin graft. *J Vis Exp*. 2020;(162):10.3791/61339. doi: 10.3791/61339 EDN: CXPOMY
19. Ulkür E, Oncül O, Karagöz H, et al. Comparison of silver-coated dressing (Acticoat), chlorhexidine acetate 0.5% (Bactigrass), and silver sulfadiazine 1% (Silverdin) for topical antibacterial effect in Pseudomonas aeruginosa-contaminated, full-skin thickness burn wounds in rats. *J Burn Care Rehabil*. 2005;26(5):430–433. doi: 10.1097/01.bcr.0000176879.27535.09
20. Anichkov NN, Volkova KG, Garshin VG. *Morphology of wound healing*. Moscow: Medgiz; 1951. (In Russ.)
21. Wang X, Ge J, Tredget EE, Wu Y. The mouse excisional wound splinting model, including applications for stem cell transplantation. *Nat Protoc*. 2013;8(2):302–309. doi: 10.1038/nprot.2013.002
22. Arkhipova AY, Kulikov DA, Moisenovich AM, et al. Fibroin-Gelatin composite stimulates the regeneration of a splinted Full-Thickness skin wound in mice. *Bull Exp Biol Med*. 2019;168(1):95–98. doi: 10.1007/s10517-019-04656-0 EDN: TVCUVJ
23. Park SA, Teixeira LB, Raghunathan VK, et al. Full-thickness splinted skin wound healing models in db/db and heterozygous mice: implications for wound healing impairment. *Wound Repair Regen*. 2014;22(3):368–380. doi: 10.1111/wrr.12172
24. Laschke MW, Menger MD. The dorsal skinfold chamber: A versatile tool for preclinical research in tissue engineering and regenerative medicine. *Eur Cell Mater*. 2016;32:202–215. doi: 10.22203/eCM.v032a13
25. Grambow E, Sorg H, Sorg CGG, Strüder D. Experimental models to study skin wound healing with a focus on angiogenesis. *Med Sci (Basel)*. 2021;9(3):55. doi: 10.3390/medsci9030055 EDN: ESFBYU
26. Furman BL. Streptozotocin-induced diabetic models in mice and rats. *Curr Protoc*. 2021;1(4):e78. doi: 10.1002/cpz1.78 EDN: ZEUGEE
27. Kottaisamy CPD, Raj DS, Prasanth Kumar V, Sankaran U. Experimental animal models for diabetes and its related complications-a review. *Lab Anim Res*. 2021;37(1):23. doi: 10.1186/s42826-021-00101-4 EDN: KUPVAF
28. Campos LF, Tagliari E, Casagrande TAC, et al. Effects of probiotics supplementation on skin wound healing in diabetic rats. *Arq Bras Cir Dig*. 2020;33(1):e1498. doi: 10.1590/0102-672020190001e1498 EDN: BXFJVX
29. Nayaka SS, Krishna V, Narayana J, et al Diabetic wound healing activity of Elaeagnus conferta Roxb. leaf ethanol extract. *Res J Biotech*. 2023;18(11):154–164. doi: 10.25303/1811rjbt01540164 EDN: QCFQGA
30. Michaels J 5th, Churgin SS, Blechman KM, et al. db/db mice exhibit severe wound-healing impairments compared with other murine diabetic strains in a silicone-splinted excisional wound model. *Wound Repair Regen*. 2007;15(5):665–670. doi: 10.1111/j.1524-475X.2007.00273.x
31. Falanga V, Schrayer D, Cha J, et al. Full-thickness wounding of the mouse tail as a model for delayed wound healing: accelerated wound closure in Smad3 knock-out mice. *Wound Repair Regen*. 2004;12(3):320–326. doi: 10.1111/j.1067-1927.2004.012316.x EDN: FPBHQP
32. Du Y, Wang J, Fan W, et al. Preclinical study of diabetic foot ulcers: From pathogenesis to vivo/vitro models and clinical therapeutic transformation. *Int Wound J*. 2023;20(10):4394-4409. doi:10.1111/iwj.14311
33. Yu CO, Leung KS, Fung KP, et al. The characterization of a full-thickness excision open foot wound model in n5-streptozotocin (STZ)-induced type 2 diabetic rats that mimics diabetic foot ulcer in terms of reduced blood circulation, higher C-reactive protein, elevated inflammation, and reduced cell proliferation. *Exp Anim*. 2017;66(3):259–269. doi: 10.1538/expanim.17-0016
34. Chang L, Xu Y, Wu Z, et al. Hyaluronic acid methacrylate/laponite hydrogel loaded with BMP4 and maintaining its bioactivity for scar-free wound healing. *Regen Biomater*. 2023;10:rbad023. doi: 10.1093/rb/rbad023 EDN: HPJDHP
35. Hu CH, Tseng YW, Chiou CY, et al. Bone marrow concentrate-induced mesenchymal stem cell conditioned medium facilitates wound healing and prevents hypertrophic scar formation in a rabbit ear model. *Stem Cell Res Ther*. 2019;10(1):275. doi: 10.1186/s13287-019-1383-x EDN: CXWTQV
36. Alapure BV, Lu Y, Peng H, Hong S. Surgical denervation of specific cutaneous nerves impedes excisional wound healing of small animal ear pinnae. *Mol Neurobiol*. 2018;55(2):1236–1243. doi: 10.1007/s12035-017-0390-0 EDN: LPHUCL
37. Trujillo AN, Kesl SL, Sherwood J, et al. Demonstration of the rat ischemic skin wound model. *J Vis Exp*. 2015;(98):e52637. doi: 10.3791/52637
38. Lovasova V, Bem R, Chlupac J, et al. Animal experimental models of ischemic wounds - A review of literature. *Wound Repair Regen*. 2022;30(2):268–281. doi: 10.1111/wrr.12996 EDN: CNRNVQ
39. Souza BR, Cardoso JF, Amadeu TP, et al. Sympathetic denervation accelerates wound contraction but delays reepithelialization in rats. *Wound Repair Regen*. 2005;13(5):498–505. doi: 10.1111/j.1067-1927.2005.00070.x
40. Shu B, Xie JL, Xu YB, et al. Effects of skin-derived precursors on wound healing of denervated skin in a nude mouse model. *Int J Clin Exp Pathol*. 2015;8(3):2660–2669.
41. Yarboro SR, Baum EJ, Dahners LE. Locally administered antibiotics for prophylaxis against surgical wound infection. An in vivo study. *J Bone Joint Surg Am*. 2007;89(5):929–933. doi: 10.2106/JBJS.F.00919
42. Kugelberg E, Norström T, Petersen TK, et al. Establishment of a superficial skin infection model in mice by using Staphylococcus aureus and Streptococcus pyogenes. *Antimicrob Agents Chemother*. 2005;49(8):3435–3441. doi: 10.1128/AAC.49.8.3435-3441.2005
43. Dai T, Kharkwal GB, Tanaka M, et al. Animal models of external traumatic wound infections. *Virulence*. 2011;2(4):296–315. doi: 10.4161/viru.2.4.16840 EDN: PHRCXZ

44. Fujita K, Nishimoto S, Fujiwara T, et al. A new rabbit model of impaired wound healing in an X-ray-irradiated field. *PLoS One*. 2017;12(9):e0184534. doi: 10.1371/journal.pone.0184534
45. Lee J, Jang H, Park S, et al. Platelet-rich plasma activates AKT signaling to promote wound healing in a mouse model of radiation-induced skin injury. *J Transl Med*. 2019;17(1):295. doi: 10.1186/s12967-019-2044-7
46. Huang SP, Huang CH, Shyu JF, et al. Promotion of wound healing using adipose-derived stem cells in radiation ulcer of a rat model. *J Biomed Sci*. 2013;20(1):51. doi: 10.1186/1423-0127-20-51 EDN: GKYZIM
47. Deshevoy YuB, Nasonova TA, Dobrynina OA, et al. Experimental conditions for the use of syngeneic multipotent mesenchymal stem cells (MMSCs) from adipose tissue for the treatment of severe radiation-induced skin lesions. *Genes & Cells*. 2019;14(3):77. (In Russ.) doi: 10.23868/gc122470 EDN: OTWUTF
48. Oliver RA, Lovric V, Yu Y, et al. Development of a novel model for the assessment of Dead-Space management in soft tissue. *PLoS One*. 2015;10(8):e0136514. doi: 10.1371/journal.pone.0136514
49. Peirce SM, Skalak TC, Rodeheaver GT. Ischemia-reperfusion injury in chronic pressure ulcer formation: a skin model in the rat. *Wound Repair Regen*. 2000;8(1):68–76. doi: 10.1046/j.1524-475x.2000.00068.x
50. Takeuchi Y, Ueno K, Mizoguchi T, et al. Development of novel mouse model of ulcers induced by implantation of magnets. *Sci Rep*. 2017;7(1):4843. doi: 10.1038/s41598-017-05250-y EDN: ZWSLMN
51. Stekelenburg A, Oomens C, Bader D. Compression-induced tissue damage: animal models. In: Bader DL, Bouten CV, Colin D, Oomens CW, editors. *Pressure ulcer research*. Berlin: Springer; 2005. P:187–204. doi: 10.1007/3-540-28804-x_12
52. Stadler I, Zhang RY, Oskoui P, et al. Development of a simple, noninvasive, clinically relevant model of pressure ulcers in the mouse. *J Invest Surg*. 2004;17(4):221–227. doi: 10.1080/08941930490472046
53. Wassermann E, van Griensven M, Gstaltner K, et al. A chronic pressure ulcer model in the nude mouse. *Wound Repair Regen*. 2009;17(4):480–484. doi: 10.1111/j.1524-475x.2009.00502.x
54. Masson-Meyers DS, Andrade TAM, Caetano GF, et al. Experimental models and methods for cutaneous wound healing assessment. *Int J Exp Pathol*. 2020;101(1-2):21–37. doi: 10.1111/iep.12346 EDN: XASXEL
55. Nunan R, Harding KG, Martin P. Clinical challenges of chronic wounds: searching for an optimal animal model to recapitulate their complexity. *Dis Model Mech*. 2014;7(11):1205–1213. doi: 10.1242/dmm.016782

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