GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 12 (369) Декабрь 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
NO 12 (369) 2025

Содержание:

GEORGIAN MEDICAL NEWS
No 12 (369) 2025

HYPERCORTICISM IN THE PATHOGENESIS OF ACUTE RADIATION SICKNESS AND CONDITIONS OF INCREASED RADIORESISTANCE

Nadezhda Omelchuk*.

**Department of Clinical Laboratory Diagnostics, Faculty of Continuous Medical Education, Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation.*

Abstract.

Objective: To investigate the role of hypercorticism in the pathogenesis of acute radiation sickness (ARS) and under conditions of increased radioresistance, assessing the theoretical and clinical significance of impaired protein-steroid interactions.

Materials and Methods: An analysis was conducted of experimental data from irradiated animal models: chinchilla rabbits (n=20), dogs (n=15), WISTAR rats (n=63), guinea pigs (n=49), and BALB/c mice (n=32). Some animals underwent adrenal autotransplantation. Fluorometric and gel filtration methods were used to assess protein-steroid interactions; total-body γ-irradiation was administered at doses inducing grade IV ARS. Data were statistically processed using Student's t-test.

Results: A biphasic adrenocortical response to radiation was observed in most species, whereas rabbits exhibited a monophasic decline in corticosteroid levels. During the peak of ARS, impaired corticosteroid-binding globulin (CBG) function led to increased levels of free, biologically active corticoids, even with normal or reduced total 11-oxycorticosteroids. A consistent radiobiological pattern was established: an increase in the free hormone fraction due to diminished CBG binding capacity. Adrenal autotransplantation prior to irradiation reduced corticoid levels, enhanced CBG binding capacity during ARS, and decreased free corticoid concentrations, resulting in a protective effect and increased radioresistance.

Conclusion: The findings underscore the critical role of corticosteroid regulation and CBG functional status in the body's response to radiation exposure. Modulation of adrenal activity and correction of protein-steroid interactions may be considered a promising strategy for enhancing radioresistance.

Key words. Acute radiation sickness, protein-steroid interaction, 11-oxycorticosteroids, binding capacity of the corticosteroid-binding globulin, free hormone, adrenal autotransplantation.

Introduction.

The development of radiobiology, pathophysiology, and experimental medicine [1] has led to the creation of a theoretical framework for the functioning of the pituitary-adrenal system, which determines the specifics of hormone synthesis in various pathological conditions of the body, including radiation sickness [2]. A leading symptom of acute radiation sickness is hypercorticism, which develops against the background of high glucocorticoid activity of the adrenal cortex [3].

The radiobiological patterns of the functional activity of the adrenal cortex under the influence of radiation were discovered more than 60 years ago. However, the main conclusions were drawn only based on the total hormone level in the blood, without considering the biological activity of various fractions. It has been established that hormones are present in free form in the blood and are bound to a specific protein, corticosteroid-binding globulin (CBG) or transcortin [4]. Only free corticosteroids have biological activity, and the hormones bound with CBG are biologically inactive [5]. Therefore, the patterns of protein-steroid interaction, considering different fractions of corticosteroids in the pathogenesis of acute radiation sickness and conditions of increased resistance, particularly in irradiated animals with autotransplanted adrenal glands, deserve scientific analysis.

The relevance of the protein-steroid interaction problem in the pathogenesis of acute radiation sickness and in conditions of increased resistance is determined by its theoretical value for the theory of radiobiology, for radiobiological and medical-clinical research, as well as its practical significance in the clinical diagnosis and treatment of patients with hormonal disorders, and in medical radiobiology for the treatment of radiation sickness.

The extent of prior research on the problem under study.

Modern radiobiological concepts of the pathogenesis of acute radiation sickness are the theoretical basis. These concepts allow, on the one hand, to observe the multilevel patterns of the radiation response to radiation damage and, on the other hand, to identify the conditions causing increased radioresistance, which allows for determining the severity and prognosis of radiation sickness [6]. Currently, the leading position in radiobiology is the systemic nature of the adaptive response of various levels and systems of the body to radiation exposure, reflected in several modern adaptive theories [7,8].

The pituitary-adrenal system plays a vital role in the pathogenesis of acute radiation syndrome. The fundamental position that has existed in radiobiology since the beginning of the 20th century is the two-phase nature of the pituitary-adrenal system reaction in radiation sickness, where the first phase is early, occurring immediately after radiation exposure, and the second is late, occurring at the height of radiation sickness and accompanied by an increase in adrenocortical function [9], which is the result of purely the damaging effect of radiation [10]. The leading mechanism of protein-steroid interaction in pathological conditions of the body, which affects the activity of the entire hypothalamic–pituitary–adrenal axis, is the binding capacity of CBG or transcortin [5]. However, the radiobiological patterns of the functional activity of the adrenal cortex under the influence of radiation are derived without considering the physiological role of different fractions of corticosteroids. To date, there is practically no modern radiobiological experimental data on the patterns of binding of corticosteroids to plasma proteins, considering its fractions and the role of free corticoids in the hormonal effect in acute radiation sickness, except for our publications on this issue [11,12].

Hypercorticism in radiation damage is becoming important in light of the mechanisms of increasing radioresistance. Autotransplantation of the adrenal glands prevents the development of hypercorticism and increases the radioresistance of irradiated animals [10]. Therefore, the study of the protein-steroid interaction, considering its fractions in the pathogenesis of acute radiation sickness on the model of resistance of irradiated animals with autotransplanted adrenal glands, will clarify some patterns that increase radioresistance [13].

Thus, further experimental studies on the binding of corticosteroids to plasma proteins are needed, considering different fractions of corticosteroids in the pathogenesis of acute radiation sickness and in conditions of increased resistance, particularly in irradiated animals with autotransplanted adrenal glands.

Aim: The study aims to summarize experimental data on the importance of hypercorticism in the pathogenesis of acute radiation sickness, considering species differences and conditions of increased radioresistance in a model of irradiated animals with autotransplanted adrenal glands.

Research objectives: 1) to identify the dynamics of the fractional composition of 11-oxycorticosteroids (11-OCS) in the pathogenesis of acute radiation sickness in various experimental animals; 2) to describe the patterns of protein-steroid interaction in the model of irradiated animals with autotransplanted adrenal glands; 3) to identify the role and significance of hypercorticism in the pathogenesis of acute radiation sickness, considering species differences and in conditions of increased radioresistance.

Materials and Methods.

A series of experiments was conducted to study the patterns of protein-steroid interaction in the pathogenesis of acute radiation sickness, considering the specific features of this mechanism. The experiments were carried out on large animals (chinchilla rabbits (n=20) and non-pedigree dogs (n=15)) and small animals (male WISTAR rats (n=63), guinea pigs (n=49), and white BALB/c mice (n=32)). All animals had previously adapted to the experimental conditions. Adaptive conditions were determined experimentally by assessing the level of corticosteroids in the blood of animals. γ-irradiation of animals was performed on the EGO-2 (Co60) installation at an average dose rate of 5.75 Gy/min for further γ-irradiation of animals at a dose equaling an acute stage IV radiation sickness: the rabbits were irradiated at a dose of 8 Gy, rats at a dose of 8.5 Gy, guinea pigs 4.5 Gy, dogs 3.5 Gy, and mice 6.5 Gy. The follow-up time after irradiation varies from animal to animal. The testing times for the fractional composition of 11-OCS (cortisol in dogs and guinea pigs; corticosterone in rats, mice, and rabbits) after irradiation differed across animal species: the rabbits were tested before irradiation and 30 minutes, 1.5-2 hours, 4, 6, and 8 days after irradiation; rats - before irradiation and 1 hour, 1, 3, and 10 days after irradiation; guinea pigs - before irradiation and 1 hour, 1, 3, 7, and 10 days after irradiation; mice - before irradiation and 10 and 15 days after irradiation; and non-pedigree dogs - before irradiation and 7 and 12 days after irradiation.

Experiments on protein-steroid interaction in the model of irradiated animals with autotransplanted adrenal glands were carried out on male rats (n=125) weighing 200-220 g. Initially, on the 3rd, 6th, 12th, 20th, 28th, and 30th days after autotransplantation of the adrenal glands in animals (n=63), the total content of 11-OCS in the blood was determined. After autotransplantation of the adrenal glands on day 28, the rats were subjected to total γ-radiation at a dose of 6.0 Gy, causing acute radiation sickness of the IV degree. Animals irradiated on the 28th day after the adrenal autotransplantation surgery were more radioresistant than those irradiated in the early stages. Two groups of animals were formed: the experimental group of rats with autotransplanted adrenal glands (n=30) and the control group of rats with intact adrenal glands (n=32). The binding capacity of CBG and the total content of 11-OCS in the blood of the studied groups were determined at different stages of radiation sickness. Before irradiation and on the 7th day after irradiation, the amount of free 11-OCS was determined in the animals.

Depending on the objectives of the experiments, we used a set of experimental methods and research techniques. The fractional composition of 11-OCS was determined using the fluorometric method developed by Guillemin et al., and we used a modified gel filtration method developed by De Moor et al. [12]. In experiments aimed at detecting protein-steroid interaction in a model of irradiated animals with autotransplanted adrenal glands, autotransplantation of the adrenal glands was performed using a modified version of the Ingle and Higgins method [14]. This modified methodology is currently in the final stage of formal registration with Rospatent, the Federal Service for Intellectual Property of the Russian Federation.

Statistical methods of quantitative data processing (descriptive statistics method, Student's t-test) were used. The differences were significant at $p<0.05$ or less.

Results.

A series of studies on the patterns of protein-steroid interaction in the pathogenesis of acute radiation sickness, considering the specific features of this mechanism, showed the dynamics of the fractional composition of 11-OCS in acute radiation sickness in various experimental animals. A monophasic radiation curve was found in rabbits since a significant increase in the total level of 11-OCS was observed only in the first hours after radiation exposure. With the development of acute radiation sickness, the secretion of adrenocortical hormones continued to decrease (Table 1).

In rats, primary hypercorticism was observed in the first hours after irradiation. A secondary increase in the total level of 11-OCS in the blood was observed on the 3rd day of acute radiation sickness ($P<0.001$), which again significantly decreased on the 10th day below the baseline level ($P<0.02$) (Table 2).

In the dynamics of acute radiation sickness in rabbits and rats, there is a period of "latent" hypercorticism, characterized by an increase in the concentration of free hormone even against the background of a reduced total corticosteroid level in blood plasma. The free fraction of the hormone significantly increases ($P<0.05$ in rabbits; $P<0.001$ in rats) in the first hours and at the height of radiation sickness ($P<0.001$). In the first hours of radiation sickness, the level of free hormone increases against the background of a significant increase in the total

Table 1. *Dynamics of the fractional composition of 11-OCS in rabbit blood plasma after irradiation at a dose of 8.0 Gy, mcg/100 ml (n=20).*

Time frame	Total level 11-OCS, M±m	Free 11-OCS, M±m	Free 11-OCS, % of the total level	Bound 11-OCS, M±m
Before irradiation	9.3±0.6	0.2±0.04	0	9.1±0.5
30 min-1 hour after irradiation	12.0±1.1*	1.8±1.0	11.9±6.5	10.1±0.7
1.5-2 hours after irradiation	13.7±1.9*	2.1±0.25*	17.4±2.5*	11.3±1.5
4 days after irradiation	8.6±0.7	2.4±0.31**	30.1±2.9**	6.1±0.7*
6 days after irradiation	6.8±1.0	0.9±0.8	13.5±13.0	6.1±1.0*
8 days after irradiation	5.6±0.5**	0.5±0.3	9.1±5.7	5.2±0.6**

*Note: P is the confidence level of the differences between the corresponding parameters in rabbits before and after irradiation. *P<0.05; **P<0.001.*

Table 2. *Dynamics of the fractional composition of 11-OCS in rat blood plasma after irradiation at a dose of 8.5 Gy (n=63).*

Time frame	Number of observations	Total 11-OCS level, mcg/100 ml	Free 11-OCS		Bound 11-OCS	Binding capacity of CBG (mcg/100 ml)
			mcg/100 ml	% of the total 11-OCS	mcg/100 ml	
Before irradiation	10	17.8±1.1	1.6±0.1	9.2	16.2±0.8	40.4±1.0
After irradiation						
1 hour	12	45.0±2.5***	10.6±1.0***	23.8***	34.7±3.1***	38.5±1.4
1 day	10	14.8±1.3	2.0±0.3	13.8	12.8±1.2	-
3 days	10	28.2±2.7***	4.9±0.7***	17.1***	23.3±1.5**	24.1±1.0***
8 days	11	17.6±1.7	-	-	-	15.4±1.3***
10 days	10	12.9±1.2*	5.4±0.7***	42***	7.5±1.0***	8.8±1.1***

Note: P is the confidence level of the differences between the corresponding rat parameters before and after irradiation. *P<0.02; **P<0.01; ***P<0.001.

corticosteroid content (P<0.05 in rabbits; P<0.001 in rats). At the height of radiation sickness, an increase in the free fraction of the hormone occurs against the background of both increased and decreased total levels of 11-OCS (P<0.001 in rabbits; P<0.02 in rats).

Thus, in both rats and rabbits, a period of "latent" hypercorticism is observed in the pathogenesis of acute radiation sickness, characterized by an increase in the concentration of free hormone against the background of even a reduced total level of corticosteroids in blood plasma. The content of the free fraction increases in the first hours and at the height of radiation sickness. In the first hours, this increase occurs against the background of an increased total corticosteroid content and at the height of radiation sickness against the background of increased and decreased total hormone levels.

In experiments on guinea pigs, the content of the free fraction of corticosteroids was significantly increased both in the first hours after irradiation (P<0.001) against the background of a significantly increased total hormone level (P<0.001) and at the height of radiation sickness (P<0.05 on day 3; P<0.001 on days 7 and 10) against the background of both elevated (P<0.001) and normal total corticosteroid levels in the blood (Table 3).

A two-phase radiation curve was also found in guinea pigs. The total hormone level significantly increased both in the first hours after exposure (P<0.001) and on day 3 (P<0.001), decreasing with the development of acute radiation sickness.

When studying the binding of 11-OCS to plasma proteins in dogs and mice, primary attention was paid to the dynamics of protein-steroid interaction at the height of acute radiation sickness (Tables 4 and 5).

In dogs at the height of acute radiation sickness, on the 7th day of acute radiation sickness, the total level of 11-OCS significantly (P<0.001) exceeded the baseline level by almost 2 times and returned to it on the 12th day. The concentration of free hormones during these periods significantly (P<0.001) exceeded the baseline level, remaining significantly higher (P<0.05) on the 12th day after irradiation. Thus, at the height of radiation sickness in dogs, the free fraction of 11-OCS in the blood increased against the background of normal and elevated total 11-OCS content.

The content of total corticosteroids in mice before irradiation and on the 10th and 15th days after irradiation did not differ from the normal level. The level of free hormone significantly increased 2-fold (P<0.05) on day 10 and 3.5-fold (P<0.001) on day 15 of radiation sickness compared with the control group (Table 5).

Thus, the experimental results showed that the free fraction of the hormone remained elevated throughout acute radiation sickness in animals with both mono- and biphasic adrenocortical response curves to radiation, regardless of fluctuations in the total level of corticosteroids. This is especially pronounced in the first hours after radiation and at the height of acute radiation sickness. The presence of non-protein-bound and more mobile steroids in the blood plasma can cause a hypercorticoid state with normal or even reduced levels of hormones in the blood.

As Table 2 shows, early hypercorticism is determined by an increase in the total secretion of 11-OCS since the binding capacity of CBG does not change. At the height of acute

Table 3. *Dynamics of the fractional composition of 11-OCS in the blood plasma of guinea pigs after irradiation at a dose of 4.5 Gy (n=49).*

Time frame	Number of observations	Total level 11-OKS	Free 11-OCS		Bound 11-OCS
			mcg/100 ml	%	mcg/100 ml
Before irradiation	9	31.5±1.9	7.0±1.0	22.5	24.5±1.6
After irradiation					
1 hour	10	119.0±7.5***	44.0±3.5***	37**	75.0±3.9***
1 day	11	35.0±2.1	-	-	-
3 days	6	75.5±6.0***	14.5±2.8*	19*	61.0±4.7***
7 days	6	62.5±5.1***	23.0±2.4***	36**	39.5±3.8**
10 days	7	37.5±2.7	18.5±2.1***	48**	19±2.0*

*Note: P is the confidence level of the differences between the corresponding values in guinea pigs before and after irradiation. *P<0.05; **P<0.01; ***P<0.001.*

Table 4. *Dynamics of the fractional composition of 11-OCS in the blood plasma of dogs after irradiation at a dose of 3.5 Gy (n=15).*

Time frame	Number of observations	Total level 11-OCS mcg/100ml	Free 11-OCS		Bound 11-OCS
			mcg/100 ml	%	mcg/100 ml
Before irradiation	15	5.5±0.4	1.6±0.2	28	4.0±0.4
After irradiation, 7 days	8	10±1.0**	4.0±0.5**	40**	6.0±0.7*
After irradiation, 12 days	5	6.5±0.9	3.0±0.4*	45*	3.5±0.6*

*Note: P is the confidence level of the differences between the corresponding indicators in dogs before and after irradiation. *P<0.05; **P<0.001.*

Table 5. *Dynamics of the fractional composition of 11-OCS in the blood plasma of mice after irradiation at a dose of 6.5 Gy (n=32).*

Time frame	Number of observations	Total level 11-OCS mcg/100ml	Free 11-OCS		Bound 11-OCS
			mcg/100 ml	%	mcg/100 ml
Before irradiation	12	16.5±1.2	2.0±0.4	12	14.5±0.9
After irradiation, 10 days	10	15.3±1.0	4.0±0.7*	26*	11.3±0.8*
After irradiation, 15 days	10	17.9±1.4	7.0±0.8**	39**	10.9±1.1*

*Note: P is the confidence level of the differences between the corresponding parameters in mice before and after irradiation. *P<0.05; **P<0.001.*

Table 6. *Dynamics of the total level of 11-OCS, the free fraction of 11-OCS, and the binding capacity of CBG in the blood of rats with intact and autotransplanted adrenal glands after irradiation at a dose of 6.0 Gy. Values are presented as mean ± SEM; n indicates the number of observations.*

Group (n)	Parameter	Before irradiation	3 days after	7 days after	14 days after	21 days after
Intact adrenal glands (32)	Total 11-OCS (μg/100 mL)	17.7 ± 1.1	20.6 ± 1.2	21.6 ± 1.5	17.8 ± 2.2	18.0 ± 2.9
	Free 11-OCS (μg/100 mL)	1.6 ± 0.2	–	4.8 ± 1.1^{a}	–	–
	CBG binding capacity (μg/100 mL)	35.8 ± 1.0	27.6 ± 2.5^{b}	16.3 ± 2.6^{c}	18.4 ± 0.6^{d}	26.8 ± 1.3^{c}
Autotransplanted adrenal glands (30)	Total 11-OCS (μg/100 mL)	9.2 ± 1.0†††	9.1 ± 1.2†††	10.7 ± 1.3†††	8.9 ± 1.4††	13.2 ± 1.5†
	Free 11-OCS (μg/100 mL)	0††	–	1.0 ± 0.4††	–	–
	CBG binding capacity (μg/100 mL)	46.5 ± 2.2†††	36.4 ± 3.5^{a,†}	32.0 ± 5.8^{a,†}	22.0 ± 1.2^{d,†}	34.5 ± 1.7^{d,††}

Note.

– not measured.

Statistical symbols:

• Within group comparisons (vs. pre irradiation baseline): $^{a}p < 0.05$; $^{b}p < 0.02$; $^{c}p < 0.01$; $^{d}p < 0.001$.

• Between group comparisons (intact vs. autotransplanted at the same time point): $^{\dagger}p < 0.05$; $^{\dagger\dagger}p < 0.01$; $^{\dagger\dagger\dagger}p < 0.001$.

radiation sickness, an increase in free corticosteroids, observed against a background of normal or even reduced total 11-OCS levels, is associated with decreased binding capacity of CBG ($P<0.001$). The reduction in CBG binding capacity during the peak of radiation sickness and the corresponding increase in free corticosteroids—irrespective of fluctuations in total hormone levels—were observed across different animal species, representing a general radiobiological pattern.

Autotransplantation of the adrenal glands in irradiated animals prevents the development of hypercorticism, which is a condition for increasing radioresistance [14]. The markedly elevated CBG binding capacity in animals with autotransplanted adrenal glands, both before irradiation and during the course of acute radiation sickness, constitutes one of the mechanisms underlying the radioprotective effect of adrenal autotransplantation. However, its applicability as a method to suppress adrenal hyperfunction could extend to the treatment of acute radiation syndrome and other conditions, such as hormone-dependent tumors and Cushing's syndrome.

Questions about the patterns of protein-steroid interaction in irradiated animals with autotransplanted adrenal glands deserve attention [10].

Initially, the total level of 11-OCS in rats (n=63) was studied at various time points after adrenal autotransplantation. On days 3 and 6, after the adrenal glands were autotransplanted, 11-OCS were not detected in the animals' peripheral blood plasma. On day 9, the corticosteroid content was 5.1±0.7 mcg/100 ml. Subsequently, the level of 11-OCS gradually increased, and on days 12, 20, 28, and 30, respectively, it amounted to 6.1±1.25, 8.1±1.4, 8.6±2.1, and 11.65±1.35 mcg/100 ml. During all study periods, the total corticosteroid content in the blood of operated animals was significantly lower ($P<0.01$-0.001) than in animals with intact adrenal glands. Autotransplantation of the adrenal glands on the 28th day after surgery, immediately before irradiation, significantly increased the binding capacity of CBG ($P<0.01$), and almost halved the content of total 11-OCS. Free corticosteroids in the blood under conditions of reduced total corticosteroid content and increased binding capacity of CBG in the blood plasma in such rats were practically absent.

To study the dynamics of the fractional composition of 11-OCS in the pathogenesis of acute radiation sickness in conditions of increased radioresistance, experiments were continued on rats with autotransplanted and intact adrenal glands exposed to a dose of 6 Gy (Table 6).

In the initial stages of acute radiation sickness, both rats with intact and autotransplanted adrenal glands showed a significant decrease in the binding capacity of blood plasma CBG ($P<0.02$, $P<0.05$, respectively).

In animals with autotransplanted adrenal glands, the decrease in the binding capacity of CBG after irradiation occurred later, and its recovery occurred earlier and more intensively than in animals with intact adrenal glands. In rats with autotransplanted adrenal glands, with a significantly reduced total level of corticosteroids ($P<0.001$) compared with the control group, the binding capacity of CBG was sharply increased, both normally ($P<0.01$) and in the dynamics of radiation sickness ($P<0.05$, $P<0.01$). At the height of acute radiation sickness, the content of free hormone was significantly reduced, both compared with the control group ($P<0.01$) and with the baseline level ($P<0.05$).

Discussion.

The experimental results show several patterns of protein-steroid interaction in the pathogenesis of acute radiation sickness, considering the specific features of this mechanism.

In acute radiation sickness, the binding capacity of CBG decreases, while the level of free hormone increases. This has been conclusively demonstrated by our extensive experimental data.

The mechanism by which irradiation causes a reduction in CBG binding capacity has been examined in detail in previously published articles. For instance, the article "The Role of the Liver in Regulating Protein-Steroid Interaction in Healthy and Irradiated Animals" presents findings on the influence of the liver on the fractional composition of 11-OCS in the blood plasma of healthy and irradiated angiostamized dogs [15].

The adrenocortical response to radiation in most studied animal species has the character of a two-phase curve. The two-phase nature of the reaction of the pituitary-adrenal system to radiation is confirmed by the analysis of experimental data on rats exposed to lethal doses [2], guinea pigs [10], dogs [16], and sheep at low and medium doses of radiation [17]. However, as our study shows, in animals with both mono- and biphasic adrenocortical response curves to radiation, regardless of fluctuations in the total level of corticosteroids, the free fraction of the hormone remained elevated throughout acute radiation sickness, which was especially pronounced in the first hours after radiation and at the height of acute radiation sickness. The effect of radiation at a dose of acute radiation sickness disturbs the binding of corticosteroids to plasma proteins, increasing free, biologically active hormones at the height of acute radiation sickness. The presence of non-protein-bound and more mobile steroids in the plasma can cause a hypercorticoid state with normal or even reduced hormone levels in the blood. The long-term effect of "latent" hypercorticism, therefore, may be a factor exacerbating the course of acute radiation sickness.

The existing concept of hypercorticism in acute radiation sickness, based on the two-phase response of the adrenal cortex, needs to be clarified since almost all acute radiation syndrome occurs against the background of an increase in free biologically active glucocorticoids.

Our results expand the understanding of the role of protein-steroid interaction, particularly the role of the free hormone, in various pathological conditions, which is confirmed by the results of modern medical and clinical research. Thus, a significant decrease in the level of CBG in blood plasma is observed with the development of acute inflammatory reactions [18], such as sepsis [19]. This leads to an increase in the level of free glucocorticoids in the blood, which can control the inflammatory response, gluconeogenesis, and stress [20]. Currently, the free hormone index is increasingly used to diagnose the functional status of the hypothalamic-pituitary-adrenal system in patients with impaired hormonal status [21,22], also relevant in radiation pathology [23]. Studies have shown that in the pathogenesis of acute radiation sickness, the biological effect of glucocorticoids is determined not by the

total level of 11-OCS but by the concentration of hormones in the blood that are not related to proteins, which is the practical value of our results.

In the experiments on a model of irradiated animals with autotransplanted adrenal glands, patterns were found, according to which the pathogenesis of acute radiation sickness in conditions of increased resistance in the mechanism of reducing radiation hypercorticism was mainly due to a lower degree of impairment of the binding capacity of CBG, rather than a change in the total level of 11-OCS in the blood. Our results confirmed the patterns of protein-steroid interaction, demonstrating an increase in the binding capacity of CBG in animals after adrenalectomy [24]. Thus, autotransplantation of the adrenal glands, which causes a decrease in corticoids, leads to an increase in the binding capacity of CBG, the purpose of which is to protect adrenocortical hormones from metabolism before their utilization by tissues and, at the height of radiation sickness, to have a protective effect by reducing the concentration of free corticosteroids in the blood of animals. In the pathogenesis of acute radiation sickness, increased animal resistance due to autotransplantation of the adrenal glands leads to the absence of radiation hypercorticism due to impaired interaction of corticosteroids with plasma proteins.

This study has certain limitations that should be acknowledged. First, the quantitative data on 11-OCS were obtained using fluorometric methods, which were the standard in radiobiological endocrinology at the time of the original experiments but have lower specificity than contemporary mass spectrometry-based assays. While this may influence the absolute hormone concentrations reported, the consistent relative patterns of change—specifically the decrease in CBG binding capacity and the concomitant rise in the free hormone fraction across all species—remain a robust and central finding. Second, the experimental model of adrenal autotransplantation is inherently prophylactic. Consequently, it is not proposed as a direct clinical intervention for acute radiation syndrome but serves as a powerful tool to elucidate the protective mechanism mediated through CBG stabilization. Finally, while the use of multiple animal species strengthens the generality of the observed radiobiological pattern, differences in their dominant glucocorticoid (corticosterone vs. cortisol) and metabolism necessitate cautious extrapolation to humans. These limitations highlight specific areas for technical refinement in future research but do not detract from the primary conclusion regarding the critical role of protein-steroid interaction dynamics in radiation response.

Conclusion.

1. The adrenocortical response to radiation in most studied animal species is a two-phase curve. Only in rabbits, after a decrease in the total level of corticosteroids in the blood, secondary hypercorticism was not noted, which manifests the specific features of the functional activity of the adrenal cortex to radiation. In all irradiated animals, at the height of acute radiation sickness, the binding of corticosteroids to plasma proteins was disrupted, leading to an increase in the free biologically active fraction observed against the background of elevated, normal, and even reduced total levels of 11-OCS.

2. A typical radiobiological pattern in the pathogenesis of acute radiation sickness was an increase in the free fraction of corticosteroids due to a decrease in the binding capacity of CBG at the height of acute radiation sickness, the value of which is an indicator of protein-steroid interaction.

3. Autotransplantation of the adrenal glands, which causes a persistent decrease in corticoids, leads to an increase in the binding capacity of CBG at the height of radiation sickness, having a protective effect that reduces the concentration of free corticosteroids in the blood.

REFERENCES

1. Kovalev AV, Kholmogorskaya OV, Korenkova MV. Structural dynamics of skin regeneration after thermal burns in controlled water environment (experimental study). Systematic Reviews in Pharmacy. 2020;11:1564-1567.
2. Abd-Elhamid TH, Ismail NS, Amin YA, et al. Treatment of corticosteroid-induced myopathy through Filgrastim induced endogenous stem cells mobilization in male albino rats. Cells Tissues Organs. 2025;11:1-36.
3. Zeng W, Zhao Y, Tu Q, et al. Network analysis and experimental validation analysis reveal the mechanism by which psoralen improves glucocorticoid-induced growth retardation. Journal of Pharmaceutical and Biomedical Analysis. 2025;260:116801.
4. Boyle LD, Miguelez-Crespo A, Paul M, et al. The NE/AAT/CBG axis regulates adipose tissue glucocorticoid exposure. Nature Communications. 2025;16:545.
5. Breuner CW, Beyl HE, Malisch JL. Corticosteroid-binding globulins: Lessons from biomedical research. Molecular and Cellular Endocrinology. 2020;514:1108-1157.
6. Obrador E, Salvador R, Villaescusa JI, et al. Radioprotection and radiomitigation: From the bench to clinical practice. Biomedicines. 2020;8:461.
7. Azizova TV, Moseeva MB, Briks KV. [Acute radiation sickness due to critical accidents at a nuclear production facility] [Published in Russian]. Mediko-biologicheskiye i sotsial'no-psikhologicheskiye problemy bezopasnosti v chrezvychaynykh situatsiyakh. 2023;1:5-12.
8. Busato F, Khouzai BE, Mognato M. Biological vechanisms to reduce radioresistance and increase the efficacy of radiotherapy: State of the art. International Journal of Molecular Sciences. 2022;23:10211.
9. Rusch JA, Layden BT, Dugas LR. Signalling cognition: The gut microbiota and hypothalamic-pituitary-adrenal axis. Frontiers in Endocrinology. 2023;14:1130689.
10. Shabdarbaeva D, Chaizhunusova N, Uzbekov D, et al. Radiation-induced adrenal gland injury. Astana Medical Journal. 2020;2:141-150.
11. Omelchuk NN. [Binding capacity of plasma corticosteroid-binding globulin as a mechanism for increasing the free fraction of the hormone in the pathogenesis of acute radiation sickness] [Published in Russian]. Radiatsiya i risk. 2022a;31:139-146.
12. Omelchuk NN. [On the problem of impaired binding of corticosteroids to blood plasma proteins in the pathogenesis of acute radiation sickness] [Published in Russian]. Radiatsiya i risk. 2022b;31:131-138.

13. Yalcin S, Sokmensuer C, Esin E. Glucagonoma. In: Yalcin S, Öberg K (eds) Neuroendocrine tumours. 2024:265-282.
14. Ingle DJ, Higgins GM. Autotransplantation and regeneration of the adrenal gland endocrinology. Endocrinology. 1938;22:458-464.
15. Omelchuk NN. Rol' pecheni v reguliatsii belkovo-steroidnogo vzaimodeistviia u zdorovykh i obluchënnykh zhivotnykh [The role of the liver in the regulation of protein-steroid interaction in healthy and irradiated animals]. Radiatsiia i risk. 2023;32:78-87.
16. Nazarov E, Khlusov I, Noda M. Homeostatic and endocrine responses as the basis for systemic therapy with medical gases: Ozone, xenon and molecular hydrogen. Medical Gas Research. 2021;11:174-186.
17. Kutlikova IV, Lysenko NP. [Analysis of the dynamics of the content of adrenocorticotropic hormone in the blood plasma of small cattle depending on the dose load] [Published in Russian]. In: Obrazovaniye i nauka: Sovremennoye sostoyaniye i perspektivy razvitiya. 2015;93-95.
18. Meyer EJ, Nenke MA, Lewis JG, et al. Corticosteroid-binding globulin: Acute and chronic inflammation. Expert Review of Endocrinology & Metabolism. 2017;12:241-251.
19. Meyer EJ, Nenke MA, Rankin W, et al. Total and high-affinity corticosteroid-binding globulin depletion in septic shock is associated with mortality. Clinical Endocrinology. 2019;90:232-240.
20. Li JX, Cummins CL. Fresh insights into glucocorticoid-induced diabetes mellitus and new therapeutic directions. Nature Reviews Endocrinology. 2022;18:540-557.
21. Bae YJ, Kratzsch J. Corticosteroid-binding globulin: Modulating mechanisms of bioavailability of cortisol and its clinical implications. Best Practice & Research Clinical Endocrinology & Metabolism. 2015;29:761-772.
22. Bancos I, Erickson D, Bryant S, et al. Performance of free versus total cortisol following cosyntropin stimulation testing in an outpatient setting. Endocrine Practice. 2015;21:1353-1363.
23. Claude F, Ubertini G, Szinnai G. Endocrine disorders in children with brain tumors: At diagnosis, after surgery, radiotherapy and chemotherapy. Children. 2022;9:1617.
24. Gulfo J, Castel R, Ledda A, et al. Corticosteroid-binding globulin is expressed in the adrenal gland and its absence impairs corticosterone synthesis and secretion in a sex-dependent manner. Scientific Reports. 2019;9:14018.