

Experimental evaluation of chemotherapy-induced models of testicular failure

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The increasing incidence of cancer among young individuals underscores the importance of preserving reproductive function and improving experimental models for the study of chemotherapy-induced testicular failure. The aim of this study was to conduct a comparative evaluation of cytostatic agents from different pharmacological classes in a mouse model of testicular dysfunction. Male Balb/c mice were treated with cyclophosphamide (250 mg/kg), doxorubicin (10 mg/kg), or cisplatin (10 mg/kg). Body weight, hematological parameters, survival, social activity, anxiety levels, and sperm parameters were assessed at 1, 4, and 8 weeks post-treatment. Doxorubicin caused early and pronounced toxicity, including weight loss, hematopoietic suppression, reduced sperm count, motility, and viability, along with an increased proportion of abnormal forms as early as one week after administration. By week 4, complete aspermatogenesis was observed, accompanied by persistent behavioral impairments and increased lethality, without recovery by the end of the study. In the cyclophosphamide group, body weight and hematological parameters stabilized within 4 weeks, although irreversible anxiety elevation and transient reduction in social activity were noted. Oligospermia peaked at week 4, accompanied by decreased motility and viability, while sperm count and morphology remained impaired up to week 8. Cisplatin demonstrated the mildest and predominantly reversible effects. Body weight progressively increased, hematological alterations were moderate with subsequent recovery, and social activity was generally preserved except for a transient decline at week 4. Anxiety levels showed a decreasing trend, while moderate oligospermia was detected without significant morphological abnormalities. By week 8, sperm count and motility showed marked improvement. In summary, cyclophosphamide represents the most suitable agent for modeling testicular failure with partial functional recovery, doxorubicin induces irreversible gonadotoxicity, and cisplatin may be employed to study mild, reversible forms of gonadal impairment.

Key words: cytostatics; chemotherapy; cyclophosphamide; doxorubicin; cisplatin; testicular failure; biomedical modeling.

INTRODUCTION

Male reproductive dysfunction caused by both age-related changes and external factors, particularly chemotherapy, remains one of the pressing medico-social problems. A significant decrease in fertility adversely affects not only quality of life and psychological well-being but also social adaptation, especially in young and middle-aged men who have undergone oncological diseases [1, 2]. One of

the critical consequences of antitumor therapy is testicular insufficiency, which can manifest as hypospermia, hormonal imbalance, irreversible damage to the germinal epithelium, and loss of fertility [3, 4]. In addition, the consequences of testicular insufficiency are manifested not only by morphological and functional changes in the gonads but also by behavioral disorders, such as reduced social and sexual activity, increased anxiety, and mood alterations [5]. The severity of these changes is largely determined by the type

and regimen of chemotherapy, which necessitates comparison of different gonadotoxicity models to identify the most informative and reproducible experimental approaches.

Chemotherapeutic agents of different classes vary in their degree and mechanisms of gonadal toxicity, determined by both their pharmacological properties and the sensitivity of spermatogenic epithelium cells. Studying the action of the most common cytostatics, such as cyclophosphamide, doxorubicin, and cisplatin, helps to deepen the understanding of the pathogenesis of testicular dysfunction and improve strategies for its prevention and treatment [6]. These drugs are widely used in the treatment of solid tumors and hematological malignancies but possess pronounced systemic toxicity, leading to multiple adverse effects, including reproductive impairment. Because the severity of gonadal injury and the rate of recovery depend on the cytostatic class, dose, and exposure duration, cytostatic administration can serve as a convenient and reproducible experimental model of testicular dysfunction [7].

The current literature widely describes morphological changes in animal testes following chemotherapy exposure [6, 8-10]. However, many aspects of gonadal toxicity and its functional outcomes, including alterations in semen parameters, remain to be elucidated. Comparative analysis of various cytostatic-induced models of testicular toxicity enables the selection of optimal approaches for further research, including studying gonadal recovery processes.

Objective: to perform a comparative evaluation of the effects of cytostatic agents from different classes in a model of testicular dysfunction.

METHODS

The study was conducted on male Balb/c mice aged 6 months and weighing 29.4 ± 0.5 g. A total of 128 animals were used. Mice were randomly divided into 4 experimental groups (32 per group) and subjected to behavioral testing, analysis of sperm parameters, body

weight dynamics, and peripheral blood cell counts. For long-term survival monitoring, 20 animals per group were followed until the end of the observation period (22 months), while 12 mice from each group were euthanized at intermediate time points for bone marrow sampling. The animals were maintained under standard vivarium conditions with free access to food and water. All experimental procedures complied with the guidelines of the "Bioethical Expertise of Preclinical and Other Scientific Research Conducted on Animals" (Kyiv, 2006), the "General Principles of Animal Experiments" (VI Congress on Bioethics, Kyiv, 2016), and the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986).

Modeling of testicular dysfunction. To model testicular dysfunction, cyclophosphamide (CPA), doxorubicin (DOX), and cisplatin (CDDP) were used. These agents represent different classes of cytostatics and induce testicular injury through distinct mechanisms involving DNA damage and apoptosis [11-14].

Animals were randomly divided into four groups ($n = 30$ per group): group 1 (control) – received no drug; group 2 (CPA) – received intraperitoneal cyclophosphamide 250 mg/kg once; group 3 (DOX) – received intraperitoneal doxorubicin 10 mg/kg once; group 4 (CDDP) – received intraperitoneal cisplatin 10 mg/kg once. Doses were selected based on published data [8, 15, 16]. General condition, body weight, behavioral responses, and semen parameters were assessed at 1, 4, and 8 weeks post-treatment.

Survival was assessed using Kaplan-Meier analysis. Group comparisons were performed with the log-rank test. In addition, the median survival age (the time point at which 50% of the population remains alive) and the age reached by 90% of the animals were determined. Statistical analyses were carried out using PAST v.3.15 software (Norway) and the online tools www.evanmiller.org, <https://www.medicalstat.org>.

Peripheral blood cell count. Blood samples were diluted in isotonic solution, loaded into a Neubauer chamber (Germany), and the number of cells was determined using the standard hemocytometric method under a light microscope at $\times 400$ magnification. The results were expressed as the absolute number of erythrocytes and leukocytes per ml of blood.

Bone marrow cell count. Bone marrow cells were isolated from the femurs of mice immediately after euthanasia under ketamine anesthesia. Both ends of the femur were cut off, and the marrow cavity was flushed with 1 ml of sterile 0.9% sodium chloride solution using a syringe with a fine needle. The obtained cell suspension was resuspended by pipetting until a homogeneous mixture was achieved. The total number of nucleated cells was counted in a Neubauer chamber under a light microscope at $\times 400$ magnification. The results were expressed as the absolute number of nucleated cells per ml of suspension.

Social activity. Social activity was assessed using the three-chamber test, which allows evaluation of the level of social interaction and interest in another conspecific. The apparatus consisted of three interconnected chambers; cages with unfamiliar mice (or empty cages) were placed in the side chambers, while the test animal was placed in the central chamber. The time spent in each chamber was recorded as a measure of social activity [17].

Anxiety level. Anxiety was assessed using the elevated plus maze test, which consisted of two open and two closed arms arranged in a cross shape and elevated above the floor. The animal was placed in the center of the maze, after which the time spent in the open and closed arms was recorded. A decrease in time spent in the open arms was interpreted as an indicator of increased anxiety [18].

Evaluation of sperm parameters. Sperm samples were obtained from the cauda epididymis and suspended in 1 ml of prewarmed (37°C)

physiological saline. Sperm count was determined in a Neubauer chamber under $\times 400$ magnification. Motility was evaluated microscopically by assessing at least 200 cells in several fields and expressed as a % of motile sperm. Viability (eosin and trypan blue staining) and morphology (hematoxylin–eosin staining) were assessed using standard criteria. Measurements were performed at 1, 4, and 8 weeks after administration of chemotherapeutic agents.

Statistical analysis. Data were analyzed using Statistica 10.0 software (StatSoft Inc., USA). Results are presented as mean \pm SD. The Mann-Whitney U test was applied to assess differences between groups [19]. Differences were considered statistically significant at $P < 0.05$.

RESULTS AND DISCUSSION

The selected cytostatic agents - cyclophosphamide (CPA), doxorubicin (DOX), and cisplatin (CDDP) – belong to different pharmacological classes and induce testicular injury through distinct molecular pathways. CPA, an alkylating agent, acts through the formation of intra- and inter-strand DNA crosslinks, leading to replication arrest and cell apoptosis [11], causing sustained damage to rapidly proliferating tissues such as the spermatogenic epithelium. DOX, an anthracycline antibiotic, intercalates into DNA by hydrogen bonding between nitrogenous bases and forms stable complexes with topoisomerase II, blocking DNA repair and replication [12, 13]. Additionally, DOX promotes the generation of reactive oxygen species, further damaging cells via inflammation, apoptosis, or ferroptosis [12, 13]. In contrast, CDDP is a platinum-based compound whose mechanism involves forming platinum-DNA adducts, resulting in replication arrest, activation of repair pathways, and apoptotic cell death [14]. These differences in cytotoxic mechanisms determine not only the pattern of testicular injury but also the degree of systemic toxicity.

Body weight and hematopoiesis are considered sensitive indicators of systemic toxicity,

and their fluctuations are regarded as the earliest markers of cytostatic side effects, reflecting both the extent of systemic damage and the organism's capacity for recovery. In this context, it was reasonable to evaluate the effects of the selected chemotherapeutic agents on these parameters over time.

Our results demonstrated that the most pronounced reduction in body weight in CPA-treated animals, compared to the control group, was observed as early as the first week after administration ($P < 0.05$), followed by stabilization of body weight (Fig. 1). By week 8, body weight had recovered to values close to those of the control group, indicating partial restoration of the general physiological state of the animals.

In mice receiving DOX, body weight decreased by 14% relative to baseline as early as week 1 ($P < 0.05$). By week 4, this reduction reached 17%, followed by only a slight increase

at week 8, with no recovery to control levels. Similar findings have been reported in the literature, where anthracycline antibiotics are described to cause cachexia and body mass loss due to enhanced free radical production, systemic inflammation, and appetite suppression [20].

In contrast, in the CDDP group, body weight remained comparable to control values during the first week, while a consistent and statistically significant increase of up to 15% was recorded at weeks 4 and 8. These data are generally consistent with published findings; for instance, study [21] reported that cisplatin administration does not invariably result in pronounced cachexia and may, in some cases, lead to compensatory weight gain. This effect may be related to the relatively lower systemic toxicity of cisplatin compared to anthracyclines and the possible activation of adaptive mechanisms.

Administration of cytostatics was accompanied by hematopoietic suppression of varying

Table 1. Dynamics of hematological parameters in mice following administration of chemotherapeutic agents

Group	Week	Leukocytes ($\times 10^9/\text{ml}$)	Erythrocytes ($\times 10^{12}/\text{ml}$)	Bone marrow cells ($\times 10^9/\text{ml}$)
Control	0	6.4 ± 0.32	4.9 ± 0.27	5.2 ± 0.26
	1	6.2 ± 0.4	5.1 ± 0.25	6 ± 0.3
	4	5.8 ± 0.27	4.7 ± 0.28	5.3 ± 0.34
	8	7.1 ± 0.31	4.8 ± 0.35	6.6 ± 0.22
Cyclophosphamide	0	5.8 ± 0.36	5.0 ± 0.35	5.4 ± 0.27
	1	$3.4 \pm 0.24^{*#}$	$4.5 \pm 0.28^*$	$3.4 \pm 0.17^{*#}$
	4	$0.8 \pm 0.06^{*#}$	$3.1 \pm 0.18^{*#}$	4.8 ± 0.24
	8	$2.5 \pm 0.18^{*#}$	4.7 ± 0.21	6.0 ± 0.35
Doxorubicin	0	$5.3 \pm 0.32^*$	5.1 ± 0.32	$6.0 \pm 0.33^*$
	1	$1.5 \pm 0.06^{*#}$	$4.3 \pm 0.22^{*#}$	5.8 ± 0.26
	4	$1.0 \pm 0.05^{*#}$	$3.3 \pm 0.24^{*#}$	$2.1 \pm 0.12^{*#}$
	8	$2.0 \pm 0.11^{*#}$	$3.3 \pm 0.2^{*#}$	$4.2 \pm 0.23^{*#}$
Cisplatin	0	6.5 ± 0.2	4.8 ± 0.28	5.8 ± 0.34
	1	$1.5 \pm 0.08^{*#}$	$4.2 \pm 0.32^*$	6.1 ± 0.41
	4	$0.8 \pm 0.12^{*#}$	$3.0 \pm 0.27^{*#}$	$4.0 \pm 0.29^{*#}$
	8	$2.0 \pm 0.14^{*#}$	5.3 ± 0.36	6.3 ± 0.37

Notes: * $P < 0.05$ vs. control; # $P < 0.05$ vs. week 0. Numbers of animals used for peripheral blood cell count were as follows: week 0 ($n = 32$), week 1 ($n = 29$), week 4 ($n = 26$), week 8 ($n = 23$); bone marrow cell analysis: $n = 3$ per time point.

severity. In the CPA group, a decrease in leukocyte count and bone marrow cellularity was observed, reaching minimal values at week 4, with partial recovery by week 8; the erythroid lineage was less affected (Table 1). DOX caused the most marked and sustained reduction in all evaluated parameters throughout the observation period, indicating profound suppression of hematopoiesis. In the CDDP group, moderate decreases were noted at the beginning of the study, followed by progressive normalization of erythroid indices, however, leukocyte recovery occurred more slowly (Table 1).

These findings indicate that all cytostatics studied induced alterations in the hematopoietic system to different extents. DOX proved to be the most toxic, causing marked and sustained suppression of leukopoiesis, erythropoiesis, and bone marrow cellularity. CPA exerted a pronounced but partially reversible myelotoxic effect, whereas CDDP showed the lowest overall toxicity, with a faster normalization of erythroid but slower leukocyte recovery.

Analysis of mouse survival curves revealed pronounced differences depending on the drug administered. In CPA-treated animals, a decline in survival was first observed at month 6, and by month 11, more than half of the animals had

died. The mean lifespan in this group was 11.05 ± 2.8 months (median 11 months), which was significantly lower than in the control group ($P = 0.0146$). The greatest mortality was observed in the DOX group, where a decline in survival began at month 5, and a marked reduction in survival occurred between months 7 and 10. The mean lifespan in this group was only 7.75 ± 1.8 months (median 7 months), significantly lower than in controls ($P < 0.0001$).

In animals receiving CDDP, survival dynamics were close to control: the curve showed a steady decline without abrupt drops, the mean lifespan was 12.9 ± 3.2 months (median 13.5 months), and no statistically significant differences from the control group were observed ($P = 0.2773$). Thus, DOX demonstrated excessive toxicity and high mortality, limiting its applicability in modeling testicular dysfunction.

It is known that testicular insufficiency can be accompanied by changes in neuroendocrine regulation, which are reflected in behavioral responses [5]. Therefore, in the next phase, the effects of cytostatics on social activity and anxiety levels of experimental animals were assessed.

Behavioral tests in the CPA and DOX groups showed a significant increase in anxiety during the first week after administration, accompa-

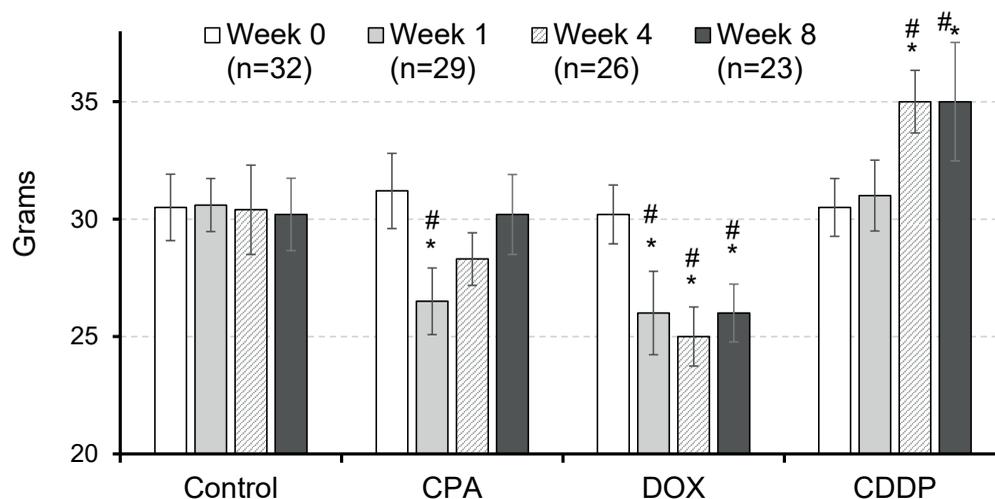


Fig. 1. Body weight of mice after administration of cytostatic agents (1-8 weeks): Groups: Control, CPA - cyclophosphamide, DOX - doxorubicin, CDDP - cisplatin. * $P < 0.05$ vs. control; # $P < 0.05$ vs. week 0

nied by a more than twofold decrease in social activity and male interest in females (Fig. 3A, B). These changes may be associated with both somatic discomfort and the toxic effects of the drugs. By week 8, social activity nearly fully recovered (~90% relative to control), but anxiety levels remained elevated, suggesting persistent behavioral changes or slow recovery of neurophysiological status.

In contrast, the effects of CDDP were less pronounced and reversible. CDDP did not cause significant changes in sexual behavior parameters (Fig. 3). Males maintained interest in females and demonstrated normal social activity throughout the observation period. Social activity decreased by 47% compared to control but only at week 4, unlike CPA and DOX, where decreases were observed from the first week. By week 8, the parameter did not differ from control values, contrasting with other groups, where social activity remained significantly affected during most of the study period. Anxiety levels increased during the first week after CDDP administration but subsequently tended toward normalization.

Comparative analysis of spermogram parameters and sperm morphology showed that CPA administration led to pronounced oligospermia, reaching its peak at week 4 (Fig. 4A). Overall, the spermogram during this period indicated a significant decrease in sperm count, reduced motility, increased proportion of abnormal forms, and membrane integrity disruption, reflecting decreased viability (Fig. 4A-D). Sperm motility, still significantly lower than control at week 8, showed a clear upward trend compared to week 4, indicating the beginning of functional recovery. Despite improvements in sperm morpho-functional characteristics at week 8 (partial restoration of count, motility, and membrane integrity), the number of abnormal sperm remained over six times higher than control (Fig. 4D). Morphological analysis of pathological sperm forms revealed a predominance of headless spermatozoa (absence of head), head hypoplasia (small head), and biflagellate forms, indicating mitotic and meiotic division defects in germline cells (Fig. 5). Nevertheless, the observed progressive improvement in key spermogram parameters suggests the activation

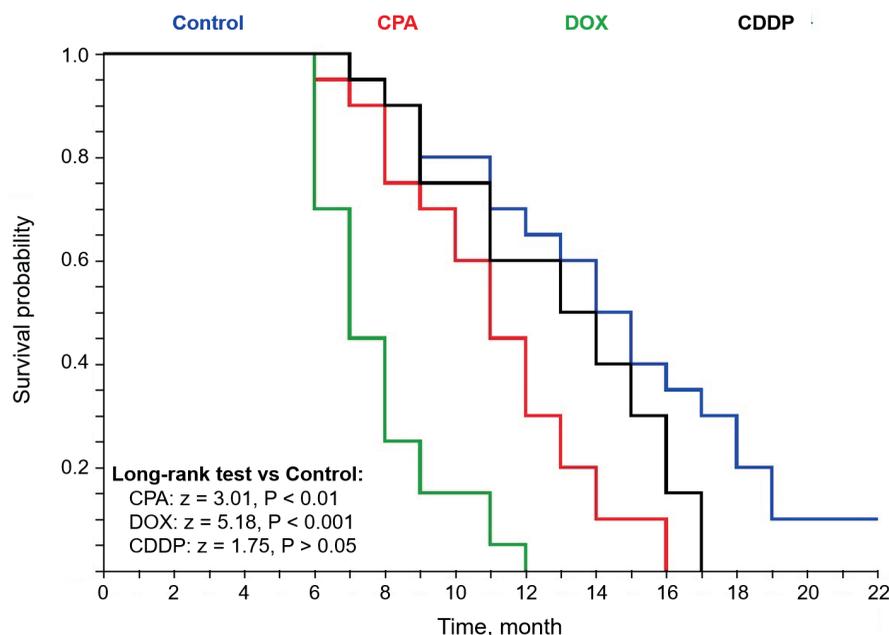


Fig. 2. Survival rates of mice in the experimental groups: Group 1 - control; Group 2 - cyclophosphamide; Group 3 - doxorubicin; Group 4 - cisplatin; $n = 20$ per group

of compensatory mechanisms and preservation of spermatogenic potential, allowing the identified changes to be considered partially reversible.

DOX administration caused severe toxic effects on the reproductive system of mice, which became evident within the first weeks following treatment. Total sperm count decreased by

73.7% compared to control, motility declined by 39%, and viability, assessed by plasma membrane integrity, reduced by 37%. Concurrently, the proportion of morphologically abnormal spermatozoa increased threefold compared to the control group (Fig. 4A-D).

During week 1, numerous morphological ab-

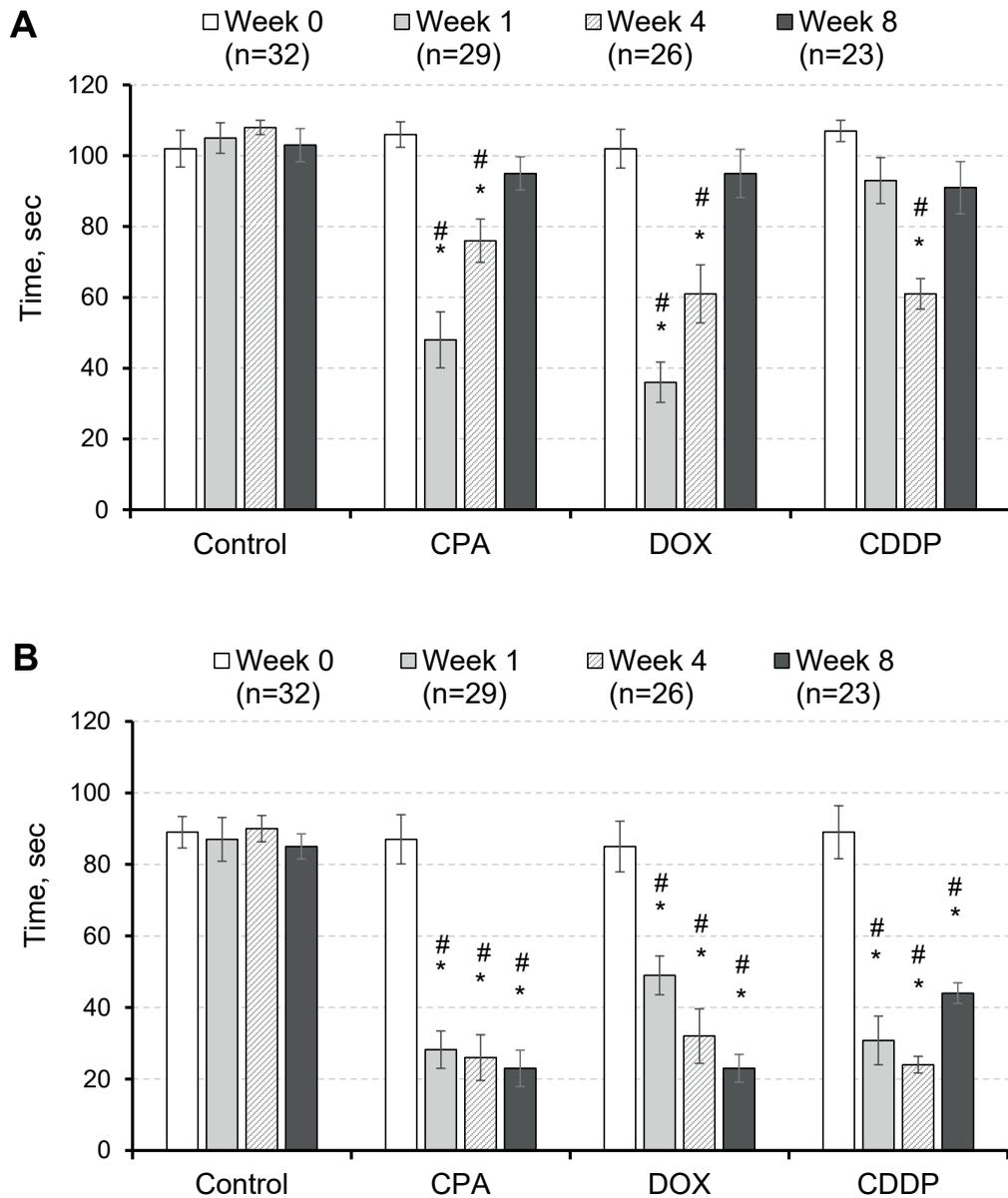
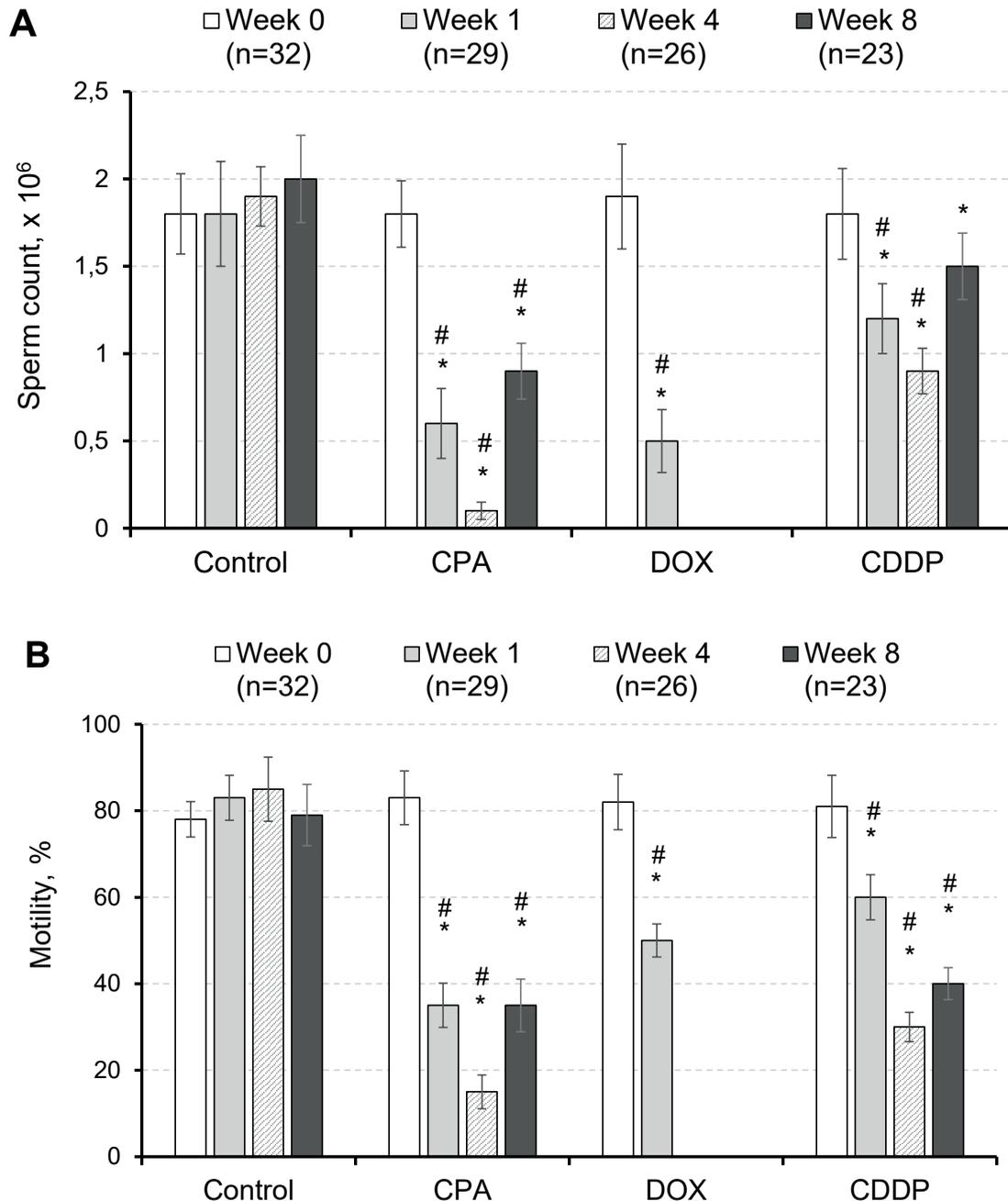


Fig. 3. Indicators of social activity (A) and anxiety (B) in mice after administration of cytostatic agents (1-8 weeks). Groups: Control, CPA - cyclophosphamide, DOX - doxorubicin, CDDP - cisplatin. *P < 0.05 vs. control; #P < 0.05 vs. week 0

normalities were detected, including pronounced bending of the midpiece and malformations of the sperm head (Fig. 5), indicative of structural damage to cellular components essential for normal spermatogenesis. At week 4, complete aspermia was recorded, suggesting profound and likely irreversible suppression of spermatogenic

activity. In contrast to CPA-treated animals, which showed partial recovery of sperm count and morphology by week 8, no evidence of reproductive recovery was observed in the DOX group throughout the entire observation period.

In addition to pronounced gonadotoxicity, DOX adversely affected the overall health status



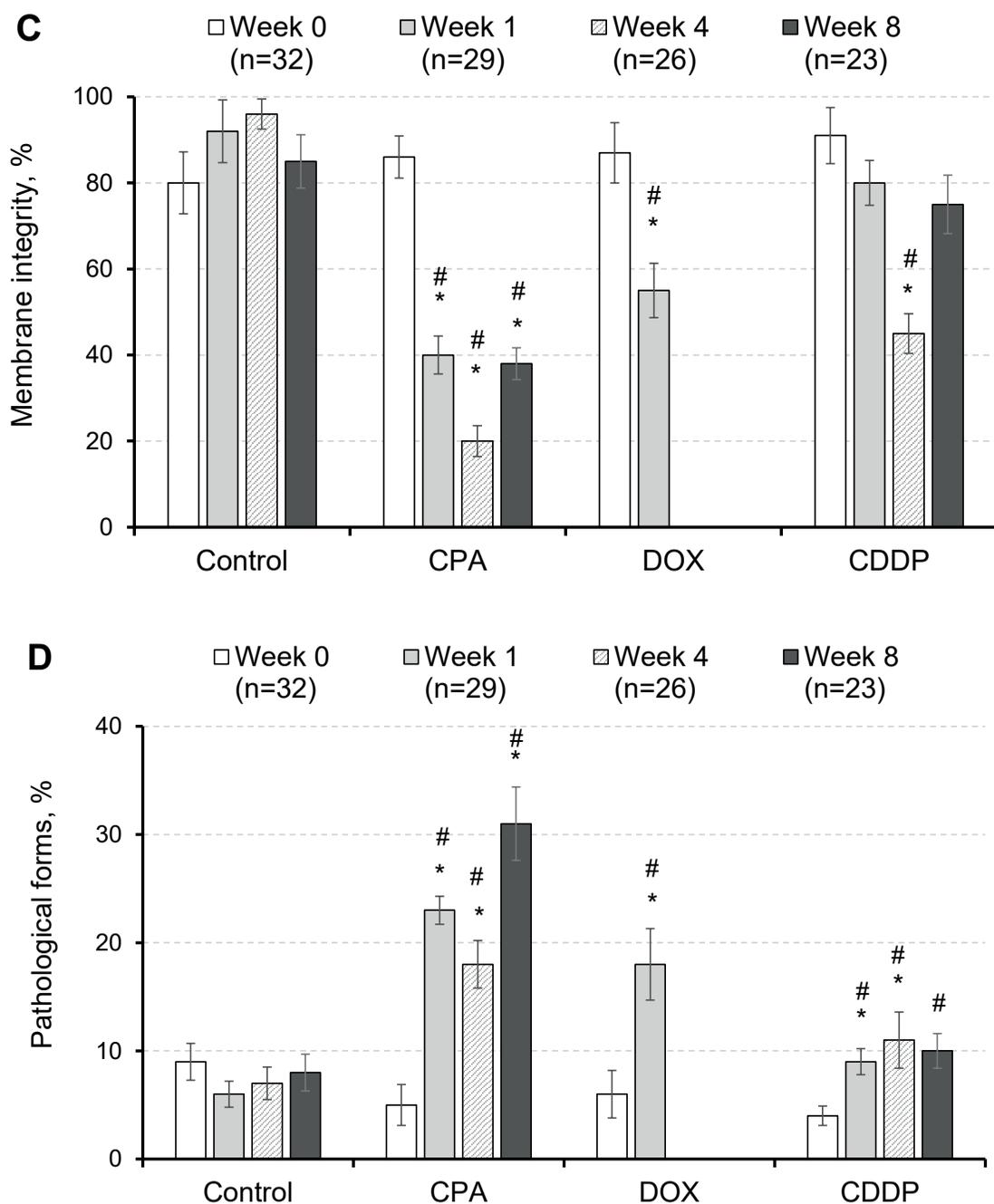


Fig. 4. Sperm parameters following the induction of spermatogenesis pathology over 1-8 weeks: sperm count (A), motility (B), viability assessed by membrane integrity (C), and % of abnormal sperm forms (D). Groups: Control, CPA - cyclophosphamide, DOX - doxorubicin, CDDP - cisplatin. *P < 0.05 vs. control; #P < 0.05 vs. week 0

of the animals. This group demonstrated an increased mortality rate compared to the other experimental groups. This effect may be associated with the systemic cardiotoxic and hepato-

toxic properties of anthracyclines, as reported in several previous studies [22-24].

In contrast, CDDP exerted a considerably milder impact on the reproductive system of

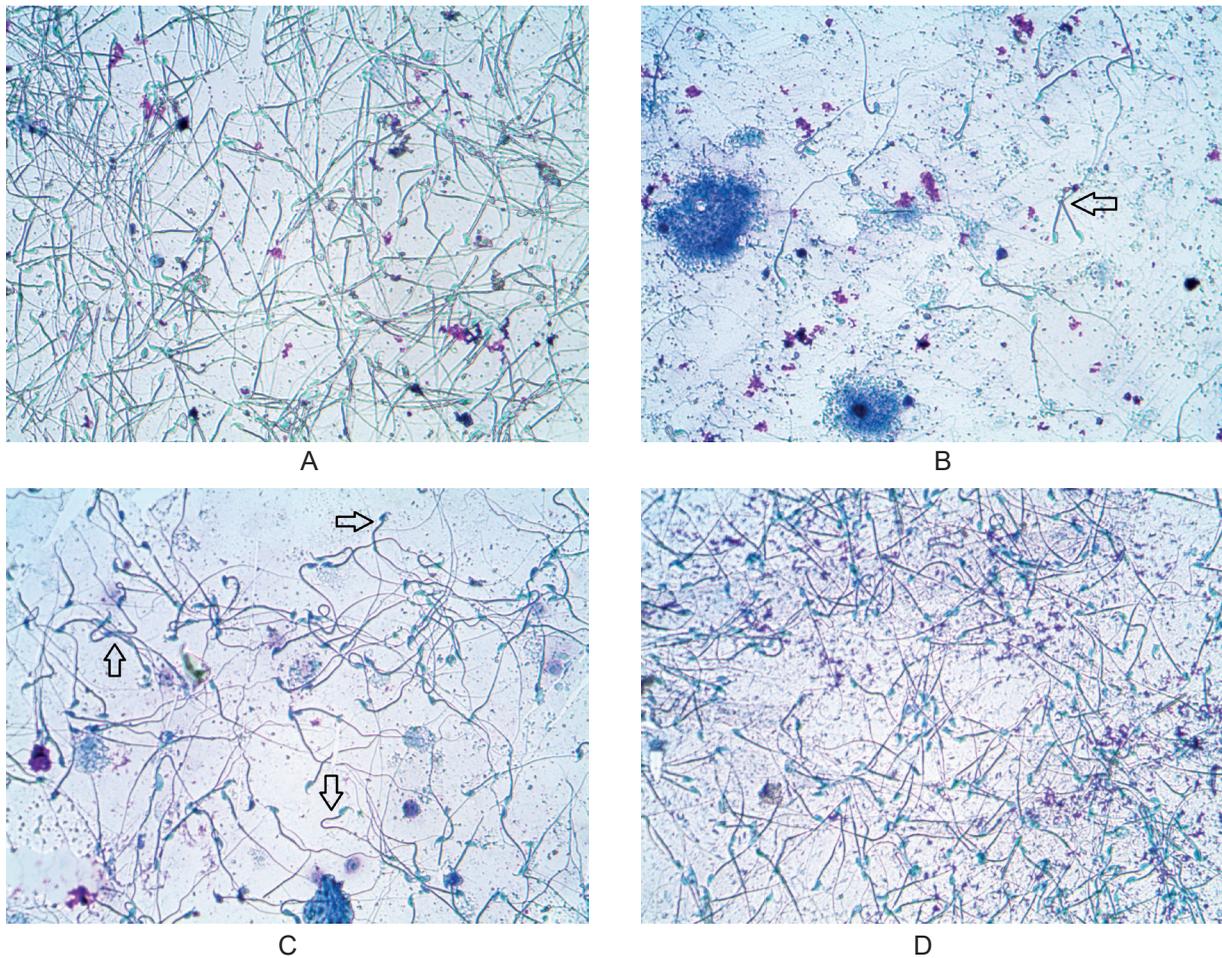


Fig. 5. Morphology of mouse spermatozoa in experimental groups: A - control; B - 4 weeks after CPA (arrows indicate double-headed spermatozoa); C - 4 weeks after CDDP; D - 1 week after DOX (arrows indicate coiled neck and tail forms). Staining: hematoxylin / eosin. Magnification $\times 1000$ (oil immersion)

mice relative to the other two agents. During the first four weeks after CDDP administration, animals developed moderately oligospermia without overt aspermia or severe morphological abnormalities of spermatozoa (Figs. 4; 5). By week 8, sperm count in most animals had returned to near-control levels, indicating the reversible nature of the damage and preservation of gonadal functional reserve. At this stage, sperm motility remained about twice as low as in the control group but showed a positive trend compared to week 4, suggesting the partial restoration of functional sperm activity. Based on these findings, CDDP may be regarded as a chemotherapeutic agent with comparatively

lower gonadotoxic potential than the other cytostatics evaluated.

Overall, the obtained data demonstrate that the tested agents exhibit varying degrees of cytotoxicity. DOX induced pronounced and irreversible damage, resulting in complete aspermia, which precludes further evaluation of sperm viability and functional activity. These findings are consistent with previous reports, which demonstrated that even seven weeks following DOX therapy, only 3-8% of seminiferous tubules exhibit repopulation with differentiated germ cells, and normalization of spermatogenesis may take up to a year unless the drug dose is reduced [25, 26].

In contrast, CDDP, despite exerting a transient effect, did not result in sustained reproductive impairment. This pattern is supported by studies showing that CDDP-induced toxicity can be attenuated by antioxidants (e.g., melatonin), suggesting a potential for rapid spermatogenic recovery under favorable conditions [27]. Consequently, the experimental utility of CDDP for modeling persistent pathological alterations in spermatogenesis is substantially limited.

In this context, CPA exhibited an optimally balanced effect, resulting in persistent yet incomplete suppression of spermatogenesis, with partial preservation of spermatozoa and potential for recovery. The data obtained are consistent with previous studies reporting sustained CPA-induced toxicity affecting sperm count and motility, germ cell apoptosis, meiotic progression, and blood-testis barrier permeability, alongside the onset of progressive recovery of spermogram recovery beginning around week ten [28].

The observed differences in the biological effects of the investigated cytostatics are primarily attributable to their distinct mechanisms of action. DOX and CDDP exert mainly direct cytotoxic effects via DNA damage and induction of oxidative stress [12-14], while CPA, as an alkylating agent, induces a more pronounced and prolonged impact on germinal epithelium cells, directly influencing spermatogenesis [11]. This feature makes CPA the most suitable agent for modeling testicular dysfunction in experimental settings, providing a sufficiently strong effect on the reproductive system while maintaining active compensatory mechanisms.

CONCLUSIONS

The results obtained demonstrate that the studied cytostatic agents exert differential effects on the general physiological status, behavioral responses, and reproductive function of mice. Doxorubicin exhibited the highest toxicity, inducing sustained body weight loss, suppression of hematopoiesis, pronounced behavioral impairments, complete

aspermia, and elevated mortality, indicative of irreversible reproductive damage. Cisplatin administration resulted in a comparatively mild and transient effect, characterized by moderate oligospermia and temporary alterations in hematological parameters and behavior, which were rapidly restored. This transient nature substantially limits its experimental utility for modeling persistent testicular pathology. Cyclophosphamide proved to be the most suitable agent for experimental modeling, eliciting marked yet partially reversible suppression of spermatogenesis, accompanied by progressive recovery of behavioral and functional reproductive parameters. These findings support the use of cyclophosphamide as an optimal agent for inducing testicular dysfunction in experimental settings.

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of co-authors of the article.

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ЕКСПЕРИМЕНТАЛЬНА ОЦІНКА МОДЕЛЕЙ ТЕСТИКУЛЯРНОЇ НЕДОСТАТ- НОСТІ, ІНДУКОВАНОЇ ХІМІОТЕРАПЕВ- ТИЧНИМИ АГЕНТАМИ

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Зростання онкозахворюваності серед молоді зумовлює актуальність збереження репродуктивної функції та вдосконалення експериментальних моделей для дослідження тестикулярної недостатності, спричиненої хіміотерапією. Метою нашої роботи було проведення порівняльної оцінки ефектів цитостатиків різних класів у моделі тестикулярної дисфункції. Для моделювання тестикулярної дисфункції у самців мишей Balb/c застосовували циклофосфамід – 250

мг/кг, доксорубіцин – 10 мг/кг або цисплатин – 10 мг/кг. Оцінювали масу тіла, гематологічні показники, виживаність, соціальну активність, рівень тривожності та спермограму через 1, 4 і 8 тижнів. Дослідження показало, що доксорубіцин чинив ранню та виражену токсичність з втратою маси тіла, пригніченням гемопоєзу, зменшенням кількості сперміїв, їх рухливості та життєздатності, а також зростанням частки аномалій вже через тиждень після введення. До 4 тижня розвивалась аспермія без ознак відновлення на завершальних етапах дослідження, виражені поведінкові порушення та підвищена летальність. При застосуванні циклофосфаміду маса тіла та гематологічні показники стабілізувались протягом 4 тижнів. Виявлено незворотне підвищення тривожності й тимчасове зниження соціальної активності. Спостерігалась олігоспермія з піком на 4 тижні, зниження рухливості та життєздатності сперміїв. До 8 тижня кількість та рухливість сперміїв залишалась зниженою, а частка патологічних форм підвищеною. Ефекти цисплатину найменш виражені і переважно оборотні. Маса тіла поступово зростала, гематологічні показники помірно знижувались з подальшим відновленням, соціальна активність зберігалась, за винятком тимчасового зниження на 4 тижні. Тривожність мала тенденцію до зниження. Виявлено помірну олігоспермію без критичних морфологічних змін. До 8 тижня кількість сперміїв відновлювалась, а їх рухливість демонструвала позитивну динаміку. Таким чином, циклофосфамід є оптимальним препаратом для моделювання тестикулярної недостатності з частковим відновленням функцій, тоді як доксорубіцин спричиняє незворотні ураження, а цисплатин доцільний для вивчення легких форм гонадотоксичності.

Ключові слова: цитостатики; хіміотерапія; циклофосфамід; доксорубіцин; цисплатин; тестикулярна недостатність; біомедичне моделювання.

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