ICBUW
International Coalition to Ban Uranium Weapons

List of Recent Research on Depleted Uranium

In recent decades, depleted uranium (DU) has garnered more attention due to its military applications and potential impact on human health. Researchers and scientists have been diligently studying this controversial substance, seeking to understand its effects and assess the associated risks. However, despite numerous investigations, the current state of affairs on depleted uranium research remains (at least in parts) inconclusive, underscoring the need for further investigation. Nonetheless, existing evidence suggests multifaceted adverse effects on human health, prompting experts to advocate a **precautionary approach** to mitigate potential risks.

The complexity of studying DU's impact on human health arises from the multitude of factors involved, including different routes of exposure, varying levels of contamination, and long-term effects that may manifest over years or even decades. Multiple studies focusing on war veterans and civil populations are restricted to the small size of the samples and the heterogeneous natures of these groups. Another factor, which has negative impact on the research efforts is the political aspect of depleted uranium use, which makes related research “unwelcomed” in many countries.

Animal studies and studies involving DU-exposed veterans have shown various health abnormalities, especially regarding **kidneys**, **lungs**, and **the reproductive system**. Furthermore, there are reports of higher rates of **cancer and birth defects** in areas where DU has been deployed. Strong evidence suggests that depleted uranium exposure leads to **kidney damage** and **oxidative stress** in many cases. This link is significantly more evident, than ,e.g., link between cancer and DU exposure. Other risks include **congenital malformations**, **neurological abnormalities**, and **developmental issues**. Also the bone damage such as the **bone mass decrease** has been observed in some studies. The effects on the immune system are multifaceted and may lead to potential health outcomes such as hypersensitivity, immune suppression, chronic inflammation and autoimmunity. The thyroid function seems to be adversely impacted when exposed to DU as well. Animal studies have demonstrated **DU-induced DNA strand breaks**, chromosomal aberrations, and alterations in DNA repair mechanisms.
Furthermore, when it comes to the radiological aspect of DU, the so-called “**bystander effect**” has been observed by the scientists.

The effect is defined as the observation of a biological response (radiation damage) in cells that are not themselves travestied by ionizing radiation but can communicate with cells that are. The phenomenon is still poorly understood by the scientists and further research on the topic is needed, especially with DU exposure in mind.

Given the potential risks and the uncertainty surrounding depleted uranium's health effects, experts have called for a precautionary approach. This approach urges policymakers, military organizations, and regulatory bodies to take proactive measures to minimize exposure to DU and protect potentially affected populations. The precautionary principle emphasizes that in situations where scientific understanding is incomplete or inconclusive, it is prudent to err on the side of caution and prioritize public health and safety.

In conclusion, research on depleted uranium has made significant strides, shedding light on potential risks but leaving many questions unanswered. While conclusive evidence regarding many aspects is still elusive, the existing body of research suggests multifaceted adverse effects on human health. Therefore, adopting a precautionary approach is essential to ensure the well-being of individuals potentially exposed to depleted uranium, and further research is warranted to enhance our understanding of its implications fully.

OVERVIEW STUDIES

These studies provide overview on the current "state of affairs" regarding the research of depleted uranium effects on health.

Title	Date	Link	Summary / Abstract Excerpt
Shaki F, Zamani E, Arjmand A, Pourahmad J. A Review on Toxicodynamics of Depleted Uranium. Iran J Pharm Res. 2019 Fall; 18(Suppl1):90-100.	01.09.2019	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7393059/	*Alterations in behavior, some neurologic adverse effects, immunotoxicity, embryo-toxicity and hepatotoxicity were observed in chronic exposure to DU. Also, the increased risk of cancer was revealed in epidemiological and experimental studies. Several mechanisms were suggested for DU toxicity such as oxidative stress, mitochondrial toxicity and inflammation. In fact, uranium like other toxic heavy metals can induce oxidative damage and apoptosis via mitochondrial pathway and inflammatory response. In this review, we have discussed the kinetic of DU including source and exposure pathway.*

Hon, Z.; Österreicher, J.; Navrátil, L. Depleted Uranium and Its Effects on Humans. Sustainability 2015, 7, 4063-4077.	08.04.2015	https://doi.org/10.3390/su7044063	*The results of the above-mentioned studies suggest that the **most important toxic mechanism of DU toxicity is the involvement of oxidative stress** and **reactive oxygen species**. In the development of cellular oxidative damage to most types of mammalian cells, the major sources of reactive oxygen species are mitochondria and also key organelles. Experimental studies demonstrated a significant mitochondrial membrane potential collapse and mitochondrial swelling after DU exposure in different cell lines. Therefore, **mitochondrial dysfunction and oxidative damage** may be responsible for the pathological consequences of DU exposure in living organism.*
Asic, A.; Kurtovic-Kozaric, A; Besic, L.; Mehinovic, L.; Hasic, A.; Kozaric, M.; Hukic, M.; Marjanovic, D. Chemical toxicity and radioactivity of depleted uranium: The evidence from in vivo and in vitro studies. Environmental Research 156 (2017), 665-573.	22.04.2017	https://doi.org/10.1016/j.envres.2017.04.032	*Critical overview of the current state of knowledge on chemical toxicity and radioactivity of depleted uranium and their effect on living systems and cell lines.*

CANCER

Several studies have been conducted to investigate this potential link, but the findings have been somewhat inconclusive. While some studies have suggested a possible association between DU exposure and certain types of cancer, such as **lung cancer** and **kidney cancer**, others have found no significant evidence of increased cancer risk.

One reason for the conflicting findings is the difficulty in isolating the effects of DU exposure from other factors that can contribute to cancer development, such as smoking, exposure to other carcinogens, and battlefield conditions. Additionally, the

long latency period of cancer makes it challenging to establish a direct cause-and-effect relationship. It is worth noting that the majority of studies conducted so far have focused on individuals with high levels of DU exposure, such as veterans of conflicts where DU weapons were used. These individuals typically experience exposure through inhalation or ingestion of DU particles. The potential risk associated with lower levels of exposure, such as environmental exposure, remains less well understood. Recent studies suggest that DU is one of the contributing factors to the development of cancer among the residents of polluted areas.

Further research is needed to establish a clear and definitive relationship.

Title	Date	Link	Summary / Abstract Excerpt
Siyah, M. A., Al-Mashhadani, A. H., & Essa, B. H. (2021). Risk Assessment for AL-Nahrawn Site that Contaminated with Depleted Uranium in Baghdad. Journal of Chemical Health Risks, 11(3), 317-328.	01.09.2021	https://jchr.damghan.iau.ir/index.php/JCHR/article/view/article_684579.html	*The total dose for the contaminated area that calculated by RESRAD code (7.2) dose from all nuclides all pathways summed in AL-Nahrawan is (1.46 mSv / year) and that more the accepted limit for dose limit exposure to public (1 mSv/A) according to the IAEA and that mean the public have limit use and action for this site. The high purity germanium analysis appears AL-Nahrawan site contaminated with Du depended on the ratio between 235U and 238U radio nuclides. The **cancer risk** from all nuclides calculated by RESRD code for AL-Nahrawan site is (2.2) ×10-3. This value **is above the global average** of 0.29×10 −3 and 1.16×10 −3 reported by UNSCEAR.*
Zhang, L.; Chu, J.; Xia, B.; Xiong, Z.; Zhang, S.; Tang, W. Health Effects of Particulate Uranium Exposure. Toxics 2022, 10, 575.	30.09.2022	https://www.mdpi.com/2305-6304/10/10/575	*Epidemiological studies from occupationally exposed populations in the uranium industry have concluded that there is a possible association between **lung cancer risk** and uranium exposure, while the **evidence for the risk of other tumors is not sufficient**. The toxicological effects of particulate uranium exposure to animals have been shown in laboratory tests to focus on respiratory and central nervous system damage. **Fibrosis and tumors can occur in the lung tissue of the respiratory tract**. Uranium particles can also induce a concentration-dependent increase in cytotoxicity, targeting mitochondria. **The understanding of the health risks and potential toxicological mechanisms of particulate uranium contamination is***

			still at a preliminary stage.
Jumaah, A.S., Al-Haddad, H.S., Mahdi, L.H. et al. Increased PTEN gene expression in patients with endometrial carcinoma from areas of high risk depleted uranium exposure. BMC Res Notes 12, 708 (2019).	29.10.2019	https://bmcresnotes.biomedcentral.com/articles/10.1186/s13104-019-4756-4#citeas	*Tumor PTEN gene expression was significantly increased in patients living in the areas of high risk DU exposure, in comparison to patient tumors from low risk areas. The results linked environmental war pollutants [DU] to* ***alterations in PTEN gene expression in endometrial carcinoma.*** *Furthermore, this finding may explain the overall increasing cancer trends observed in Iraq.*
Francesco Cappello, Alberto J.L. Macario, Depleted uranium induces human carcinogenesis involving the immune and chaperoning systems: Realities and working hypotheses, Medical Hypotheses, Volume 124, 2019, Pages 26-30.	24.01.2019	https://doi.org/10.1016/j.mehy.2019.01.018	*Cancer is caused by a combination of factors, genetic, epigenetics and environmental. Among the latter, environmental pollutants absorbed by contact, inhalation, or ingestion are major proven or suspected culprits. Depleted uranium (DU) is one of them directly pertinent to the military and civilians working in militarized areas. It is considered a* ***weak carcinogen but its implication in cancer development in exposed individuals is supported by various data****.*
Ahmed, R.S., Mohammed, R.S. Assessment of uranium concentration in blood of Iraqi females diagnosed with breast cancer. Radiat Environ Biophys 60, 193–201 (2021).	22.11.2020	https://doi.org/10.1007/s00411-020-00881-8	*It is concluded that there is a* ***correlation*** *between the incidence of breast cancer in Iraqi women and elevated levels of uranium concentrations in their blood.* ***Whether this is a casual relationship is unclear, because cancer can be caused by various carcinogens, including environmental pollution in the region.***

GESTATION PROCESS, FETUS

Some studies have suggested a possible association between DU exposure and an increased risk of birth defects, such as congenital malformations, neurological abnormalities, and developmental issues.

One of the challenges in studying this potential association is the difficulty in isolating the effects of DU exposure from other factors that can contribute to birth defects and adverse pregnancy outcomes, such as maternal health, genetics, socioeconomic factors, and exposure to other environmental toxins.

Recent studies suggest that the exposure to depleted uranium may lead to external anomalies in embryos, as well as other adverse effects related to gestation process. Some studies even suggest a link between behavioral abnormalities; however, more research is required.

Title	Date	Link	Summary / Abstract Excerpt
Mirderikvand N, Mohammadzadeh Asl B, Naserzadeh P, Shaki F, Shokrzadeh M, Pourahmad J. Embryo toxic effects of depleted uranium on the morphology of the mouse fetus. Iran J Pharm Res. 2014 Winter;13(1):199-206.	01.11.2013	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3985252/	*Although the biokinetics, metabolism, and chemical toxicity of uranium are well known, until recently little attention was paid to the potential toxic effects of uranium on reproduction and development in mammals. In recent years, it has been shown that uranium is a* ***developmental toxicant when given orally or subcutaneously (SC)*** *to mice.* ***Decreased fertility, embryo/fetal toxicity including teratogenicity, and reduced growth of the offspring*** *have been observed following uranium exposure at different gestation periods. For investigating the effects of DU on pregnant animals, three groups (control, sham and test) of NMRI mice were chosen. In test group 4 mg/Kg of DU were administered intraperitonealy at 11 day of gestation, in sham group only normal saline injected to interior peritoneum as indicated in the test group and in Control group which was considered as the comparison base line of our research, no injection was made. Caesarean sections were performed at 15 day of the gestation; and their placentas were examined externally. Based on our results* ***DU caused significant external anomalies, and caused a significant decrease (p < 0.05) in the***

			weight and diameter of placentas, the number of the embryos, their body weight and crown-rump length of fetuses.
Weiping Zhang, Wenyu Liu, Shuangshuang Bao, Hongxiu Liu, Yuzeng Zhang, Bin Zhang, Aifen Zhou, Jia Chen, Ke Hao, Wei Xia, Yuanyuan Li, Xia Sheng, Shunqing Xu, Association of adverse birth outcomes with prenatal uranium exposure: A population-based cohort study, Environment International, Volume 135, 2020.	23.12.2019	https://doi.org/10.1016/j.envint.2019.105391	*Uranium (U) is a well-recognized hazardous heavy metal with embryotoxicity and fetotoxicity. However, little is known about its association with adverse birth outcomes. We aimed to investigate the potential correlation between prenatal U exposure and birth outcomes. Urine samples of 8500 women were collected before delivery from a birth cohort in Wuhan, China. Concentrations of urinary U and other metals were measured by inductively coupled plasma mass spectrometry. We used multivariable logistic regressions to evaluate the associations between urinary U concentrations and adverse birth outcomes, such as preterm birth (PTB), low birth weight (LBW) and small for gestational age (SGA). Associations of urinary U concentrations with gestational age, birth weight, and birth length were investigated by linear regressions. The geometric mean of U concentration was 0.03 μg/L. After adjustment for potential confounders, we found each Log2-unit increase in U concentration was associated with a significant decrease in gestational age [adjusted β = −0.32 day; 95% confidence interval (CI): −0.44, −0.20] and a significant increased likelihood of PTB (adjusted OR = 1.18, 95% CI: 1.07, 1.29).* ***This birth cohort uncovered an association of maternal exposure to U during pregnancy with decreased gestational age and increased risk of PTB. Our findings reveal an association of maternal exposure to U during pregnancy with decreased gestational age and increased risk of PTB.***
M. Legrand, S. Lam, I. Anselme, C. Gloaguen, C. Ibanez, P. Eriksson, P. Lestaevel, C. Dinocourt,	14.09.2016	https://doi.org/10.1016/j.neuro.2016.09.006	*{…} Therefore, these* ***data strongly suggest that exposure to DU during gestation and lactation affects brain development in embryos, fetuses and neonates with behavioral consequences in the offspring****.*

Exposure to depleted uranium during development affects neuronal differentiation in the hippocampal dentate gyrus and induces depressive-like behavior in offspring, NeuroToxicology, Volume 57, 2016, Pages 153-162.			

BONES

Recent evidence suggests links between bone malignancies, specifically bone mass decrease, with depleted uranium exposure.

Title	Date	Link	Summary / Abstract Excerpt
Yue, YC., Li, MH., Wang, HB. et al. The toxicological mechanisms and detoxification of depleted uranium exposure. Environ Health Prev Med 23, 18 (2018).	16.05.2018	https://environhealthprevmed.biomedcentral.com/articles/10.1186/s12199-018-0706-3	*In humans and animals, DU can induce multiple health effects, such as **renal tubular necrosis and bone malignancies**. This review summarizes the known information on DU's routes of entry, mechanisms of toxicity, and health effects.*
McDiarmid, Melissa A.; Gaitens, Joanna M.; Hines, Stella; Cloeren, Marianne; Breyer, Richard; Condon, Marian; Oliver, Marc; Roth,	01.06.2021	https://journals.lww.com/health-physics/Abstract/2021/06000	*In addition, a measure of bone resorption, N-telopeptide, showed a statistically significant increase in those in the high DU subgroup, a finding consistent with a statistically significant **decrease in bone mass** also observed in this high DU subgroup compared to the low DU subgroup.*

Tracy; Gucer, Patricia; Kaup, Bruce; Brown, Lawrence; Brown, Clayton H.; Dux, Moira; Glick, Danielle; Lewin-Smith, Michael R.; Strathmann, Frederick; Xu, Hanna; Velez-Quinones, Maria A.; Streeten, Elizabeth. Surveillance of Depleted Uranium-exposed Gulf War Veterans: More Evidence for Bone Effects. Health Physics 120(6):p 671-682, June 2021.		/Surveillance_of_Depleted_Uranium_exposed_Gulf_War.9.aspx	

KIDNEY & OXIDATIVE STRESS

The kidneys are vital organs responsible for maintaining fluid balance, regulating electrolyte levels, and excreting metabolic waste products from the body. They are also highly susceptible to toxic insults, including exposure to heavy metals like DU. Oxidative stress, a state characterized by an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, has been implicated as a key mediator in DU-induced renal damage.

Oxidative stress contributes to kidney damage through various mechanisms. ROS can induce lipid peroxidation, causing damage to cell membranes and impairing renal function. Additionally, ROS can promote inflammation by activating pro-inflammatory signaling pathways, attracting immune cells, and exacerbating tissue injury. Moreover, oxidative stress can lead to DNA damage, protein oxidation, and mitochondrial dysfunction, further compromising renal integrity.

Multiple experimental studies have provided evidence supporting the association between DU exposure, oxidative stress, and

kidney damage. Animal models exposed to DU have exhibited increased levels of oxidative stress markers, such as lipid peroxidation products and antioxidant enzyme alterations, along with histopathological changes in renal tissue. Additionally, human studies have reported associations between DU exposure and markers of oxidative stress in individuals occupationally or environmentally exposed to DU.

Overall, strong evidence suggests that depleted uranium exposure leads to kidney damage and oxidative stress in many cases. **This link is significantly more evident, than ,e.g., link between cancer and DU exposure.**

Title	Date	Link	Summary / Abstract Excerpt
Briner, W. The Toxicity of Depleted Uranium. Int. J. Environ. Res. Public Health 2010, 7, 303-313.	25.01.2010	https://www.mdpi.com/1660-4601/7/1/303	*While depleted uranium is less radioactive than natural uranium, it still retains all the chemical toxicity associated with the original element. In large doses the kidney is the target organ for the acute chemical toxicity of this metal,* ***producing potentially lethal tubular necrosis****. In contrast, chronic low dose exposure to depleted uranium may not produce a clear and defined set of symptoms. Chronic low-dose, or subacute, exposure to depleted uranium alters the appearance of milestones in developing organisms.*
Suiyi Liu, Shuang Wang, Yazhen Zhao, Juan Li, Chang Shu, Yong Li, Jie Li, Binghui Lu, Zeheng Xu, Yonghong Ran, Yuhui Hao, Depleted uranium causes renal mitochondrial dysfunction through the ETHE1/Nrf2 pathway, Chemico-Biological Interactions, Volume 372, 2023, 110356.	19.01.2023	https://doi.org/10.1016/j.cbi.2023.110356	*In summary, this study demonstrates that* ***DU induces renal oxidative stress and mitochondrial dysfunction*** *in vitro and vivo. Researchers have suggested that increased oxidative stress can damage mitochondria, suggesting that DU may lead to mitochondrial dysfunction by causing renal oxidative stress. Previous studies have shown that DU leads to a significant decrease in ETHE1 expression and that ETHE1 is closely related to mitochondrial function.*
Hu, Q, Zheng, J, Xu, XN,	19.01.2022	https://doi.org/	*Taken together, these* ***data strongly suggest that U treatment induces***

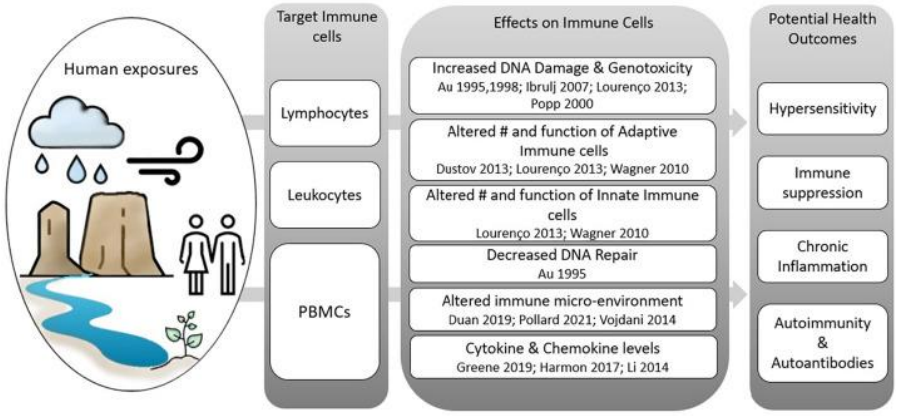
Gu, C, Li, W. Uranium induces kidney cells apoptosis via reactive oxygen species generation, endoplasmic reticulum stress and inhibition of PI3K/AKT/mTOR signaling in culture. Environmental Toxicology.		10.1002/tox.23453	***NRK-52E cells apoptosis through ROS production, ER stress, and down-regulation of PI3K/AKT/mTOR signaling.***
Xabier Arzuaga, Susan H. Rieth, Ambika Bathija & Glinda S. Cooper (2010) Renal Effects of Exposure to Natural and Depleted Uranium: A Review of the Epidemiologic and Experimental Data, Journal of Toxicology and Environmental Health, Part B, 13:7-8, 527-545.	17.12.2010	https://doi.org/10.1080/10937404.2010.509015	*However, occupational and community-based studies of populations chronically exposed to elevated drinking-water concentrations of uranium provide some evidence of* ***adverse renal effects****, as assessed by biomarkers of proximal tubule damage such as urinary levels of glucose, calcium, and various low-molecular-weight proteins. Indications of proximal tubule effects, as evidenced by increased urinary β(2)-microglobulin and retinol binding protein levels, were also seen in the most recent follow-up surveillance study of Gulf War veterans exposed to DU. The reported β(2)-microglobulin levels in these studies were generally considered to be within normal limits, but the long-term implications of the observed variation in these levels are not established.* ***The kidney was observed to be a target of uranium toxicity following oral and implantation exposure routes in several animal species.***

IMMUNE SYSTEM

Depleted Uranium has been proven to have adverse effects on the immune function of humans and animals. The effects are multifaceted and may lead to potential health outcomes such as hypersensitivity, immune suppression, chronic inflammation and

autoimmunity.

Title	Date	Link	Summary / Abstract Excerpt
Y. Hao, J. Ren, J. Liu, Z. Yang, C. Liu, R. Li, Y. Su Immunological changes of chronic oral exposure to depleted uranium in mice Toxicology, 309 (2013), pp. 81-90.	5.07.2013	https://doi.org/10.1016/j.tox.2013.04.013	*The results revealed that after 4 months of consuming the DU-containing feed, the immune function of the mice was changed in a concentration-dependent manner. When the DU dose in the feed reached 300 mg/kg, the immune function of the mice was significantly inhibited, compromising the innate immune function of the mice, thereby leading to the abnormalities in the acquired immune function and increasing the number of splenic mIgM+ cells and the proportion of mIgM+mIgD+ double-positive cells; however, the number of splenic CD3+ cells and the ratio of splenic CD4+/CD8+ T cells were decreased. In addition, the release of cytokines from the splenic was abnormal, inhibiting the levels of Th1-derived cytokines while increasing the levels of Th2-derived cytokines, thereby promoting the shift to Th2 cells. However, the dose of less than 30 mg/kg in the DU-containing feed exhibited little or no impact on the immune function.* ***This study verified the hypothesis that with sufficient doses and durations of exposure, DU may cause a systematic shift of Th1 cytokines to Th2 cytokines.***
Schilz, Dashner-Titus, Simmons, Erdei, Bolt, MacKenzie, Hudson, The immunotoxicity of natural and depleted uranium: From cells to people, in: Toxicology and Applied Pharmacology, Volume 454, 116252.	1.11.2022	https://www.sciencedirect.com/science/article/pii/S0041008X22003970#s0035	*The purpose of this review was to summarize findings on uranium immunotoxicity obtained from cell, rodent and human population studies.*

BLOOD, CHEMICAL TOXICITY, MUTATIONS

Depleted uranium can directly interact with DNA through several mechanisms. DU can penetrate cells and bind to DNA molecules, interfering with their normal structure and function. Additionally, DU can induce the production of reactive oxygen species (ROS), which can cause oxidative damage to DNA. ROS generated by DU exposure can lead to DNA strand breaks, base modifications, and cross-linking of DNA molecules, compromising the integrity of the genetic material.

DNA damage induced by DU exposure has significant implications for cellular function and health. Genetic mutations resulting from DU exposure can disrupt normal cellular processes, including DNA replication, transcription, and repair mechanisms. Accumulated DNA damage can increase the risk of genomic instability, impair cell viability, and potentially contribute to the development of various diseases, including cancer.

Numerous studies have provided evidence linking DU exposure to DNA damage in both experimental models and human populations. Animal studies have demonstrated DU-induced DNA strand breaks, chromosomal aberrations, and alterations in DNA repair mechanisms. Moreover, studies on individuals occupationally exposed to DU or those living in DU-contaminated areas have reported increased levels of DNA damage markers, such as DNA adducts and chromosomal abnormalities.

Title	Date	Link	Summary / Abstract Excerpt
Milacic S. Health investigations of depleted-uranium clean-up workers. La Medicina del Lavoro. 2008 Sep-Oct;99(5):366-370. PMID: 18828536.	01.09.2008	https://europepmc.org/article/med/18828536	*The total number of blood cells did not change, but **variations of the relative number (percentage) of cells in the leukocyte formula** were observed. The total number of DNA alterations was higher immediately after decontamination than before decontamination. Four years after decontamination the number of DNA alterations had decreased. However, the number of damaged cells (lymphocytes containing chromosome lesions) was higher in both medical examinations, immediately after and four years after decontamination.*
Carolyne LaCerte, Hong Xie, AbouEl-Makarim Aboueissa, John Pierce Wise, Particulate depleted uranium is cytotoxic and clastogenic to human lung epithelial cells, Mutation Research/Genetic Toxicology and Environmental Mutagenesis, Volume 697, Issues 1–2, 2010, Pages 33-37.	19.02.2010	https://www.sciencedirect.com/science/article/abs/pii/S138357181000051 3	*(…) we determined the **cytotoxicity and clastogenicity of particulate DU in human bronchial epithelial cells** (BEP2D cells). DU-induced concentration-dependent cytotoxicity in human bronchial epithelial cells, and was not clastogenic after 24 h but induced chromosomal aberrations after 48 h. These data indicate that if DU is a **human bronchial carcinogen**, it is likely acting through a mechanism that involves DNA breaks after longer exposures.*
Geir Bjørklund, Lyudmila Pivina, Maryam Dadar, Yuliya Semenova, Md Mostafizur Rahman, Salvatore Chirumbolo, Jan Aaseth,	01.02.2020	https://www.sciencedirect.com/science/article/abs/pii/S001393511930724 8	*Indications of **proximal tubule effects** have been observed in recent surveillance study of Gulf War veterans exposed to depleted uranium (DU). This gives some support for the suspicion that DU may represent one of the causes for the so-called Persian Gulf syndrome. Proposed effects may be especially harmful if the toxicity hits the mitochondrial DNA since the mitochondria lack the nucleotide excision repair*

Depleted uranium and Gulf War Illness: Updates and comments on possible mechanisms behind the syndrome, Environmental Research, Volume 181, 2020, 108927.			*mechanism, which is needed for repairing bulky adducts that have been associated with DU. It is a plausible* ***working hypothesis*** *that a significant part of the symptoms from various organs, which have been observed among veterans from Gulf War and that have been grouped under the name of the Persian Gulf syndrome, may be explained as a consequence of* ***mitochondrial DNA damage*** *in various cell types and organs. Interpretation of observations, on military personnel and civilians after Gulf War 1, is associated with difficulties because of the abundance of potential confounding factors. The symptoms observed on veterans from Gulf War may be attributed to a multiplicity of substances functioning directly or indirectly as mitochondrial mutagens. A concise analysis of the cascade of toxic effects initiated by DU exposure in the human body is the subject of this article.*
Miller, A. C., Rivas, R., & Tesoro, L., et al. (2017). Radiation exposure from depleted uranium: The radiation bystander effect. Toxicology and Applied Pharmacology, 331, 135-141.	15.09.2017	https://doi.org/10.1016/j.taap.2017.06.004	*DU possesses a radiological and chemical component but is generally considered a chemical biohazard. Exposure can occur via wounding, ingestion or inhalation. In vitro investigations have demonstrated that* ***DU is mutagenic, genotoxic, and exposure can induce neoplastic transformation and genomic instability****. It is also responsible for cellular damage. In vivo studies have demonstrated carcinogenic, neurotoxic and leukemogenic effects, renal dysfunction, genotoxicity, affects on rodent behaviour, accumulation in the brain and inhibition of vitamin metabolism. DU exposure can also induce chromosomal dicentrics which are considered a radiation-specific chromosomal damage.* *There is also a biological phenomenon called '****the bystander effect****'. This effect is defined as the observation of a biological response in cells that are not themselves traversed by ionizing radiation, but which can communicate with cells that are. The effect is a poorly understood phenomenon. The study demonstrates that non-DU exposed cells, the so-called bystander cells, are influenced by their proximity to DU*

			exposed cells and that this phenomenon is not observed with carcinogenic non-radioactive heavy metals. It appears that different cell types respond differently to bystander signalling.
Yellowhair, M., Romanotto, M. R., & Stearns, D. M., et al. (2018). Uranyl acetate induced DNA single strand breaks and AP sites in Chinese hamster ovary cells. Toxicology and Applied Pharmacology, 349, 29-38.	15.06.2018	https://doi.org/10.1016/j.taap.2018.04.022	*The purpose of this specific in vitro study was to characterize the types of DNA damage produced by DU in the form of soluble uranyl acetate (UA) at environmentally relevant concentration ranges. Uranium enters the cell via endocytosis as observed with nickel. The clonogenic assay showed that UA had a significant cytotoxic effect.* *As observed in other metals,* ***uranium is considered carcinogenic, mutagenic, and genotoxic by more than one mechanism****. The results of the study indicate that* ***DU induces DNA damage via strand breaks and uranium-DNA adducts in treated cells****. This suggests that DU is genotoxic in CHO cells and is inducing single strand breaks rather than double strand breaks in vitro.*

THYROID DAMAGE

Recent study suggests the link between DU exposure and adverse effects on the thyroid function.

Title	Date	Link	Summary / Abstract Excerpt
Chang Shu, Jie Li, Suiyi Liu, Yong Li, Yonghong Ran, Yazhen Zhao, Juan Li, Yuhui Hao, Depleted uranium induces thyroid damage through activation of ER stress via the thrombospondin 1-PERK pathway, Chemico-	1.09.2023	https://www.sciencedirect.com/science/article/abs/pii/S0009279723002594	*The purpose of this study was to investigate the DU-induced* ***thyroid damage*** *and its potential mechanism in order to find new targets for detoxification after DU poisoning. A model of acute exposure to DU was constructed in rats. It was observed that* ***DU accumulated in the thyroid, induced thyroid structure disorder and cell apoptosis, and decreased the serum T4 and FT4 levels****. Gene screening showed that thrombospondin 1 (TSP-1) was a sensitive gene of DU, and the expression of TSP-1 decreased with the increase of DU exposure dose and time.*

Biological Interactions, Volume 382, 2023, 110592.			

CRITICAL STUDIES

There still are several studies that are denying some of the links between DU and adverse health effects. Such studies mainly cover the potential link between DU and cancer. Especially consistent in this denial are the studies on US veterans who were exposed to DU during the Gulf War. However, even in these studies, it is usually emphasized, that the DU exposure either is a concern or that DU might be a weak carcinogen. It must be (again) noted, that further research is essential.

Squibb, Katherine S., et al. "Surveillance for Long-Term Health Effects Associated With Depleted Uranium Exposure and Retained Embedded Fragments in US Veterans." Journal of Occupational and Environmental Medicine, vol. 54, no. 6, 2012, pp. 724–32.	6.06.2012	https://www.jstor.org/stable/45010139	*Elevated systemic exposure to depleted uranium (DU) that continues to occur in veterans with DU fragments* ***remains a concern****, although no clinically significant DU-related health effects have been observed to date. Other metals and local tissue reactions to embedded fragments are also of concern.*
Hines, Stella E., et al. "Pulmonary Health Effects in Gulf War I Service Members Exposed to Depleted Uranium." Journal of Occupational and Environmental Medicine, vol. 55, no. 8, 2013, pp. 937–	15.06.2013	https://www.jstor.org/stable/48509558	*We found no significant differences in respiratory symptoms. ab normal pulmonary function values, or prevalence of chest computed tomography abnormalities between which ark low urine uranium groups, Overall, the cohort's pulmonary function values fell within the expected clinical range.*

44.			
M.V. Bakhmutsky, M.S. Oliver, M.A. McDiarmid, K.S. Squibb, J.D. Tucker, Long term depleted uranium exposure in Gulf War I veterans does not cause elevated numbers of micronuclei in peripheral blood lymphocytes, Mutation Research/Genetic Toxicology and Environmental Mutagenesis, Volume 720, Issues 1–2, 2011, Pages 53-57.	28.02.2011	https://www.sciencedirect.com/science/article/abs/pii/S1383571810004092	*Our results indicate that on-going systemic exposure to DU occurring in Gulf War I Veterans with DU embedded fragments does not induce significant increases in MN in peripheral blood lymphocytes compared to MN frequencies in Veterans with normal U body burdens.*
Francesco Cappello, Alberto J.L. Macario, Depleted uranium induces human carcinogenesis involving the immune and chaperoning systems: Realities and working hypotheses, Medical Hypotheses, Volume 124, 2019, Pages 26-30.	01.03.2019	https://www.sciencedirect.com/science/article/abs/pii/S0306987718311940	*Depleted uranium (DU) is one of them directly pertinent to the military and civilians working in militarized areas. It is considered a* ***weak carcinogen but its implication in cancer development in exposed individuals is supported by various data****. Since not all subjects exposed to DU develop cancer, it is likely that DU-dependent carcinogenesis requires cofactors, such as genetic predisposition and deficiencies of the chaperoning and immune systems.*
Parrish, R.R., Haley, R.W. Resolving whether inhalation of depleted uranium contributed to Gulf War Illness using high-	18.02.2021	https://doi.org/10.1038/s41598-021-82535-3	*The findings show that even the highest likely levels of DU inhalation played no role in the development of GWI, leaving exposure to aerosolized organophosphate compounds (pesticides and sarin nerve agent) as the most likely cause(s) of GWI.*

sensitivity mass spectrometry. Sci Rep 11, 3218 (2021).			