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Artículo de Revisión

Healthcare professionals and cytotoxic agents: routes of exposure, sources of contamination, and means of prevention

Profesionales de la salud y agentes citotóxicos: vías de exposición, fuentes de contaminación y medios de prevención

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ABSTRACT

Introduction: Occupational exposure to antineoplastic agents poses a significant health risk to healthcare professionals and personnel involved in their preparation, administration or disposal. These cytotoxic substances, widely used in oncology, can cause to serious adverse health effects following repeated or accidental exposure.

Objective: To identify the primary routes and sources of occupational exposure to antineoplastic agents and to propose evidence-based preventive strategies for a safer work environment.

Methods: A narrative review was conducted using scientific literature and guidelines from authorized bodies (NIOSH, WHO) to synthesize current one exposure pathways and prevention measures.

Results: Multiple routes of exposure were identified: dermal, inhalation, ocular and oral. Exposure risk exists throughout the drug-handling process, from receipt and compounding to administration and waste disposal. Patient excreta (urine, feces, sweat) represent a significant secondary source of exposure. The review also outlines immediate response protocols for exposure incident to minimize health risk and maintain workplace safety.

Conclusions: Effective risk mitigation requires an integrated approach based on three pillars: (1) engineering controls (e.g., closed-system transfer devices, ventilated cabinets), (2) administrative protocols with appropriate personal protective equipment, and (3) continuous education and training. Prioritizing healthcare worker safety as an ethical obligation is fundamental to sustainable and responsible oncology care.

RESUMEN

Introducción: La exposición a agentes antineoplásicos representa un riesgo para la salud de profesionales sanitarios y trabajadores que participan en su manipulación. Estas sustancias, utilizadas habitualmente en oncología, son conocidas por sus efectos citotóxicos, que pueden provocar graves consecuencias para la salud en caso de exposición repetida o accidental.

Objetivo: Identificar las principales vías de contaminación y las fuentes de exposición profesional a los agentes antineoplásicos, y proponer estrategias preventivas destinadas a garantizar un entorno laboral más saludable y seguro.

Métodos: Se realizó una revisión narrativa de la literatura científica y de las directrices de organismos especializados para sintetizar las vías de contaminación por medicamentos antineoplásicos y elaborar recomendaciones de prevención.

Resultados: La literatura científica destaca múltiples vías de contaminación asociadas a la manipulación de agentes antineoplásicos, incluidas las cutánea, respiratoria, ocular y oral. Destaca que el riesgo de exposición puede producirse en las etapas del circuito, desde la recepción del producto hasta la gestión final de los residuos. Los excrementos de los pacientes que reciben quimioterapia también representan un vector potencial de transmisión. Además, la revisión identifica varios procedimientos que deben seguirse en caso de accidente de exposición, con el fin de limitar los riesgos para los profesionales sanitarios y preservar la integridad del entorno de trabajo.

Conclusiones: La mitigación de los riesgos asociados a los agentes antineoplásicos requiere una estrategia de prevención integrada y sistémica, construida sobre tres pilares fundamentales: controles técnicos robustos, protocolos estrictos con equipo de protección personal y formación continua del personal.

INTRODUCTION

Working in oncology departments entails significant occupational health hazards for healthcare personnel. Although antineoplastic agents provide therapeutic benefits to patients, they also pose serious risks to those involved in their handling. These hazardous drugs have being detected in ambient air, on workplace surfaces, and in patient excreta, underscoring the potential for widespread environmental contamination in healthcare settings.[1]

Although occupational exposure levels are several orders of magnitude lower than those received by patients (approximately 10^6-fold lower), such exposure is often repeated over extended periods and may involve multiple antineoplastic agents simultaneously.[2,3]

Due to their widespread use and well-documented carcinogenic, mutagenic and reprotoxic (CMR) properties, antineoplastic agents represent a major concern in the occupational health and a critical component of occupational risk assessment (ORA) in healthcare facilities.[4]

Occupational exposure primarily occurs through dermal contact (skin, mucous membranes, conjunctivae), inhalation of aerosols, or accidental incidents (e.g. vial breakage, splashes, or needlestick injuries).[5] Additional exposure risks arise during drug preparation, administration, waste handling, management of patient excreta, and decontamination of work surfaces.[5]

Therefore, all personnel who interact with patients receiving chemotherapy or handle antineoplastic agents must implement appropriate protective measures at all times.[5,6] Nevertheless, occupational exposure remains underestimated and underrecognized by some healthcare workers, emphasizing the need for objective tools to assess and monitor exposure levels.[1,4]

This review argues that effective protection against the pervasive risks of antineoplastic agents cannot rely on isolated interventions. Instead, a comprehensive, systemic prevention strategy is required, one build upon three interdependent pillars: (1) engineering controls, (2) administrative controls, and (3) appropriate use of personal protective equipment, supported by continuous education and training.

METHODS

This narrative review was conducted using a structured analytical-synthetic approach to synthetize and interpret current evidence on occupational exposure to antineoplastic agents in hospital settings.

A comprehensive literature search was performed in PubMed, Scopus, ScienceDirect and Google Scholar. The search was supplemented with official

guidelines and technical documents from internationally recognized organizations specializing in occupational health in oncology, including the National Institute for Occupational Safety and Health (NIOSH), the World Health Organization (WHO), the Observatory of Medicines, Medical Devices, and Therapeutic Innovations (OMMEDIT), the French National Research Institute (INRS), and the United States Pharmacopeia (USP).

Search terms included: "antineoplastic agents", "occupational exposure", "routes of exposure", "prevention", "hospital hygiene" and "healthcare personnel safety". Searches were carried out in French, English and Spanish.

The inclusion criteria were: (a) original research articles; (b) systematic reviews and evidence-based professional guidelines on occupational exposure to antineoplastic agents in healthcare settings; (c) publications detailing risks associated with drug preparation, administration, waste handling and surface decontamination; and (d) studies evaluating or validating preventive interventions.

Exclusion criteria were: (a) non-scientific publications (e.g., opinion pieces, editorials without data); and (b) articles that did not address occupational risks related to antineoplastic agents.

RESULTS

Of 120 identified publications, 29 were selected based on methodological rigor and thematic relevance.

Thematic analysis revealed that occupational risk from antineoplastic agents in hospitals is pervasive and multifaceted, organized into four key domains:

Exposed personnel: Includes pharmacists, nurses, physicians, pharmacy technicians, cleaners and waste handlers.

Routes of exposure: Dermal (cutaneous), inhalation (respiratory), ingestion (oral), and ocular contact.

Sources of exposure: Risk occurs across the entire antineoplastic drug-handling continuum, from receipt and storage of vials, through compounding and transport, to drug administration, patient excreta (urine, feces, and sweat) and cytotoxic waste management.

Preventive strategies and an integrated framework: Emphasizes the need for a systematic approach combining engineering controls, administrative protocols, personal protective equipment, and ongoing training to ensure sustainable workplace safety.

DISCUSSION

Exposed Professionals

Occupational exposure to antineoplastic agents affects a broad spectrum of hospital personnel, not only pharmacy technicians and nurses, but also physicians, nursing assistants, cleaners, receptionists, transport staff, laundry workers, and even administrative staff. These findings align with recent studies by Ndaw and Remy[1] and Kennedy, et al.[7] which documented urinary and environmental contamination among healthcare workers, particularly during drug administration and patient excreta handling, but also among staff with no direct contact with medications. Multicenter studies have further confirmed the presence of cytotoxic residues on surfaces and hands beyond compounding areas, as well as urinary biomarkers in "non-handling" personnel.[8] The detection of cytotoxic traces in administrative staff, and persistent contamination of drug vials upon receipt,[9,10] reinforce the hypothesis of early dissemination throughout the pharmaceutical supply chain. Collectively, these data demonstrate that exposure can occur via contaminated surfaces, packaging, or airborne particles, even in the absence of direct drug handling.

This diversity of affected roles confirms that risk extends beyond direct handlers to the entire hospital ecosystem. International guidelines,[5,11] therefore advocate a comprehensive prevention strategy encompassing all personnel potentially exposed to antineoplastic agents or their residues. Institutional protocols similarly recommend expanding prevention efforts to include logistics and support services, coupled with reinforced continuing education.[12,13]

Routes of exposure

a) Dermal route:

The skin is the primary exposure pathway, due to frequent contamination of gloves, hands, forearms, and work surfaces.[1] This is corroborated by Beigzadeh, et al.,[14] who reported high rates of skin contamination despite glove use. Environmental surveys consistently detect cytotoxic residues on workbenches, door handles, telephones, floors, and equipment,[1,9] explaining chronic dermal exposure, even among non-handling staff.[1] A Moroccan study found that 67% of healthcare workers experienced skin-related incidents, underscoring the risk in routine practice.[15] Critically, residues persist after standard cleaning with detergents or disinfectants, indicating that conventional decontamination protocols are insufficient.[16]

International recommendations emphasize frequent glove changes and use of fluid-resistant gowns to mitigate dermal exposure.[6,11] However, adherence remains suboptimal. In Morocco, nurses often retained gloves until visibly soiled or torn, increasing contamination risk.[13] Conversely, double gloving has proven highly effective: Kennedy, et al.[7] reported a ~70% reduction in hand

contamination with double gloves, while Ndaw and Remy[1] observed 60-75% lower cytotoxic detection in skin and urine samples, and 50% lower urinary biomarkers, among nurses using two glove pairs. These findings strongly support universal adoption of double gloving in oncology settings, where single-glove use remains prevalent.[1,7]

b) Respiratory route:

Inhalation exposure occurs during drug reconstitution, line purging, tubing handling, or opening pressurized vials.[17] Air sampling has detected measurable antineoplastic concentrations in clinical areas.[14] Ndaw & Remy[1] confirmed airborne cyclophosphamide and ifosfamide despite engineering controls (e.g., hoods, isolators) supporting guidelines that classify inhalation as a significant exposure route,[5] Respiratory symptoms, including rhinitis and nasal irritation, have been reported in 15-25% of exposed personnel across cohorts.[1,14,18]

c) Oral route:

Unintentional ingestion of residues from contaminated hands or food in clinical areas poses a documented risk.[17] Poor hand hygiene facilitates transfer from surfaces to mouth.[1,19] Additionally, handling oral chemotherapy formulations (tablets, capsules) contributes to exposure, a route often overlooked.[7] The World Health Organization[19] and international guidelines strictly prohibit eating, drinking, gum chewing, or food storage in preparation areas to prevent ingestion. These measures align with containment principles requiring dedicated, food-free compounding spaces.[5,11,20]

d) Ocular route:

Splash incidents during vial handling or administration can cause eye exposures.[21] Campbell and Dicksit[17] noted accidental droplet projection as a key mechanism, while Ndaw & Remy[1] emphasized indirect transfer via contaminated hands or gloves. Reported symptoms include irritation, redness, and pain,[7] confirming ocular mucosa vulnerability, and justifying mandatory protective eyewear.[6] Nevertheless, compliance is poor. Elmortaji & Zahir[15] observed zero eyewear use among nurses, and Mahdy et al.[18] found most staff deemed goggles "non-essential", highlighting eye-wear as the most neglected PPE component.

Hierarchy of exposure risks

This review establishes a clear risk hierarchy:

- Dermal exposure is predominant, evidenced by widespread surface and skin contamination, even among indirect-contact staff.[1,14] Chronic low-dose exposure constitutes the core occupational hazard.[2,3]
- Respiratory exposure persists despite engineering controls, particularly during non-isolated procedures (e.g., line purging) and via particle resuspension.[1,13]
- Oral and ocular routes, though less frequent, represent critical accidental risks tied to PPE noncompliance and hygiene lapses.[11,15]

This hierarchy should guide resource allocation, prioritizing skin protection, surface decontamination and strict adherence to PPE protocols.

Critical discussion of identified exposure sources

Healthcare professionals are exposed to occupational risks throughout the entire drug handling process, including the receipt, preparation, reconstitution, and administration of antineoplastic agents. In addition, exposure may occur through contact with patients' excreta, which can remain contaminated for several days following chemotherapy administration. With the increasing use of cytotoxic drugs worldwide, staff in direct contact with these patients faces a heightened risk of contamination and toxicity.[11,19]

a) Receipt of antineoplastic vials

Several studies have demonstrated that the outer surfaces of vials are contaminated in 56% to 71% of cases.[9,10] This early contamination confirms that occupational risk begins upon drugs receipt, even prior to preparation. Recent evidence corroborate this observation, emphasizing that the absence of systematic cleaning protocols exposes staff during this initial stage.[7] Although guidelines advocate strict control and decontamination upon receipt, these measures remain inconsistently applied in many clinical settings.[6] Furthermore, staff frequently omit systematical vial cleaning before storage or preparation, thereby promoting secondary contamination of workbenches and isolators.[1] This oversight facilitates the spread of cytotoxic residues in the work environment and increases the risk of dermal and respiratory exposure. Conversely, experimental studies have confirmed the efficacy of pre-handling decontamination. Gonzalo, et al.[22] demonstrated that the use of detergent solutions or disinfectant wipes significantly reduces platinum concentrations on external surfaces. The pre-disinfection of vials interrupts the contamination chain of and limits the dispersion of cytostatics in preparation areas.[16] These findings reinforce the importance of incorporating systematic vial cleaning into hospital protocols, in accordance with the recommendations.[5,11]

b) Storage of antineoplastic drugs

Several studies indicate that drug storage areas constitute a significant contamination source, occasionally reaching very high levels (up to 20,000 ng/100 cm²).[1] Similarly, Sessink et al.[20] documented cytotoxic residues in cabinets and storage bins, despite staff rarely perceives these areas as exposure risk. Storage therefore represents a critical stage in indirect environmental contamination. International standards emphasize the necessity of specific labeling and routine cleaning of these zones.[5] Additionally, evidence highlights the need for systematic maintenance of storage areas. Hilliquin & Bussières[10] reported that inadequate container disinfection promotes residue transfer to workbenches and isolators. Viegas, et al.[16] confirm that regular cleaning of storage surfaces significantly reduces measurable cytotoxic concentrations and limits secondary spread. These data support the integration of routine storage area decontamination into institutional protocols, aligning with international guidelines.[6,11]

c) Preparation of antineoplastic drugs

The preparation of antineoplastic agents presents substantial occupational hazard. Concerns regarding risks to nursing staff during the preparation and administration of anticancer treatments were first documented in the late 1970s, following reports of clinical toxicity. Numerous occupational hazards associated with these agents have since been documented in the literature.[4] Technical procedures such as reconstituting lyophilized products, diluting liquid formulations, or opening glass ampoules carry a high risk of splashing, putting staff members at risk of contamination.[4] Needle removal from vial stopper may generate air currents and potential aerosolization. Liquid transfer using syringes or tubing connection to infusion bags can result in spillage, while air expulsion from syringes or tubing may release droplets.[5] When preparations are performed outside biological safety cabinets, measurable airborne contamination is detectable, exposing workers to toxic aerosols.[1,5] The introduction of biological safety cabinets and closed-system isolators has significantly reduced inhalation risks during the preparation phase.[4,23] However, these engineering controls do not eliminate all exposure routes; the risk of dermal contamination of hands or forearms persists, necessitating the use of double gloves and long-sleeved, impermeable gowns. Aerosols generated by overpressure when introducing diluent into a vial may contaminate work surfaces and, subsequently, operators if appropriate personal protective equipment is not used.[1,4] A multicenter study carried out in hospitals and pharmacies in the Czech Republic and Slovakia, highlighted recurrent environmental contamination by antineoplastic agents, including within controlled-access preparation areas.[23] Measured surface concentrations ranged from a few ng/cm² to several tens, confirming residue persistence despite cleaning protocols. A subsequent study focusing on cyclophosphamide and fluorouracil detection in laminar flow hoods, isolators, work surfaces, and preparation equipment reported persistent contamination in the majority of samples. Glove exteriors and preparation

workstations were among the most affected surfaces. The authors emphasized the stability of contamination risks over time, despite evolving safety practices, and stressed the need to combine engineering controls with organizational measures and consistent personal protective equipment use (gloves, gowns, masks).[19]

d) Transport of antineoplastic preparations

Beyond preparation hazards, the transport of chemotherapy drugs represents a critical node in the safety chain. Evidence indicates that infusion bags and syringes delivered to clinical units may be externally contaminated, particularly on packaging and transport trays.[4] Handling of bins, carriers, or delivery equipment can also contribute to secondary environmental contamination.[24] To mitigate these risks, international guidelines recommend that preparations be securely sealed, packaged in shock-resistant, leak-proof containers, and externally decontaminated before leaving the preparation area.[5,11] Clear labeling and container traceability are also essential to prevent medication errors and ensure staff safety.[4,6] These integrated technical and organizational measures, combined with consistent protective personal equipment use, effectively limit contamination risk during drug transport.[5]

e) Administration of antineoplastic preparations.

Injectable formulations represent the primary source of occupational exposure during drug administration.[5] Nursing techniques for connecting, administering, and disconnecting infusion lines, as well as performing subcutaneous or intravenous injection, constitute critical moments for potential contamination. Risk is particularly high during line disconnections, where leakages or aerosol generation may occur.[4] Environmental monitoring has detected antineoplastic traces on infusion sets, bedside tables, IV poles, floors, and especially on nurses' gloves in treatment rooms.[25] Additionally, line flushing procedures performed post-administration have been identified as secondary contamination sources, potentially dispersing cytotoxic residues into the immediate clinical environment.[5] Oral formulations also pose occupational risks, particularly when tablets are split or crushed for pediatric patients or individuals with dysphagia. These practices expose healthcare workers and caregivers to inhalation or ingestion of drug dust.[11] Safer administration alternatives should be prioritized, such as tablets dissolution in closed-system syringes, enabling safe liquid administration for patients with swallowing difficulties.[18] Oral formulations and their packaging therefore constitute potential contamination vector, raising concerns not only for healthcare staff, but also for patients and family caregivers.[11]

f) Patient excreta

Patients themselves constitute a potential contamination source through their excreta. These include urine and feces, as well as sputum, saliva, sweat, and

vomit, particularly with oral treatments, in which the drug or its active metabolites may be detected.[5] High concentrations of antineoplastic agents have been measure in excreta throughout treatment and up to several days post-therapy, typically between 3 and 7 days for most compounds, although slower excretion kinetics have been reported for certain agents.[4] Few studies have specifically evaluated the toxicity of excreta handling, and standardized disposal guidelines remain lacking. Nevertheless, the occupational hazard for staff managing these wastes is well established and constitutes a significant risk of dermal exposure.[11] Furthermore, hospital excreta contribute to wastewater contamination, with cytotoxic drugs such as cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and docetaxel consistently detected in hospital effluents,[26] highlighting the environment persistence of these compounds and the limitations of conventional water treatment systems.[16,26] These findings underscore the need for specific protocols for excreta and effluents management, including mandatory PPE use, dedicated dual-flush toilet systems, and the implementation of advanced treatment technologies.[26]

g) Management of cytotoxic and contaminated waste:

Cytotoxic waste encompasses any material that has contacted anticancer drugs during reconstitution or administration. This include syringes, needles, empty or partially used vials, gloves, single-use PPE, respiratory masks, spill cleanup materials, and air filters from preparation workstations (e.g., biological safety cabinets or isolators). Expired or compromised hazardous drugs must also be classified and disposed of as cytotoxic waste.[11] This type of waste, referred to as "low-level contaminated waste," must also be classified and disposed as cytotoxic waste.[5,11] Contaminated waste refers to medical devices used on patients receiving chemotherapy, such as syringes, needless, catheters or used infusion bags. Classified as "low-level contaminated waste," these items must be discarded in designated chemotherapy waste containers to prevent staff injury or exposure.[6] In some jurisdictions, waste is not stratified by contamination level; in such cases, all cytotoxic-related waste is consolidated in dedicated containers.[11] Given the evidence presented, adherence to international preventive guidelines remains essential to minimize occupational exposure.

The interpretation of environmental and biological contamination data, particularly urinary biomonitoring results, requires careful consideration. While such data unequivocally demonstrate internal exposure, methodological variability across analytical platforms and the absence of universally accepted occupational exposure limits complicate quantitative risk assessment and cross-study comparisons.[1,8] Moreover, the gap between stringent international recommendations and routine clinical practice reveals multifactorial implementation barriers. Studies indicate that some healthcare workers underestimate chronic low-dose exposure, prioritizing acute or visible hazardous risks instead.[15] Physical discomfort and workflow disruptions associated with prolonged use of double gloves, impermeable gowns, and protective eyewear

are frequently cited as major compliance barriers.[15,18] Finally, the complexity and financial burden of collective protective equipment such as closed-system drug transfer devices (CSTDs) and preparation isolators, may limit widespread adoption, particularly in resource-constrained settings.[24] Effective occupational prevention must therefore extend beyond protocol dissemination and actively address behavioral, ergonomic, and economic determinants of compliance.

Preventive Measures

The prevention of occupational exposure to antineoplastic agents is most effective when based on a multi-level approach, commonly structured as a hierarchy of controls. The measures outlined below are organized into three complementary categories: (1) technical and collective measures, which aim to eliminate or contain hazards at the source; (2) administrative controls and personal protective equipment (PPE), which manage residual risks through standardized procedures and final barriers; and (3) training and competence assurance, which ensure the consistent and effective implementation of all protocols. This framework aligns with internationally recognized occupational health and safety standards, ensuring that preventive strategies are applied systematically and synergistically.[5,15]

a) Personal protective equipment (PPE):

Hand protection: Glove use is the minimum requirement when handling cytotoxic drugs. Powder-free nitrile, neoprene, or latex gloves with extended cuffs that overlap the gown should be worn and replaced at least every 30 minutes, or immediately upon visible contamination or puncture. Glove removal must always be followed by thorough hand hygiene to prevent secondary transfer.[5,27] Current guidelines strongly recommend double gloving, which significantly reduces permeability and dermal exposure during prolonged or high-risk handling.[11,28]

Body protection: A long-sleeved, fitted, splash-resistant gown is mandatory during drug administration, waste handling, or contact with potentially contaminated materials (e.g., linens, patient clothing). In scenarios with a high risk of splashing, an impermeable apron should be worn over the gown.[4]

Face and eye protection: A splash-resistant mask and protective eyewear are required for any procedure involving a risk of droplet or aerosol generations. In high-risk preparation or administration environments, the use of full-face shields or appropriate respiratory protection may be indicated.[5,11]

b) Specific preventive measures:

Receipt and storage: Personnel responsible for receiving and inventorying antineoplastic drugs must be trained on the risk of external vial contamination. To minimize exposure, staff should: (i) wear single-use chemotherapy-tested

gloves when handling containers; (ii) perform hand hygiene after each handling event.[5,11] Environmental monitoring studies have shown that storage bins and shelves frequently harbor cytotoxic residues, with concentrations exceeding tens of ng/cm².[23,28] Although literature lacks consensus on the optimal decontamination agent, aqueous detergent solution have proven effective at significantly reducing surface contamination.[6,10] Alternatively, pre-wiping vials with disinfectant wipes before isolator placement and immediately after preparation effectively removes detectable chemical residues.[28] All stored cytotoxic agents must be clearly identifiable; outer packaging should display standardized hazard labels or universally recognized cytotoxic symbols.[5,11]

Preparation: Preparation must occur in a designated, access-controlled room equipped with appropriate engineering controls, such as Class II biological safety cabinets or closed-system isolators.[11] These containment devices are essential for minimizing airborne and surface contamination during compounding.

Administration: All antineoplastic preparation should be considered potentially contaminated. Handling requires double gloving with chemotherapy-tested gloves, to ensure optimal protection during infusion line connection and disconnection.[5,11] Environmental studies confirm that external surfaces of infusion bags and tubing frequently become contaminated during transport and administration, posing a direct risk to nursing staff.[28] Gloves must be discarded immediately after line manipulation and placed in designated cytotoxic waste containers to prevent secondary spread.[6] While closed-system drug transfer devices (CSTDs) substantially reduce exposure, contamination may still occur via leakage or aerosolization during routine handling.[10] Therefore, strict hand hygiene before and after each administration step remains a critical preventive measure.[5,11]

Waste disposal: Potentially contaminated materials should be collected in *plastic* bags of appropriate thickness (typically ≥0.02 mm for polypropylene and ≥0.04 mm for polyethylene). Bags must be color-coded, clearly labeled with cytotoxic hazard warning, and kept separated from general waste. Sharps must be placed in puncture-resistant, leak-proof containers prior to bagging. Each institution must establish a comprehensive waste management policy that, at a minimum, complies with national or regional hazardous waste regulations.[5,27] Environmental services personnel must wear appropriated PPE when handling waste containers. Cytotoxic waste must never be commingled with municipal waste and must be processed according with hazardous materials protocols. If incinerated, waste should not be placed in airtight containers to prevent pressure-related explosions; temperatures of 1,000–1,600°C are required to thermally degrade antineoplastic compounds.[11]

c) Occupational exposure monitoring and risk stratification:

Some occupational health frameworks utilize the Cytotoxic Contact Index (CCI) to quantify exposure risk. The CCI is calculated as the ratio of total cytotoxic

drug preparations and administrations performed by a worker to their total working hours. A higher CCI correlates with increased frequency of exposure, and elevated risk of chronic toxicity. Exposure is typically stratified into three risk levels, each mandating specific control measures:

Level 1 (CCI<1): Occasional preparation/administration → individual PPE and standard precautions.

Level 2 (1≤CCI≤3): Moderate preparation/administration → implementation of collective controls (e.g., dedicated preparation stations, CSTDs).

Level 3 (CCI > 3): Intensive preparation/administration → centralized compounding units with advanced engineering controls and restricted access.[19]

d) Training, medical surveillance, and special populations:

The integration of collective and individual protective measures is essential for ensuring worker safety. Rigorous occupational health surveillance must accompany these controls, particularly for staff exposed to carcinogenic, mutagenic, or reproductive toxicants (CMR agents). Surveillance should include a comprehensive pre-employment medical assessment and annual periodic evaluations to monitor health status and early signs of toxicity.[11] All personnel involved in the handling of cytotoxic drugs must undergo mandatory, competence-based training covering hazards recognition, safe compounding and disposal techniques, patient care protocols, proper PPE use, spill management, and equipment maintenance. Departments managing antineoplastic agents must maintain an updated registry of drug toxicological profiles, handling procedures, solubility, stability data, and physicochemical properties.[6,27]

Pregnancy and lactation are formal contraindications to the preparation, administration, or disposal of cytotoxic drugs. Affected employees must promptly notify occupational health services and their direct supervisors. Occupational health records must include an individual exposure log, an inventory of handled agents, and a cumulative exposure summary upon reassignment or termination of duties.[5,11]

Additional Controls

Special controls are required for environmental services and maintenance personnel when handling linen or other materials potentially contaminated with biological fluids from patients receiving cytotoxic therapy. It is essential to develop safe work procedures for handling these materials and to provide systematic training to all personnel involved. Clear and appropriate signage must be displayed in visible areas to inform staff of the presence of cytotoxic drugs and the associated risks.[5,11]

Technical Controls

The following technical control measures must be implemented when handling cytotoxic drugs.

At a minimum, a Class II biological safety cabinet (BSC) equipped with HEPA filtration systems that prevent contaminated air from being reintroduced into the room must be used during preparation.[27] The preparation area inside the enclosure should be covered with plastic-lined absorbent material to reduce dispersion and facilitate clean-up of any spills.[28] Puncture-proof containers must be provided for the disposal of needles, syringes, and vials, and labeled waste bags with leak-proof closures should be available in the preparation area for the disposal of these containers. Contaminated needles, syringes, and vials must be disposed of intact, without being crushed or dismantled, to prevent aerosolization or leakage. These technical measures, combined with collective and individual protective equipment, are essential to reduce occupational exposure and ensure compliance with international safety standards.[11,27]

Towards a comprehensive and integrated prevention framework

Occupational exposure to antineoplastic agents remains a complex challenge that cannot be mitigated by isolated interventions. To move beyond fragmented practices, preventive measures must be synthesized into a systemic framework reflecting the internationally recognized hierarchy of controls. This framework rests on three complementary pillars, each addressing a distinct level of risk management.

Pillar 1: Technical and collective measures (engineering controls)

Technical and collective measures represent the first and most reliable line of defense, aiming to eliminate hazards at their source. The use of Class II biological safety cabinets (BSCs) equipped with HEPA filters, isolators, and closed-system transfer devices (CSTDs) significantly reduces the release of aerosols and vapors during drug preparation.[6] Ventilation systems and negative-pressure rooms further limit environmental contamination. Secure waste management, including puncture-proof containers and leak-proof bags, ensures safe disposal of contaminated materials. These engineering controls are indispensable, as they minimize exposure before reliance on individual behavior.

Pillar 2: Strict protocols and personal protective equipment (Administrative controls & PPE)

Administrative controls and PPE serve as procedural safeguards and final barriers. Standardized protocols must govern every stage of the drug circuit: receipt, storage, preparation, administration, and waste handling.[15] Compliance with these procedures reduces variability and ensures consistency across institutions. PPE, including double gloves, impermeable gowns, masks, and eye

protection, provides essential protection when technical measures cannot fully eliminate risk. Evidence consistently supports the effectiveness of double-gloving and protective eyewear in reducing dermal and mucosal contamination.[28] However, PPE should be viewed as complementary rather than primary, reinforcing the importance of strict adherence to protocols.

Pillar 3: Ongoing and engaging staff training

Training is the dynamic element that brings the other two pillars to life. Beyond initial instruction, it must be continuous, interactive, and tailored to address behavioral barriers such as risk perception, discomfort, or resistance to change. Practical demonstrations, simulation exercises, and regular competency assessments foster adherence and empower staff to integrate safety measures into daily practice. Training also reinforces the ethical dimension of occupational safety, reminding healthcare professionals that their protection is inseparable from the sustainability of oncologic care.[11]

The transition to a systemic prevention strategy, as outlined in this review, has major implications for both practice and investment. Although engineering controls and training programs require an initial financial commitment, this should be regarded as a strategic investment. The expenses linked to acquiring CSTDs and high-quality PPE are expected to be offset by long-term reductions in occupational disease and absenteeism,[5] reinforcing this approach as both economically sound and ethically imperative. Accordingly, healthcare institutions must implement harmonized, facility-wide safety protocols and commit to continuous, engaging staff training. The conceptual framework (figure 1) underscores that safety is a collective responsibility, relying on the synergy between leadership providing resources and organizational support, and frontline staff ensuring strict adherence to safety standards.

In addition to these immediate practical implications, this review identifies critical avenues for future research. While the three-pillar framework is grounded in existing evidence, there is a pressing need for longitudinal studies to evaluate its real-world effectiveness in diverse healthcare settings. Future research should quantitatively assess the impact of such integrated strategies on key outcomes: the reduction of surface and biological contamination levels, the incidence of occupational health symptoms among staff, and the long-term cost-benefit ratio for healthcare institutions. Furthermore, developing and validating standardized biomarkers for monitoring low-level chronic exposure remains a priority to objectively measure the success of prevention programs.

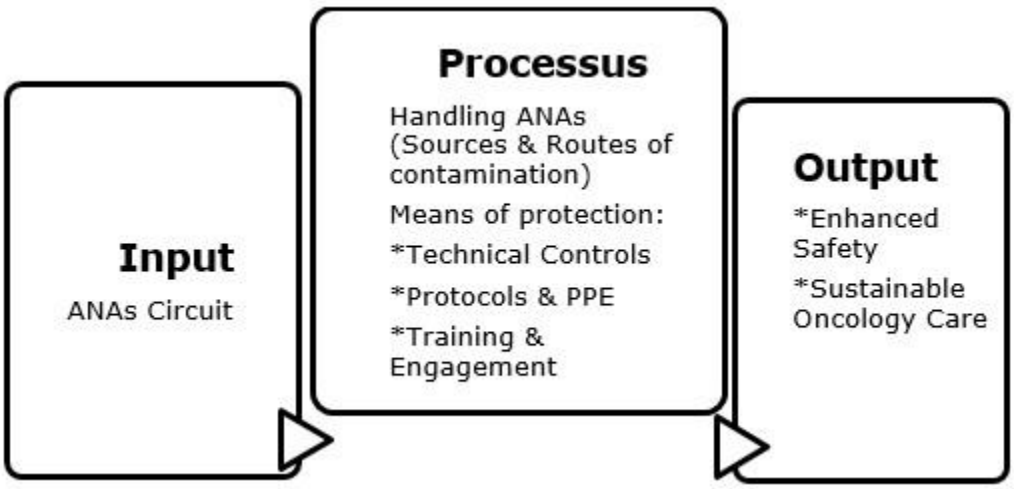

Fig. 1. Conceptual input-output framework for systemic prevention of occupational exposure to antineoplastic agents.

Management of Occupational Exposure to Antineoplastic Agents:

It is essential that all personnel involved in the handling of these drugs know how to react quickly and effectively in the event of an accident, and how to manage accidental contamination.[5,6,11] (Figs. 2, 3, and 4)

Accidental exposure to antineoplastic agents

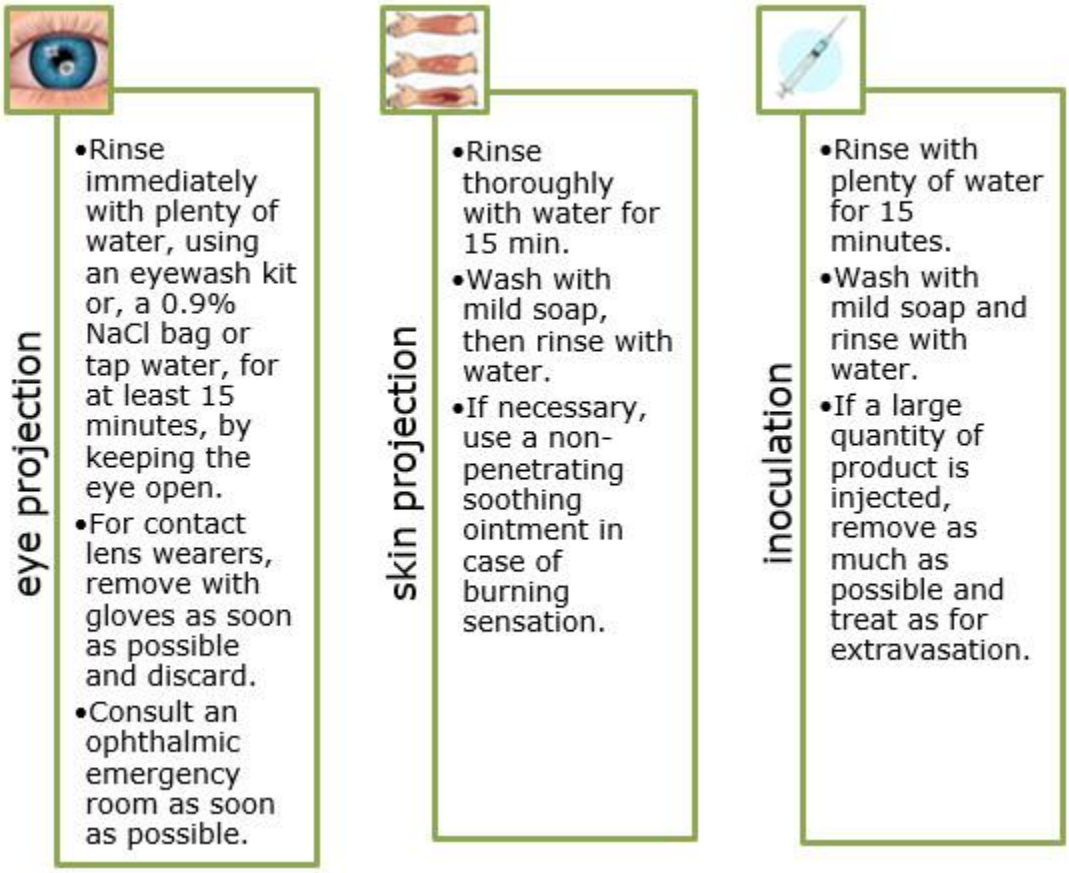

Fig. 2. Management algorithm for accidental exposure to antineoplastic agents, based on ISOPP, USP, and NIOSH guidelines.

Contamination of gloves and clothing

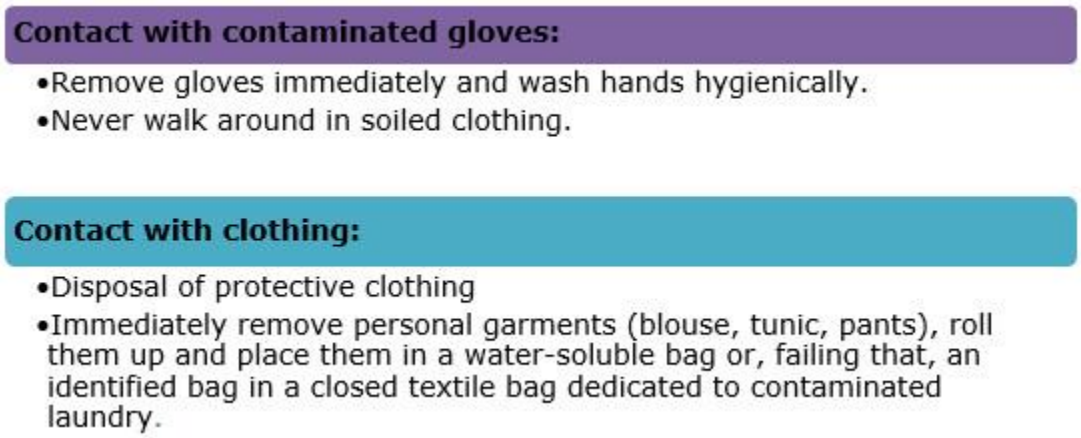

Fig. 3. Management protocol for glove and clothing contamination based on ISOPP, USP, and NIOSH guidelines.

Spill management: vial breakage, liquid leakage, or tablet/capsule crushing

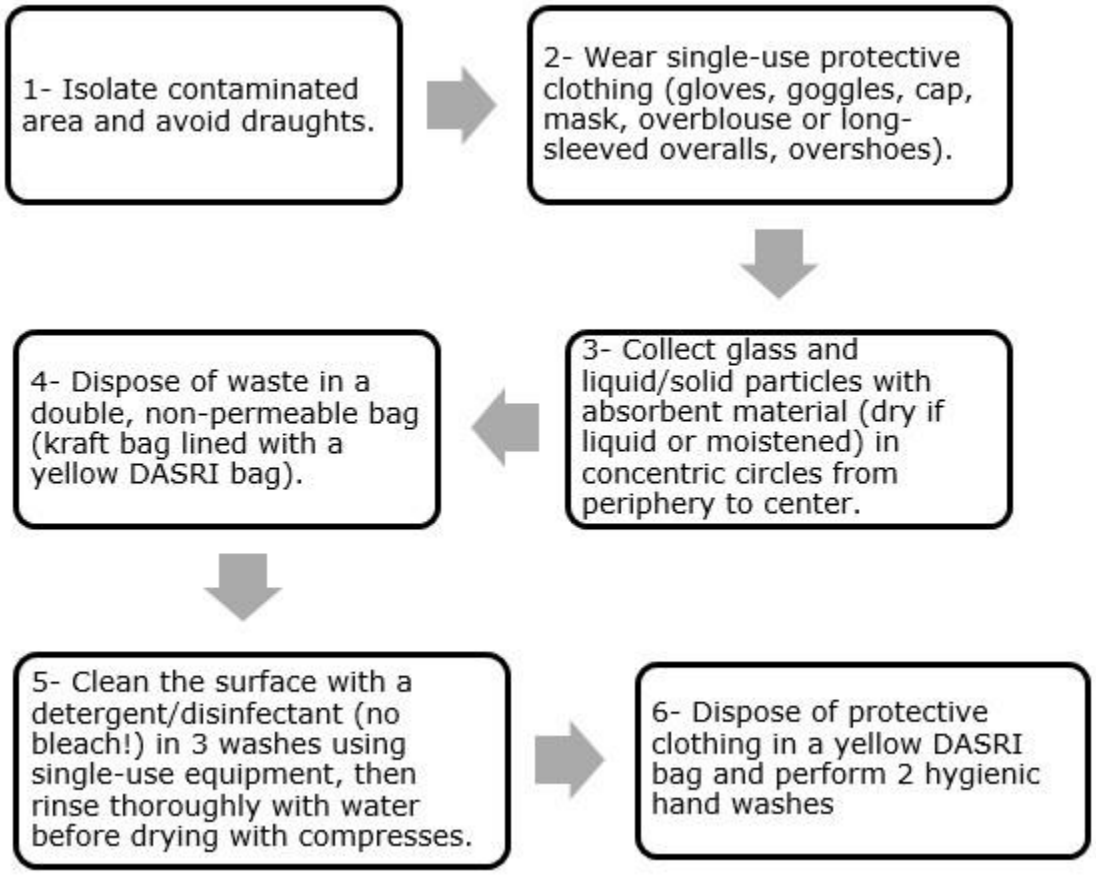

Fig. 4. Spill management protocol for vial breakage, liquid leakage, or tablet/capsule crushing, based on ISOPP, USP, and NIOSH guidelines.

CONCLUSION

In conclusion, the handling of antineoplastic agents in healthcare settings presents a pervasive and multifaceted occupational risk. This review underscores the breadth of exposed populations, the predominance of dermal exposure, and the persistence of contamination sources throughout the drug circuit. To address these challenges, preventive measures must be applied within an integrated framework that combines technical controls, strict protocols and PPE, and continuous staff training. Ensuring the safety of healthcare professionals is not optional; it is a prerequisite for the sustainability and ethics of oncologic care.

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Conflict of interest

The authors have no conflicts of interest relevant to this article.