

Table 1. Identification and description of the main findings. Vitória, 2014.

IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS							
Identification of the Article	Periodical	Year	Study Location	Objectives	Methodology	Population	Main Conclusions
<p>Cancer incidence and adverse pregnancy outcome in registered nurses potentially exposed to antineoplastic drugs</p> <p>Ratner <i>et al.</i>¹⁰</p>	BMC Nursing	2010	Canada	To determine if nurses who have been exposed to antineoplastic drugs have a higher risk of developing cancer, and if their children are more likely to be born with congenital anomalies.	Those who participated were nurses that had been registered in a professional organization for over a year, with their registrations going from 1974 to 2000. They had to have worked in oncology. Their contact with antineoplastic drugs was evaluated according to the number of years they had worked and their level of exposure. A cohort group of babies born in 1986 was evaluated. Exposure during pregnancy was considered as follows: Estimated exposure in the first trimester of pregnancy; and cumulative exposure over a 10 year period preceding the child's birth.	56,213 nurses 22,491 children, born alive.	Nurses who have worked in cancer centers or oncology units had a higher risk of getting breast cancer. The children of nurses exposed to chemotherapy drugs during pregnancy were significantly susceptible to congenital abnormalities in the eye. The risk of cleft palate and/or cleft lip was significantly higher among those born to women who had a cumulative exposure of 10 years prior to their pregnancy. Nurses with higher exposure had higher risk of rectal cancer
<p>Evaluation of genotoxicity induced by exposure to antineoplastic drugs in lymphocytes of oncology nurses and pharmacists.</p> <p>El-Ebiary <i>et al.</i>⁵</p>	Journal of Applied Toxicology	2013	Egypt	To assess the damage in the genome associated with the handling of antineoplastic drugs to oncology nurses and pharmacists working in a major cancer center in Egypt	A questionnaire about socio-demographics, health, habits of living and working. The subjects were neither smokers nor alcoholics. The subjects of the case study had worked with antineoplastic drugs for 2 to 20 years. Blood samples were taken. Lymphocytes were isolated. Genotoxic effects were evaluated for chromosome aberrations, and tests were performed with manganese. Cells in metaphase and binucleate lymphocytes were evaluated for the presence of micronuclei	20 nurses and 18 pharmacists as the case group; and 30 nurses as the control group	There was a difference regarding the years of exposure between pharmacists and nurses, being higher for the latter group, which also had higher levels of chromosome damage and aberrant lymphocytes. Aberrations such as deletions, gaps, and ruptures were found. The age of the individuals showed a positive correlation to chromosomal damage. The control group showed significantly less damage to the genome. The study infers that the reason for the difference between nurses and pharmacists is due to the fact that the latter adopt stricter protection when handling antineoplastic drugs, with gloves, masks, and gowns, while the nurses would only don gloves.

IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 2)

Identification of the Article	Periodical	Year	Study Location	Objectives	Methodology	Population	Main Conclusions
Assessment of chromosomal aberrations, micronuclei and proliferation rate index in peripheral lymphocytes from Tunisian nurses handling cytotoxic drugs. Bouraoui S. <i>et al.</i>⁸	Environmental Toxicology and Pharmacology	2011	Tunisia	To verify the genotoxicity of the exposure to antineoplastic drugs among nurses.	A questionnaire was filled out regarding socioeconomic status and lifestyle habits. Blood samples were collected for posterior testing for chromosomal aberrations and cells with binucleated micronuclei.	20 nurses (4 men and 16 women) who had been exposed and 20 matched controls.	Among those who had been exposed, chromosomal damage was assessed as being 5.7 times higher than in the control group. Chromosomal aberration was 3.75 times higher in chromatids and 5 times higher in chromosomes in the case group. No associations were found between exposure time and genetic changes. The index of the lymphocyte proliferation rate was significantly lower in the case group.
Occupational risk assessment of genotoxicity and oxidative stress in workers handling anti-neoplastic drugs during a working week. Rombaldi, F. <i>et al.</i>⁶	Mutagenesis	2009	Brazil	To assess oxidative parameters and genotoxicity in hospital workers who handle antineoplastic drugs.	The three oxidative stress parameters used were the concentration of catalase, the antioxidant enzyme superoxide dismutase and substances that are reactive to thiobarbituric acid. Genotoxicity was evaluated by comet assay and by the frequency of micronuclei in lymphocytes. All participants answered a questionnaire on health. Protective equipment use was also evaluated. There was blood collection, which underwent a clinical trial, and the slides were coded for blind analysis. The damage index (DI) to the DNA was ranked 0-4 in ascending order.	20 nurses and pharmacists in the case group, and 20 nurses and pharmacists in the control group.	The DI of the DNA of exposed workers, as well as the concentration of manganese and catalase, increased significantly compared to those in the control group. Nurses who handled antineoplastic drugs had a higher frequency of micronuclei as compared to the other groups. Alcohol consumption was associated with higher DI of the DNA. The frequency of micronuclei increased with the working time and age. Contact with antineoplastic substances led to the breaking down, cross-linking disruptions, and intercalation of the DNA.

IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 3)

Identification of the Article	Periodical	Year	Study Location	Objectives	Methodology	Population	Main Conclusions
<p>Occupational exposures to antineoplastic drugs in an Oncology-Hematology Department. –</p> <p>Derry Stover Chandran Achutan¹⁵</p>	Journal of Occupational and Environmental Hygiene	2011	Nebraska (USA)	To evaluate the occupational hazards of exposure to antineoplastic drugs in the hematology department of an oncology hospital; as well as complying with guidelines set forth in the document of the <i>National Institute for Occupational Safety and Health</i> (NIOSH).	The questionnaire was applied for four days at the beginning of the morning and night shifts. Demographic variables, level of exposure to chemotherapy, level of training and the use of personal protective equipment were evaluated. Samples from the surfaces of the nursing staff's workplaces, as well as from the rooms of patients, were collected with sterile gauze and sodium hydroxide to measure the level of contamination by antineoplastic drugs. All samples were stored at -20 °C.	40 nurses and 10 nursing technicians and/or nurse aids	The average time they had been employed was 3.66 years. The handling of the medications occurred only at the time of administration. The drugs that were handled the most were cytarabine, cyclophosphamide, etoposide, methotrexate, and ifosfamide. More than 65% of the sample handled the drug at least once a month, 46% had a certificate from the institution for administering chemotherapeutic drugs, and 82% had received training to handle these drugs safely. About 96% of nurses wore a pair of gloves that are resistant to chemotherapeutic drugs when handling them, 49% wore two pairs, and did so often or always, and 51% rarely or never wore two pairs. To remove the plastic in which the medication is placed, 69% reported wearing gloves, 86% usually wore protective gowns, and 18.9% would reuse this equipment. Less than 3% always used all the PPE that exists and is recommended, and 87% washed their hands after contact with the chemotherapeutic drugs. There was no association between the amount of training and the use of PPE. Seven of the 13 samples collected contained chemotherapeutic drugs.
<p>The genotoxic risk in health care workers occupationally exposed to cytotoxic drugs--a comprehensive evaluation by the SCE assay.</p> <p>Kopjar <i>et al.</i>⁹</p>	Journal of Environmental Science and Health Part A	2009	Croatia	To evaluate the frequency of sister chromatid exchange in health care workers who had been exposed to cytotoxic drugs.	A study carried out in health-care workers who had been exposed in 22 hospitals in Croatia. During the regular check-up, during the years from 1997 to 2007, tests were performed on the samples and analyses of sister chromatid exchange (TCI) in circulating lymphocytes. Blood samples were collected, the lymphocytes were cultured and analyzed in accordance with a standard protocol. Exchanges in the middle of the chromosomes, the chromatids, were recorded as 2 events, while the exchanges on the tips were counted as only 1 event.	Nurses and Nursing Technicians (376) Doctors (26) 402 individuals (392 women and 10 men)	Nurses and technicians manipulated 96% of the antineoplastic drugs; only 2% were by pharmacists and the other 2% were by technicians in a pharmacy. Different PPE were used, the most used were gloves. Age, smoking, and being a woman influenced to increase the amount of TCI and high-frequency cells (HFC). Having other types of exposure to carcinogens such as radiation and ultrasound (which could be considered a confounding factor), significantly increased the number of TCI. The duration of exposure to antineoplastic drugs increased TCI and HFC events

IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 4)

Identification of the Article	Periodical	Year	Study Location	Objectives	Methodology	Population	Main Conclusions
Assessment of genotoxic risks in Croatian health care workers occupationally exposed to cytotoxic drugs: a multi-biomarker approach. Kopjar N <i>et al.</i> ¹¹	International Journal of Hygiene and Environmental Health	2009	Croatia	To evaluate the genome damage induced in the lymphocytes of peripheral blood of health care workers who are exposed to cytotoxic drugs	A standardized, socio-cultural questionnaire was applied to know the additional data handling and manipulation of antineoplastic drugs. In groups, 25 smokers and 25 nonsmokers were selected. Blood samples were taken from those in the case study group at their annual check-up, whereas those in the control group donated spontaneously. The samples were treated equally. For assessing damage to DNA, cytogenetic analysis and alkaline comet assay were used. The slides were microscopically analyzed at 250X. Two slides per individual were replicated and analyzed at 50-100 comets. The measurement of the tail length was used to assess DNA damage, as well as the frequency of the nuclei with long tails. There was culture of lymphocytes, an aberration test, and a micronucleus count	100 female volunteers (50 female workers who had been exposed to chemotherapeutic drugs and 50 in the control group, all of whom were matched regarding gender, age and smoking habits)	Regarding the use of PPE, many stated that they only wear gloves (40%) or gloves and other safety devices (60%), gloves, gowns and vertical air flow (38%), gloves and masks (16%) and all of the aforementioned simultaneously (6%). Older nurses were less likely to use PPE. Using PPE greatly reduced the primary DNA damage. In the case group four types of chromosomal aberrations were observed: chromatid breaks, acentric fragments, chromosome breakage and dicentric chromosomes. In the control group, only the first three aberrations were present. Also in the case group, all values except the breakage of chromosomes were statistically higher than in the control group. Among non-smokers, age significantly influenced the DNA damage. In the population that had been exposed, smokers had higher frequencies of sister chromatid exchange and high-frequency cells. There were miscarriages. The study confirmed that handling these drugs without the proper safety precautions provides various genotoxic risks. Cytogenetic vigilance is recommended.

IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 5)

Identification of the Article	Periodical	Year	Study Location	Objectives	Methodology	Population	Main Conclusions
Evaluation of antineoplastic drug exposure of health care workers at three university-based US cancer centers. Cannon <i>et al.</i> ²⁴	JOEM	2010	USA	To evaluate the multiple factors that can result in contamination of the working environment and of workers exposed to a group of antineoplastic drugs.	Inclusion criteria: exposure to antineoplastic drugs for at least six months, and having worked with the handling of chemotherapeutic drugs for at least 24 hours during the week before the evaluation. Unexposed group: individuals with a similar job, but without any contact with antineoplastic drugs. Workers who currently smoked, who had received chemotherapy and/or radiation therapy,	80 nurses; 21 pharmacists; 10 pharmacy technicians; 10 nursing technicians. 68 Cases that had been exposed and that had handled	During the six weeks, 9762 events of handling antineoplastic drugs were reported. Samples of antineoplastic drugs on the floor were probably underestimated, due to the low recovery of those agents. The number of events of handling was linked to the increase of some antineoplastic drugs in the areas investigated. Paclitaxel was the most manipulated antineoplastic, but it was only found in 16% of samples collected. Ifosfamide was the drug with the lowest rate of handling, however it was found in 26% of the

or who were using antineoplastic drugs, and men who had undergone hormone therapy for less than 6 months were excluded from the study. A socio-cultural questionnaire was applied, information on the use of PPE and a daily description of the frequency of handling antineoplastic drugs were also collected. The drug measurement method took into account samples from the surface, location, air samples and the breathing zone of the persons. A measurement was taken of the drugs in the urine of workers and genetic damage biomarkers (comet assay). All the subjects wrote information regarding the handling of antineoplastic drugs in a diary for 6 weeks. The nursing technicians were not included in the individual analyses of handling because it was not possible to measure their exposure to antineoplastic drugs due to the variability of their tasks.

antineoplastic drugs
53 in the control group who had not handled nor had been exposed.

samples. Cyclophosphamide was found in 46% of the cleaning samples. Pharmacy areas showed high levels of contamination, since the nursing areas had low concentrations as compared to the pharmacy area. Most of the air samples showed low concentrations of the drugs, and in the control group most were without any of the agents studied. Only 3 of the urine samples showed the substances that were investigated. The DNA changes were not different for the case group and the control group.

IDENTIFICATION AND DESCRIPTION OF THE MAIN FINDINGS (Part 6)

Identification of the Article	Periodical	Year	Study Location	Objectives	Methodology	Population	Main Conclusions
Assessment of primary, oxidative and excision repaired DNA damage in hospital personnel handling antineoplastic drugs. Villarini M <i>et al.</i> ⁷	Mutagenesis	2011	Itália	To evaluate the contamination of the working environment by antineoplastic drugs in a hospital in Italy, and assess the risks associated with handling these genotoxic drugs	A sociocultural questionnaire was applied. Swabs were used to replace the skin, assessing its exposure to antineoplastic drugs. Each of the workers who had been exposed used 6 swabs, three from the inside of his work clothes, and three from the outside. The model compound (fluorouracil and cytarabine) was determined by using the liquid chromatography method for detecting ultraviolet rays. The actual exposure was assessed by urinary excretion of cyclophosphamide which was determined by gas chromatography/mass spectrometry. The alkaline comet assay measured DNA damage in peripheral blood lymphocytes. The study subjects were genotyped.	52 Cases (6 pharmacy technicians, 16 nurses from the day hospital, 22 nurses from wards and 8 attendants) and 52 controls who were matched as to gender, age and lifestyle.	The prevalence of GSTM1 genotype was 63 individuals. The null count of GSTT1 was 9, whereas of GSTP1 it was 56 subjects, and polymorphism of the TP53 gene was found in 54 participants. Environmental monitoring showed different concentrations of antineoplastic drugs in the locations of administration and preparation, and the latter had the highest concentration of medications. There was contamination in the clothing of the cases. In some urine samples it was possible to detect the markers. There were obvious changes in the genetic material of those who had been exposed. The DNA damage was higher in the nurses who had exposed, as compared to the control group and pharmacists. The use of PPE was associated with a decreased in data of the genetic material.