Cancer and the use of antineoplastic agents

In 2012, over 14 million new cases of cancer were diagnosed worldwide (3). Projections of new cancer rates show further increases in the future: more than 19 million new cases per year are expected by 2025 (3). Given that chemotherapy is one of the principal treatments for a number of cancers, there are global increases in the development and use of antineoplastic agents worldwide.

Antineoplastic agents are drugs used to treat cancer. Also known as chemotherapy drugs or cytotoxic drugs, these agents disrupt the cell cycle and kill cells that are rapidly dividing (e.g. cancer cells). Over 100 different antineoplastic agents are currently available (1). Based on their mechanism of action, these agents are classified into different types. Table 1 shows examples of different types of antineoplastic drugs.

Occupational exposure to antineoplastic agents

Although cancer cells are typically more susceptible to the toxic effects of antineoplastic agents because of their rapid growth, these drugs are non-selective and affect normal cells. Both acute and chronic toxicities of antineoplastic agents are well known for chemotherapy patients receiving large doses of the drugs. However, studies have also shown that negative health effects are associated with workers exposed to antineoplastic agents (5). Because these drugs are designed to block cell growth and division, many antineoplastic agents are carcinogenic (Table 1) and teratogenic, meaning that exposure could cause cancer and affect fetal development (4,5). Toxicities to reproductive and other organ systems are also common among antineoplastic agents (4,5).

Table 1. Examples of different types of antineoplastic agents and their carcinogenicity

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Carcinogenicity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylating agents</td>
<td>Melphalan, Chlorambucil, Cisplatin, Cyclophosphamide</td>
<td>Group 1</td>
</tr>
<tr>
<td>Anti-metabolites</td>
<td>Methotrexate, Thioguanine</td>
<td>Group 2A</td>
</tr>
<tr>
<td>Anti-microtubule agents</td>
<td>Paclitaxel, Vincristine</td>
<td>Group 2B</td>
</tr>
<tr>
<td>Others</td>
<td>Arsenic trioxide, Bleomycin</td>
<td>Group 3</td>
</tr>
<tr>
<td>Topoisomerase inhibitors</td>
<td>Doxorubicin, Etoposide</td>
<td>Not classified</td>
</tr>
</tbody>
</table>

*Based on classification of the International Agency for Research on Cancer (IARC) (2). Group 1: carcinogenic to humans; Group 2A: probably carcinogenic to humans; Group 2B: possibly carcinogenic to humans, Group 3: not classifiable as to its carcinogenicity to humans.
Occupational exposure to antineoplastic agents may occur during the manufacturing, shipping and handling, preparation, administration, and disposal of the drugs (6). Workers who come into contact with body fluids, contaminated clothing, dressings, linens and other materials related to patient chemotherapy are also at risk of exposure. Exposure typically occurs through dermal contact with antineoplastic agents or contaminated materials and surfaces (which may result in exposure via dermal absorption or accidental ingestion from hand-to-mouth contact) or inhalation of contaminated aerosol and particulates. Occasionally, injection exposure may occur through unintentional needle pricks and sharp injuries.

Occupations with potential exposure to antineoplastic agents include: pharmacists and pharmacy assistants, nurses, physicians, veterinarians and veterinarian assistants, environmental service workers (e.g. janitors and caretakers), shippers and receivers, industrial laundry workers, and pharmaceutical manufacturing workers (6, 7).

CAREX Canada estimates that more than 63,000 Canadian workers were exposed to antineoplastic agents (specifically chlorambucil, cisplatin, cyclophosphamide, doxorubicin, and melphalan) in 2006 (Figure 1) (7). Occupational groups with the largest number of workers exposed include pharmacy assistants (21,000 exposed, or 58% of all pharmacy assistants), nurses (19,000 exposed, or 6% of all nurses), and pharmacists (18,500 exposed, or 58% of all pharmacists) (7). Most of the exposed workers were female (79%). Based on the CAREX Canada estimates, pharmacists and pharmacist assistants working in pharmacies in the community were likely to have high or moderate exposure to antineoplastic agents (Figure 2). Other workers in hospital and veterinary settings were likely to have moderate or low exposure. Detailed methods and results of the exposure estimates are available online on the CAREX Canada website (7).

The prevalence and level of exposure to antineoplastic agents may differ across countries and regions with varying exposure-control resources and handling practices.
Levels of exposure

- Low Frequency, Low Control
- High Frequency, Low Control
- Low Frequency, High Control
- High Frequency, High Control

Figure 2. CAREX Canada level of exposure estimate for antineoplastic agents for 2006.

Total Exposed (n)

- High exposure
- Moderate exposure
- Low exposure

Community Pharmacy (Pharmacists, Pharmacy Assistants)
- 30,000a
- 6,800d

Hospital Nurses (Registered Nurses, Practical Nurses)
- 12,500c
- 6,800c

Hospital Pharmacy
- 4,600d

Veterinary (Veterinarians, Veterinary Assistants)
- 3,700a

Hospital Physicians
- 500d

Exposure control

Worker exposure to antineoplastic agents is best controlled using a combination of strategies (4,6):

- Engineering control: devices or workspace designs that physically isolate workers from sources of exposure (e.g. preparing antineoplastic drugs inside a biological safety cabinet).
- Administrative control: work procedures and practices that minimize worker exposure (e.g. wiping all vials and ampoules prior to puncturing and opening).
- Personal protective equipment (PPE): barriers that protect workers from exposure (e.g. gloves and gowns).

In low-resource countries, engineering controls may be too expensive to implement. Greater emphasis is therefore placed on administratie control and proper use of PPE to limit work exposure to antineoplastic drugs. More information on exposure control strategies is available from the US National Institute for Occupational Safety and Health (NIOSH) and Pan America Health Organization (PAHO) publications (4, 6).

References

Prepared by the Occupational Cancer Research Centre and CAREX Canada. Visit our websites:
http://occupationalcancer.ca/
http://www.carexcanada.ca/en/