FACT SHEET

Infectious causes of cancer

KEY MESSAGES

- 3.3% of all cancers in Australia can be attributed to infectious agents.
- Cancers caused by infectious agents are more prevalent in developing regions of the world.
- Infections that cause cancer are common among humans. However, most people’s immune systems will clear these infections. It is chronic infection with viruses, bacteria, and parasites that leads to the development of cancer in a small proportion of the population.
- All cervical cancer, adult T-cell leukaemia/lymphomas, and Kaposi’s sarcomas can be attributed to an infectious agent.
- Effective vaccinations are available for human papillomavirus strains responsible for most of cervical cancer, and the hepatitis B virus.
- Effective antiviral treatments have been developed for hepatitis B virus, human immunodeficiency virus 1, and hepatitis C virus.

Infections and Cancer

In 2008, about 2 million new cases of cancer worldwide were attributed to infections by certain viruses, bacteria, and parasites.\(^1\) This equates to approximately 16% of all cancers worldwide.\(^1\) As can be seen in Table 1, the proportion is higher in developing countries, where 23% of all cancers were attributed to infections, and lower in developed countries, where 7.4% of cancers were attributed to infectious causes.\(^1\) In Australia this proportion was estimated to be even lower, at 3.3% of all cancers.\(^1\)

Table 1: Number of new cancer cases globally in 2008 attributable to infectious agents, by cancer type.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Number of new cancer cases</th>
<th>Number of new cancer cases attributable to infection in less developed regions(^a)</th>
<th>Number of new cancer cases attributable to infection in more developed regions(^b)</th>
<th>PAF(^*) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-cardia gastric</td>
<td>870 000</td>
<td>470 000</td>
<td>180 000</td>
<td>74.4%</td>
</tr>
<tr>
<td>Liver(^b)</td>
<td>750 000</td>
<td>510 000</td>
<td>69 000</td>
<td>76.9%</td>
</tr>
<tr>
<td>Cervix uteri</td>
<td>530 000</td>
<td>450 000</td>
<td>77 000</td>
<td>100.0%</td>
</tr>
<tr>
<td>Vulva</td>
<td>27 000</td>
<td>4 100</td>
<td>7 500</td>
<td>43.0%</td>
</tr>
<tr>
<td>Anus</td>
<td>27 000</td>
<td>12 000</td>
<td>12 000</td>
<td>88.0%</td>
</tr>
<tr>
<td>Penis</td>
<td>22 000</td>
<td>7 600</td>
<td>3 200</td>
<td>50.0%</td>
</tr>
</tbody>
</table>
### Table 1

<table>
<thead>
<tr>
<th>Site</th>
<th>Risk Factors</th>
<th>Number of Annual Deaths</th>
<th>Number of Cases</th>
<th>Number of Deaths</th>
<th>PAF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vagina</strong></td>
<td></td>
<td>13 000</td>
<td>5 700</td>
<td>3 400</td>
<td>70.0%</td>
</tr>
<tr>
<td><strong>Oropharynx</strong></td>
<td></td>
<td>85 000</td>
<td>6 400</td>
<td>15 000</td>
<td>25.6%</td>
</tr>
<tr>
<td><strong>Nasopharynx</strong></td>
<td></td>
<td>84 000</td>
<td>66 000</td>
<td>5 900</td>
<td>85.5%</td>
</tr>
<tr>
<td><strong>Bladder</strong></td>
<td></td>
<td>260 000</td>
<td>6 000</td>
<td>0</td>
<td>2.3%</td>
</tr>
<tr>
<td><strong>Lymphoma and leukaemia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hodgkin’s</td>
<td></td>
<td>68 000</td>
<td>23 000</td>
<td>10 000</td>
<td>49.1%</td>
</tr>
<tr>
<td>Non-Hodgkin’s gastric</td>
<td></td>
<td>18 000</td>
<td>6 500</td>
<td>6 700</td>
<td>74.1%</td>
</tr>
<tr>
<td>Burkitt</td>
<td></td>
<td>11 000</td>
<td>6 300</td>
<td>530</td>
<td>62.5%</td>
</tr>
<tr>
<td>Hepatitis C virus associated non-Hodgkin</td>
<td></td>
<td>360 000</td>
<td>18 000</td>
<td>11 000</td>
<td>8.2%</td>
</tr>
<tr>
<td>Adult T-cell leukemia/lymphoma</td>
<td></td>
<td>2 100</td>
<td>660</td>
<td>1 500</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Kaposi’s sarcoma</strong></td>
<td></td>
<td>43 000</td>
<td>39 000</td>
<td>4 100</td>
<td>100.0%</td>
</tr>
<tr>
<td><strong>Total infectious-disease related sites</strong></td>
<td></td>
<td>3 200 000</td>
<td>1 600 000</td>
<td>410 000</td>
<td>64.4%</td>
</tr>
</tbody>
</table>

*PAF = Population attributable fraction. Estimate of the proportion of cases of cancer that could be avoided if exposure to the infectious agent were modified or removed.

### Table 2

The types of viruses, bacteria and parasites that are linked to cancer are common in the normal healthy population, worldwide. Most people’s immune systems will clear these infections quickly. It is chronic infection with these viruses, bacteria and parasites that leads to cancer development. It is however rare for an infection to develop into cancer. The many ways in which chronic infections lead to cancer are not fully understood. There is evidence to suggest that infections lead to cancer either directly, through accumulation of DNA damage (viral DNA integrating itself into the human DNA) or through chronic inflammation causing cells to rapidly divide. Evidence also suggests that infections can lead to cancer indirectly, through chronic suppression of the immune system, or tissue damage caused by the immune system’s attempts to fight off infection.²⁴ Table 1 also illustrates that for cervical, adult T-cell leukemia/lymphoma, and Kaposi’s sarcoma, all cancers can be attributed to their respective infectious causes. However, for others, such as bladder cancer only a small proportion of cancers are attributed to infectious causes.¹

Table 2 presents the infectious agents that the International Agency for Research on Cancer (IARC) have classified as either carcinogenic (cancer causing) or probably carcinogenic (contributing to cancer development) in humans. IARC is a part of the World Health Organization.

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α Less developed regions = Africa; Caribbean; Central America; South America; Asia excluding Japan; and Oceania excluding Australia and New Zealand.
β More developed regions = Australia and New Zealand; Europe; Japan; and Northern America.
φ Including cholangiocarcinoma.
Source - de Martel et al Lancet Oncology 2012
Organization which convenes international expert working groups to evaluate the evidence of the carcinogenicity of specific exposures.

Table 2: Infectious agents that are carcinogenic or probably carcinogenic to humans

<table>
<thead>
<tr>
<th>Infectious agent</th>
<th>Associated cancers</th>
</tr>
</thead>
</table>
| Epstein-Barr virus | Burkitt lymphoma  
Hodgkin lymphoma  
Non-Hodgkin lymphoma  
Nasopharyngeal carcinoma  
NK/T-cell lymphoma |
| Hepatitis B virus | Hepatocellular carcinoma (a type of liver cancer) |
| Hepatitis C virus | Hepatocellular carcinoma (including cholangiocarcinoma, which is a type of liver cancer)  
Non-Hodgkin lymphoma |
| Human papillomavirus types 16, 18, and others | Anal cancer  
Cervical cancer  
Oral cancer  
Oropharyngeal cancer (cancer of the base of the tongue, tonsils, or upper throat)  
Penile cancer  
Vaginal cancer  
Vulvar cancer |
| Human immunodeficiency virus 1 | Anal cancer  
Cervical cancer  
Conjunctiva cancer (in the eye)  
Hodgkin lymphoma  
Kaposi sarcoma  
Non-Hodgkin lymphoma |
| Human T-cell lymphotropic virus 1 | Adult T-cell leukemia/lymphoma |
| Kaposi sarcoma herpesvirus/ human herpesvirus 8 | Kaposi sarcoma  
Primary effusion lymphoma |
| *Helicobacter pylori* (bacterium) | Non-cardia gastric carcinoma  
B-cell MALT gastric cancer |
| *Opisthorchis viverrini and Clonorchis sinensis* (parasites) | Cholangiocarcinoma |
| *Schistosoma haematobium* (parasite) | Bladder cancer |

Source - IARC Monograph Vol 100B, 2012
The infectious agents responsible for the majority of infection-related cancers are: *Helicobacter pylori (H. pylori)*; cancer-causing strains of the human papillomavirus (HPV); and the hepatitis B and C viruses. These four infectious agents alone cause more than 15% of all cancers globally.²

In addition, Merkel cell polyomavirus (MCV) is a common human tumour virus. MCV is a major risk factor for Merkel cell carcinoma (MCC), a rare but aggressive type of skin cancer, most common in elderly and immune suppressed people. A 2008 study found that MCV causes approximately 80% of MCCs.⁵

**Epstein Barr Virus**

Epstein-Barr Virus (EBV) is most commonly transmitted by oral exposure (for example pre-chewing food for infants or transfer via saliva). Whereas almost every adult has been exposed to EBV at some point in their lives, in very rare circumstances it can cause certain types of lymphoma.⁶ Immuno-suppressed organ transplant patients with EBV infection have an increased risk of developing certain post-transplant lymphomas. EBV is also strongly linked to Burkitt lymphoma, a common childhood cancer in equatorial Africa and Papua New Guinea.⁶ Hodgkin’s lymphoma is associated with EBV worldwide, with EBV genome detected in up to 50% of Hodgkin’s Lymphoma cases in western countries. Nasopharyngeal carcinoma is a type of cancer most common in South East Asia, however all cases worldwide are associated with EBV, suggesting that this virus is key to cancer development.⁶

**Hepatitis B and hepatitis C**

Globally, hepatitis B virus (HBV) is one of the most common infectious viruses. HBV is highly contagious and is transmitted via exposure to infected blood, semen, vaginal fluid and saliva.⁶ Hepatitis C virus (HCV) is transmitted via exposure to blood and blood products.⁶ Infection with HBV and HCV are established risk factors for liver cancer⁶ and these two viral infections cause the majority of cases of liver cancer in Australia. Vaccination against HBV is recommended for all babies and adolescents in Australia,⁷ and for certain high-risk adults, e.g., immigrants from areas with high rates of Hepatitis B, people who have unprotected sex with multiple partners and people who inject drugs who share injecting equipment.⁸ Currently there is no vaccination available for HCV.⁹ Safe and effective anti-viral treatments are available for the control of HBV and HCV have been shown to reduce the risk of developing liver cancer.⁶,¹⁰ HCV treatment is also safe and effective among people who inject drugs,¹¹,¹² and guidelines encourage treatment in this group.¹³-¹⁵ Nevertheless, due to the extended treatment regimens and adverse side-effects, rates of antiviral therapy among this group remain low.¹⁶,¹⁷ Fortunately, safe, well-tolerated and highly effective therapies for HCV infection have become available.¹⁸,¹⁹

**Human papilloma virus**

Human papilloma virus (HPV) is transmitted through skin-to-skin or skin-to-mucosa contact.⁶ HPV is a virus that comprises many types, some of which (the so-called “high risk” types) can lead to cervical cancer. Most people will have HPV at some time in their life but not know. Both men and women are commonly infected with HPV, and inadvertently transmit it to others. The body's immune system usually clears the virus in around 12 months.⁴
Although HPV infection is very common, most women with HPV will not develop cervical cancer. However, when high risk HPV infections (especially types 16 and 18) take longer than usual to clear from the body, they increase the risk of cervical cancer. When cervical cancer occurs, HPV is found in almost all cases. Additionally, HPV types 16 and 18 have been found to cause up to 50 percent of vaginal, vulvar, and penile cancers.

HPV is also associated with anal and other genital cancers. Approximately 85% of anal cancer cases are caused by HPV type 16. More recently, researchers have estimated that HPV type 16 is associated with more than 50% of cases of oropharynx cancer (cancer of the middle part of the throat including the soft palate, the base of the tongue, and the tonsils). The incidence of HPV-associated oropharyngeal cancer has increased over the past 20 years, especially among men; and it is estimated that by the end of the next decade, HPV will cause more oropharyngeal cancers than cervical cancers. Some studies have found that skin cancers in people with weakened immune systems contain HPV, however ongoing research is needed to determine the role of HPV in skin cancers.

The HPV vaccine can prevent more than 70% of infections associated with the development of cervical abnormalities that can progress to cancer. Gardasil is the HPV vaccine used in Australia, whereas Cervaix is another competing HPV vaccine used in the UK. Australia’s National Human Papillomavirus vaccination program began in 2007 to protect young women against HPV infections that can lead to cancer. From 2013, the current school based program for young women aged 12-13 years was extended to males aged 12-13 years, with a catch up program in 2013 and 2014 for males aged 14-15 years.

Human immunodeficiency virus
People who have unprotected sex with multiple partners, people who inject drugs and share injecting equipment, and infants of mothers living with human immunodeficiency virus (HIV) are at increased risk of acquiring HIV. At the early stages of discovery of HIV some people acquired HIV via blood transfusions, before appropriate tests of the blood supply became available. All blood products in Australia are extensively tested for HIV, so the likelihood of acquiring HIV from a blood transfusion in Australia is extremely low. People with HIV and acquired immunodeficiency syndrome (AIDS) have weakened immune systems and are at risk of developing a number of cancers, including Kaposi sarcoma, non-Hodgkin lymphoma, anal cancer, Hodgkin lymphoma, and cervical cancer.

Human T-cell lymphotropic virus 1
Human T-cell lymphotropic virus 1 (HTLV-1) is transmitted via breast feeding, sexual contact, blood transfusions, and the sharing of injecting equipment among people who inject drugs. Regions that have high rates of HTLV-1 include south western Japan, parts of sub-Saharan Africa, the Caribbean Islands, and South America. Infection has also been detected among Australia’s Aboriginal peoples. Found in at least 90 percent of cases of adult T-cell leukemia/lymphomas, HTLV-1 is a diagnostic criterion for this cancer.

Kaposi Sarcoma Associated Herpesvirus
Kaposi Sarcoma Associated Herpesvirus (KSHV), also known as Human Herpesvirus 8 (HHV8) is a common infection, primarily transmitted via saliva. KSHV/HHV8 has been linked to Kaposi Sarcoma, a rare type of cancer in western countries. Only some groups of people
who are immune suppressed (HIV patients, organ transplant patients) are at higher risk of developing Kaposi Sarcoma. KSHV has also been associated with Primary Effusion Lymphoma, a type of blood cancer which is a rare complication occurring mainly among people with HIV.\textsuperscript{6}

*Helicobacter pylori*

*Helicobacter pylori* (*H. pylori*) is a bacterium which was discovered as causing ulcers in the stomach and duodenum (the first section of the small intestine), in Australia in 1982. In 1994, the International Agency for Research on Cancer (IARC) classified chronic infection with *H. pylori* as carcinogenic (cancer causing) to humans. A review of the evidence conducted by IARC in 2012 concluded that chronic infection with *H. pylori* causes stomach cancer and a rare type of lymphoma, low-grade B-cell MALT gastric lymphoma. As with many other infections associated with cancers, *H. pylori* is a common infection in the human population. Symptoms can range from none to serious upper gastric discomfort and ulcers. Cancer only occurs in a small proportion of those people with the bacteria.\textsuperscript{6}

*Opisthorchis viverrine and Clonorchis sinensis (liver flukes)*

A person may become infected by the liver fluke after ingesting raw or undercooked fish. Liver fluke infection occurs frequently in countries whose residents traditionally eat raw/undercooked fish, including Thailand, China, Republic of Korea, Laos and Cambodia. Chronic infection with liver flukes can cause cholangiocarcinoma, a type of liver cancer. Cholangiocarcinoma is a common cancer in those countries that have high rates of chronic liver fluke infection, especially Thailand and the Republic of Korea.\textsuperscript{6}

*Schistosoma haematobium*

*Schistosomes* are parasitic blood dwelling flatworms found mainly in sub-Saharan Africa. *Schistosoma* infections occur after direct contact with fresh water that contain newly hatched *Schistosoma* worms. Chronic infection with *Schistosoma haematobium* (*S. haematobium*) can cause bladder cancer. *S. haematobium* eggs have been found in bladder tumours in 85% of bladder cancer patients in South Africa.\textsuperscript{6}

The following websites are recommended for further information and support:

- National Cancer Institute
- Cancer Research UK
- International Agency for Research on Cancer
- Cancer Council Helpline on (freecall) 13 11 20

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