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### **GENERAL EPIDEMIOLOGY: TESTICULAR CANCER**

Although not common, incidence rates of testicular cancer have been on the rise in the last few decades<sup>1</sup>. In 2021, the American Cancer Society (ACS) estimated 9,470 new cases of testicular cancer will be diagnosed, while 440 people will die from it. The lifetime risk of development is 1 in 250 for men<sup>1</sup>. Testicular cancer is usually treated successfully, leading to a low risk of dying. When testicular cancer is diagnosed at Stage 1, the survival rate is 99% and when diagnosed at Stage 4, it drops to 73%. A man's lifetime risk of dying is 1 in 5,000<sup>1</sup>, leading to a combined 5-year relative survival rate of 95%<sup>2</sup>.

# INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (IARC)

In June 2022, IARC convened an international meeting of scientists to re-evaluate firefighting as an exposure related to cancer. They determined the literature supports reclassifying *firefighting* to a Group 1 carcinogen (carcinogenic to humans) based on "sufficient" evidence<sup>3</sup>. This is the *highest* classification of exposure only assigned when there is scientific certainty.

Their statement indicated:

There was also "strong" mechanistic evidence that occupational exposure as a firefighter shows the following key characteristics of carcinogens in exposed humans: "is genotoxic", "induces epigenetic alterations", "induces oxidative stress", "induces chronic inflammation", and "modulates receptor-mediated effects".

Specific to melanoma, IARC *noted "limited" evidence in humans for testicular cancer as related to firefighting*. While typical use of the word "limited" implies a lack of evidence or support, IARC's classification with the word limited "means that *a positive association has been observed* between exposure to the agent and cancer but that other explanations for the observations (technically termed "chance", "bias", or "confounding") could not be ruled out with reasonable confidence." *It should be noted that IARC criteria and classifications are focused on scientific levels of certainty which are more stringent than those focused on the "weight of the evidence"* which is often used in cases of workers compensation.

### **GENERAL RISK FACTORS FOR TESTICULAR CANCER**

Most cases of testicular cancer were not related to any known risk factors, however, known risk factors include:

- **Age:** Males between the ages of 20 and 34 years of age are at the highest risk, as half of testicular cancer cases occur in that age group<sup>5</sup>.
- Race and ethnicity: The risk of developing testicular cancer is 4 to 5 times greater for Caucasians than African Americans or Asian Americans<sup>5</sup>.
- Body size: Taller men tend to be at slightly higher risk of developing testicular cancer.
- Personal health history: Having an undescended testicle is the main risk factor for developing testicular cancer. Additionally, being infected with the human immunodeficiency virus (HIV) increases risk<sup>5</sup>.
- Family health history: Having a father or brother with testicular cancer raises the risk of developing it as well<sup>5</sup>.

### OCCUPATIONAL EXPOSURES RELATED TO TESTICULAR CANCER

Firefighters are exposed to a broad range of chemicals, both in the firehouse and during emergency response. Recent research conducted with live burns has begun to identify and quantify the presence of carcinogens that are typically present on the fire ground. Most alarming are findings that, even when the air appears "clear" there are often ultra-fine respirable particles and gaseous chemicals of several known carcinogens present. Unfortunately, this time period when there is no visible smoke is typically when firefighters remove their personal protective equipment and self-contained breathing apparatus. Particularly noted in the research is the presence of carcinogens such as perfluorooctanoic and perfluorooctanesulfonic acids (PFOA and PFOS), phthalates, dioxins, benzene, polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), vinyl chloride, and heavy metals<sup>6–13</sup>. Firefighters face several routes of exposure including inhalation, dermal absorption, secondary exposure through contaminated dust from particulates post incident, and potentially the semi-volatile off-gassing of gear. Many of these same chemicals have been implicated in the development of testicular cancer<sup>14,15</sup>.

**Benzene.** Benzene is present as a product of combustion from several standard household materials (e.g. PVC pipe, PVC siding, Christmas trees)<sup>6</sup>, from exposure to diesel exhaust, and has been found to off-gas from firefighters' PPE<sup>10</sup> and is widely recognized as a fire ground risk. Benzene is not only present on the fire ground as a product of combustion, but also at high rates in many fire stations as trucks and ambulances are housed in the bay areas. While efforts are being made to increase the use of exhaust mitigation devices in the firehouse, their introduction and use is relatively new to the fire service. Exposure to benzene has been found to increase testicular cancer risk<sup>15,16</sup>.

**PFOA.** This classification of chemicals is widely used in industrial applications including upholstery, carpeting, firefighting foam and sealants. IARC has identified PFOA as having limited evidence of being linked to the development of testicular cancer<sup>17</sup>.

# **Endocrine Disrupting Chemicals**

The Endocrine Society has released two statements over the past decade outlining what have been identified as endocrine disrupting chemicals. These synthetic chemicals include polychlorinated biphenyls (PCBs), plastics (bisphenol A), plasticizers (phthalates), dioxins, and some metals<sup>18,19</sup>. Evidence suggests that these chemicals disrupt normal hormone functioning and interrupt normal homeostatic control and reproduction, and play a role in the development of testicular cancer<sup>20–22</sup>.

Endocrine disruptors that have also been found to be present as products of combustion on the fire ground include:

- **Dioxins.** Dioxins are a group of chemicals that are present in chlorine containing chemicals and products (e.g. PVC pipes used as building materials). During incineration, dioxins are released. These chemicals have been found as products of combustion on the fire ground<sup>23</sup>, and have been linked to testicular cancer<sup>22</sup>.
- **Polychlorinated biphenyls (PCBs).** PCBs are man-made organic chemicals commonly used as coolants, lubricants in transformers, capacitors, and other electrical equipment.

While the chemicals have been banned since the late 1970s due to evidence that they are a probable human carcinogen, they remain in products manufactured prior to the ban and have been found in the fire environment as a product of combustion<sup>24</sup>. Exposure to PCBs has been linked to an elevated risk of testicular cancer<sup>21</sup>.

### RISK OF TESTICULAR CANCER AMONG FIREFIGHTERS

Lee et al<sup>25</sup>. examined over 100,000 career Florida firefighters over a 34-year period, identifying 3,760 male firefighter primary cancer incidence using the Florida State Fire Marshall's Office and Florida Cancer Data System. After adjusting for age and year of cancer diagnosis, the authors found **male firefighters had a significantly elevated risk of testicular cancer** (aOR = 1.66, 95% CI = 1.34 - 2.06). Data from male firefighters in California found the 3,659 firefighters had a **54% increased risk** of testicular cancer (OR=1.54, 95% CI=1.18-2.02)<sup>26</sup>.

Additional meta-analyses have found continued evidence of a relationship between firefighting and testicular cancer. LeMasters and colleagues<sup>27</sup> found an **increased risk of testicular cancer** (SRE=2.02, 95% Cl=1.30-3.13). A more recent meta-analysis echoed those results as Jalilian and colleagues found firefighters **were at a 34% higher risk of developing testicular cancer** (SIREs=1.34, 95% Cl=1.08-1.68)<sup>28</sup>.

International research found New Zealand firefighters were at a statistically **significant increased risk** for testicular cancer (SIR=3.0, 95% CI=1.30-5.90)<sup>29</sup>. The International Agency for Research on Cancer (IARC) undertook a monograph exploring the risk of cancers among firefighters and reported a standardized incidence ratio of 1.47 (95% CI=1.20-1.80) indicating a **47% increased risk of developing testicular cancer among firefighters**<sup>30</sup>.

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