Understanding the development of cancer for pesticide applicators and handlers

Pam Bryer
Board of Pesticides Control
Maine Department Agriculture, Conservation, & Forestry

Commercial Pesticide Applicator Meeting for Field and Forages
Middlebury American Legion
April 5, 2019
PERSONAL PROTECTIVE EQUIPMENT (PPE)

SAFETY GOGGLES
Protects the eye and surrounding area from water, chemicals or particles.

SAFETY HELMET
Prevents from head injuries due to falling objects and falls.

EAR MUFFS
Noise absorbing pads that protect the ears from excessive noise and foreign objects.

RESPIRATORY MASK
Filters out unwanted particles and limits absorption of pesticide vapours.

SAFETY GLOVES
Protects the hands against pesticide contact and injuries.

LONG SLEEVED SHIRT & PANTS
Acts as protection for the skin from pests, pesticides and injuries.

SAFETY BOOTS
Protects the feet from pesticide spills, falling objects and punctures from below.
Why talk about cancer?

• Cancer is not the only concern with pesticide exposure!

• I’ve been asked to speak about glyphosate recently
  ➢ Highlighted some basic misunderstandings about cancer

• Also, ...
Why talk about cancer?

... because it affects nearly everybody either directly or indirectly

38.4%

Of all men and women in the US will receive a cancer diagnosis at some point in their lives.
In the US, the lifetime risk of developing cancer is 1 in 2 men & 1 in 3 women.

THE OVERALL CANCER DEATH RATE IN THE UNITED STATES FELL 26%}

Note: this is death rate not incidence rate.
1991 → 2015
THE OVERALL CANCER DEATH RATE IN THE UNITED STATES FELL

Note: this is death rate not incidence rate.
NIH’s cancer-causing chemicals in the environment:

- Aflatoxins
- Aristolochic Acids
- Arsenic
- Asbestos
- Benzene
- Benzidine
- Beryllium
- 1,3-Butadiene
- Cadmium
- Coal Tar and Coal-Tar Pitch
- Coke-Oven Emissions
- Crystalline Silica (respirable size)
- Erionite
- Ethylene Oxide
- Formaldehyde
- Hexavalent Chromium Compounds
- Indoor Emissions from the Household Combustion of Coal
- Mineral Oils: Untreated and Mildly Treated
- Nickel Compounds
- Radon
- Secondhand Tobacco Smoke (Environmental Tobacco Smoke)
- Soot
- Strong Inorganic Acid Mists Containing Sulfuric Acid
- Thorium
- Trichloroethylene
- Vinyl Chloride
- Wood Dust
• Constantly exposed to carcinogens in our ideal diet
  • Estimated we consume 1.5 grams of pesticide daily
  • These are naturally occurring plant protectants
  • Only a few (< 100) tested but ~50% of them are mutagens

• Begs the question:
  if we eat this many cancer causing foods,
  how do we not all die of cancer?
• Reality is that our body is full of mechanisms that prevent cancer.
• The development of a metastatic aggressive cancer is the result of failures at multiple levels throughout the development of cancer.
  • It takes many ‘hits’ to set cancer development in motion
• Reality is that our body is full of mechanisms that prevent cancer.
• The development of a metastatic aggressive cancer is the result of failures at multiple levels throughout the development of cancer.
  • It takes many ‘hits’ to set cancer development in motion

➤ This is a reason why applicators are more at risk than the general population. Applicators have repeat exposures over long periods of time.
Mutagens / Carcinogens

- Any substance which increase rate of mutation
- All mutagens are carcinogens.
- Examples are......
  - Radiations like X-ray, UV-ray, gamma ray
  - Chemicals like benzopyrenes, Aflatoxins
  - Hormones like estrogen
Nomenclature of Cancer

Some common carcinomas:
- Lung
- Breast (women)
- Colon
- Bladder
- Prostate (men)

Leukemias:
- Bloodstream

Lymphomas:
- Lymph nodes

Some common sarcomas:
- Fat
- Bone
- Muscle
Tumors are what we typically think of when we think of cancer.

https://www.bu.edu/eng/2013/04/24/computer-simulations-suggest-new-pathways-for-cancer-progression/
Normal: regulated cell growth

Cancer: uncontrolled cell growth
So, on to the details
Loss of Normal Growth Control

Normal cell division

Cell damage—no repair

Cell Suicide or Apoptosis

First mutation

Second mutation

Third mutation

Fourth mutation

Malignant cells tumor growth
Stages of cancer development

• Stage 0 means there's no cancer, only abnormal cells with the potential to become cancer.
• Stage I means the cancer is small and only in one area. This is also called early-stage cancer.
• Stage II and III mean the cancer is larger and has grown into nearby tissues or lymph nodes.
• Stage IV means the cancer has spread to other parts of your body. It's also called advanced or metastatic cancer.
Stages of cancer development

- **Genetically altered epithelial cell**
  - Cell divides more rapidly than normal

- **Hyperplasia**
  - Cells change form

- **Dysplasia**
  - Cells stay in one place

- **In situ cancer**
  - Cancer cells invade normal tissue and enter blood and lymph
  - Metastases form at distant sites

**Blood vessel**
- Direction of flow
- Normal underlying connective or muscle tissue
- Invasion
Etiology of Cancer

- Genetic factors
- Hormonal
- Racial & geographic factors
- Environmental factors
- Chemical factors
- Age
- Sex
Genes involved with cancer

- Oncogenes: genes that promote cancer
- Proto-oncogenes: normal gene before mutations
- Tumor suppressor genes: genes that normally restrain cell growth but can break
- Mutator /DNA repair genes: normally fix broken DNA but can break
Mutations in Tumor Suppressor Genes

1. Normal genes (regulate cell growth)
2. 1st mutation (susceptible carrier)
3. 2nd mutation or loss (leads to cancer)
4. Active oncogene

Tumor suppressor genes

No brakes!

Active oncogene

Cancer
Viruses and Cancer

- Viruses promoting human cancer. These include both DNA viruses and retroviruses, type of RNA viruses.

### Tumor Viruses

<table>
<thead>
<tr>
<th>Virus</th>
<th>Type of Cancer</th>
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<tbody>
<tr>
<td>Epstein-Barr virus</td>
<td>Burkitt’s lymphoma</td>
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<tr>
<td>Human papillomavirus</td>
<td>Cervical cancer</td>
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<td>Hepatitis B virus</td>
<td>Liver cancer</td>
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<tr>
<td>Human T-cell lymphotrophic virus</td>
<td>Adult T-cell leukemia</td>
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<tr>
<td>Kaposi’s sarcoma-associated herpesvirus</td>
<td>Kaposi’s sarcoma</td>
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</tbody>
</table>
Tobacco Use and Cancer
Some Cancer-Causing Chemicals in Tobacco Smoke

- aminostilbene
- arsenic
- benz[a]anthracene
- benz[a]pyrene
- benzene
- benzo[a]fluoranthene
- benzo[a]pyrene
- benzo[e]pyrene
- cadmium
- chrysene
dibenz[a]anthracene
dibenz[a]chrysenene
dibenz[a]pyrene
dibenz[a]pyrenene
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dibenz[a]pyrene
-N,N-dimethylamine
-N,N-dimethylamine
-N,N-dimethylamine
-N,N-dimethylamine
Cancer Arises From DNA Mutations in Cells

Normal cell → DNA mutations → Uncontrolled proliferation

Last DNA mutation from:
- heredity
- radiation or chemicals
- spontaneous errors during DNA duplication
mismatch

Recruitment of MMR proteins

Excision (exonuclease 1)

DNA resynthesis (DNA polymerase III) & ligation (ligase I)
How does EPA classify carcinogenicity of pesticides?

• Carcinogenic to humans.
• Likely to be carcinogenic to humans.
• Suggestive evidence of carcinogenic potential.
• Inadequate information to assess carcinogenic potential.
• Not likely to be carcinogenic to humans.
• Multiple descriptors (differing routes).

(2005)
In our daily lives what causes cancer?
In our daily lives what causes cancer?

• I’m warning you this answer is really boring.
In our daily lives what causes cancer?

• I’m warning you this answer is really boring.

    ---> Do the things your mother told you to do.
For example: breast cancer
How many cancers can be prevented?

All cancers

Together we will beat cancer
# 10 Leading Causes of Death by Age Group, United States – 2016

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<th>Age Groups</th>
<th>Rank</th>
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## 10 Leading Causes of Injury Deaths by Age Group Highlighting Unintentional Injury Deaths, United States – 2016

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Overdose Death Rates Involving Opioids, by Type, United States, 2000-2017

- Any Opioid
- Other Synthetic Opioids (e.g., fentanyl, tramadol)
- Commonly Prescribed Opioids (Natural & Semi-Synthetic Opioids and Methadone)
- Heroin

"You mean pesticides and herbicides aren't the same?"
Please feel free to reach out to me at:

pamela.j.bryer@maine.gov
People also ask

- Is Pesticide a carcinogen?
- What is a carcinogen and list some examples?
- What is a Group 3 carcinogen?
- What can cause cancer list?

Risk Assessment for Carcinogenic Effects | Air: Fate, Exposure ... - EPA
https://www.epa.gov/fera/risk-assessment-carcinogenic-effects
Jan 31, 2017 - EPA has since gained considerable experience in applying cancer risk assessment approaches. Concurrently, the science of risk assessment ...

Evaluating Pesticides for Carcinogenic Potential | Pesticide ... - EPA
A.

B.

**% of comet-positive cells**

**Concentration of chlorpyrifos (μM)**
BIOCHEMICAL CHANGES IN CANCER CELLS AND NORMAL CELLS

CANCER CELLS

- Loss of contact inhibition
- Growing cells forms multilayer
- Increased Synthesis of RNA & DNA
- Decreased catabolism of pyrimidine
- ↑glycolysis leads to lactic acidosis
- Synthesis of fetal protein
- Increase in growth factor secretion
- Increase in oncogene expression
- Loss of tumor suppressor genes

NORMAL CELLS

- Contact inhibition
- Forms single layer
- Synthesis of RNA & DNA is normal.
- catabolism of pyrimidine also normal
- Mostly aerobic glycolysis
- Oncogene expression is rare
- Intermittent or co-ordinated growth factor secretion
- oncogene expression is absent
- Presence of tumor suppressor genes

https://www.slideshare.net/ashoktt/biochemistry-of-cancer-37948337
Pesticides

1. Premutagenic damages: DNA strand breaks, DNA adducts
2. Mutagenic damages (in base pairs)
3. Chromosomal aberrations

- Micronucleus
- Chromosomal break
- Irregular number of homologous chromosomes
- Sister chromatids exchange

- Wrong Base
- DNA single strand break
- DNA double strand break
- DNA adduct

Genetic damages
How does EPA classify carcinogenicity of pesticides?

**Standard EPA classification categorization descriptions**

**Group A: "Human Carcinogen"

"This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer."

**Group B (1 and 2): "Probable Human Carcinogen"

"This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is "limited" and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is "sufficient". The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiological studies. It is reasonable, for practical purposes, to regard an agent for which there is "sufficient evidence of carcinogenicity" in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is "sufficient" evidence from animal studies and for which there is "inadequate evidence" or "no data" from epidemiologic studies would usually be categorized under Group B2."

**Group C: "Possible Human Carcinogen"

"This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-conducted experiment that does not meet conditions for sufficient evidence, (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) responses of marginal statistical significance in a tissue known to have a high or variable background rate."

**Group D: "Not Classifiable as to Human Carcinogenicity"

"This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available."

**Group E: "Evidence of Non-Carcinogenicity for Humans"

"This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies. The designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances."
A common misconception is that all man-made chemicals are harmful, and all natural chemicals are good for us. However, many natural chemicals are just as harmful to human health, if not more so, than man-made chemicals.

"Everything is poison, there is poison in everything. Only the dose makes a thing not a poison."

Paracelsus, 1493-1541, "The Father of Toxicology"