What Is Toxicology? Why Is It Important?

Alexandra Noël, BSc, MSc, PhD
Comparative Biomedical Sciences
School of Veterinary Medicine
Louisiana State University
Overview

• What is toxicology?
• Toxicology in the news
• What do toxicologist do?
• Basic concepts in toxicology—exposure sources
• Basic concepts in toxicology—risk assessment
• Career opportunities in toxicology
• SOT and undergraduate students
What Is Toxicology?

• Toxicology helps create a safer world

• Definition: The study of the adverse effects of chemical, physical, or biological agents on living organisms and the ecosystem, including the prevention and amelioration of such adverse effects.
Toxicology Affects Us Every Day

FDA Issues New Label Changes for Common Antibiotics Based on Toxic Side Effects (abcnews.com, May 12, 2016)

US Companies Replace Teflon Toxin with Chemical Cousin. Is It Safe? (nepr.net, June 9, 2016)

How Tap Water Became Toxic in Flint, Michigan (cnn.com, Jan. 13, 2016)

Study Links Caffeine with Pregnancy Loss (nbcnes.com, Mar. 24, 2016)
• Toxicology is arguably the oldest scientific discipline, as the earliest humans had to recognize which plants were safe to eat.

• Humans are exposed to chemicals both deliberately and inadvertently.

• Most exposure of humans to chemicals is via naturally occurring compounds consumed in the diet from food plants.
Toxicology in the News: Everyday Products

- Reduction of blood lead levels provides economic gains
  - Children in late 1990s had IQs 2.2–4.7 higher than they would have if they had the same blood level as children in the late 1970s
  - Estimated about 2% increase in worker productivity
    *EHP 110(6):563–569*

- Increased blood lead levels of children <6 years old living in Flint, Michigan
  - Children in Flint had blood lead levels ≥ 5 μg/dl
  - Residents advised to use bottled or filtered water
    *MMWR (2016) 65 (25) 650–654*
Toxicology in the News: Everyday Products

• Chemicals are natural, biological, or synthetic in origin
  – Natural (food, metals, minerals)
  – Biological (toxins from bacteria)
  – Synthetic (manufactured through chemical processes)

• Approximately **100,000** chemicals are currently in use worldwide. **500** new formulations enter the marketplace annually.
Toxins and Toxicants

Which of the following statement is TRUE?

A. Natural products are all good, while man-made products are all bad.

B. Natural products are always safer than man-made products.

C. Of the 10 most toxic compounds known, only one is a natural toxin.

D. Any substance can be toxic if present at a specific dose and under specific circumstances.
Toxicology in the News: Food

• Does mercury matter?
  • Fish has health benefits (high protein, low fat, omega-3 fatty acids)
  • Fish contain some mercury, which can bioaccumulate
  • Mercury can lead to neurological deficits

• Bisphenol A (BPA)
  • Used as a sealant in metal cans, some baby bottles, sports bottles, and sippy cups
    • US FDA and the National Toxicology Program have concern about the potential effects of BPA on the brain, behavior, and prostate gland of fetuses, infants, and children
Toxicology in the News: Politics

July 3, 2004 © AP Images/Anatoly Medzyk

Nov. 5, 2004 © AP Images/Sergei Supinksy
Toxicology in the News: Preventative Health

• Thimerosal and Vaccines
  • Two 2004 UK studies found no evidence that thimerosal in vaccines caused neurodevelopmental or psychological problems, nor that early exposure is harmful
  • Cost of discounting the scientific evidence about thimerosal
  • Failure to vaccinate children puts them at risk, and put others at risk
  • Expense for litigation for groups seeking monetary awards for punitive damages

Toxicology in the News: Preventative Health

• Developmental origins of disease
  • Exposure to environmental stressors during development and lead to increased susceptibility to disease/dysfunctions later in life
  • Suggests epigenetic basis for health and disease

*Endocrinology 156(10):3408–3415*
What Do Toxicologists Do?

Many toxicologists work to develop a MECHANISTIC understanding of how chemicals affect living systems

• Develop safer chemical products
• Develop safer drugs and medicines
• Determine risks for chemical exposures
• Develop treatments for chemical exposures
• Ensure a safe food supply
• Forensics
Modern Mechanism-Based Toxicology Developed from Increased Public Awareness of Environmental Toxicology (DDT)

RACHEL CARSON (1907–1964) 

Silent Spring
What Are Major Areas of Specialization in Toxicology?

- Mechanistic toxicology (basic biology and chemistry)
- Descriptive toxicology (testing)
- Regulatory toxicology (rule-making and compliance)
- Risk assessment (modeling)
What Are the Research Tools Used in Toxicology?

• Uses carefully selected models, ethical practices
  • *In vitro* vs. *in vivo*
  • Clinical studies
  • Appropriate model organism (mouse, rat, *C. elegans*)

• Determine toxicological endpoints
Do *in utero* JUUL aerosol exposures aggravate house dust mite–induced *asthma* in adult mice?
Descriptive/Mechanistic Toxicology—An Example
The Science of Toxicology Helps People Make Informed Decisions and Balance RISKS versus BENEFITS
Exposure Sources

- Environmental
- Occupational
- Therapeutic
- Dietary
- Accidental
- Deliberate
Exposure Routes

- The route or site of exposure often determines how much (i.e., the dose) is absorbed
  - Dermal (skin)
  - Inhalation (lung) \{RfC\}
  - Oral (GI) \{RfD\}
  - Injection
- The route of exposure may be important if there are tissue-specific toxic responses
- Toxic effects may be local or systemic
Exposure Routes

What would be an approximate descending order of effectiveness for the routes of exposure?

A. Dermal, inhalation, oral, intravenous.
B. Intravenous, inhalation, oral, dermal.
C. Inhalation, oral, intravenous, dermal.
D. Oral, dermal, intravenous, inhalation.

Other factors to consider:
- “Vehicle” substance in which the agent is dissolved.
- Absorption rate is route dependent.
**Beneficial or Poisonous?**
**What Determines These Factors?**

<table>
<thead>
<tr>
<th></th>
<th>Beneficial Dose</th>
<th>Toxic Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>300 mg–1,000 mg</td>
<td>1,000 mg–30,000 mg</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>5000 Units/Day</td>
<td>50,000 Units/Day</td>
</tr>
<tr>
<td>Oxygen</td>
<td>20% (Air)</td>
<td>50%–80% (Air)</td>
</tr>
</tbody>
</table>
The Key Concept in Toxicology

Father of Modern Toxicology

Paracelsus 1493–1541

“Solely the dose determines that a thing is not a poison.”

All chemicals—synthetic or natural—have the capacity to be toxic
How to Calculate Risk?

Paracelsus Understood Risk Assessment

- Risk = Toxicity x Dose
- Exposure = Dose
- Risk = Toxicity x Exposure
Risk Assessment

Which statement better defines risk assessment?

A. Scientific characterization of potential adverse effects resulting from exposures to hazardous agents or situations.

B. Scientific calculation related to the probability that a random adverse effect will occur.

C. Scientific evaluation of the toxicity of a compound.

D. Scientific analysis of the physical and chemical properties of a compound.
Dose-Response Terminology

- **Dose-Response**: provides a quantitative description of the hazard potential that can be used to assess the concern for effects to people who may be exposed
- **Endpoint**: toxic effect upon which the risk assessment is based
- **Lowest Observed Adverse Effect Level (LOAEL)**: lowest dose from a study at which adverse toxic effects were observed
- **No Observed Adverse Effects Level (NOAEL)**: the dose below the LOAEL at which no adverse toxic effects are observed
- **Point of Departure (POD)**: point on the dose-response curve at or above which a significant biological and/or statistical change in response occurs
Career Opportunities in Toxicology

- Companies
  - Pharmaceutical
  - Agrochemical
  - Consumer Products
- Government
  - Basic Research
  - Develop Regulations
  - Risk Assessment
- Academics
  - Research
  - Teaching
  - Clinical Science
- Diverse Other Possibilities
  - Science Communication
  - Administration
  - Marketing and Sales
Toxicology Employment by Sector

- Industry: 44%
- Academic: 16%
- Consulting: 12%
- Contract Laboratory: 14%
- Government: 11%
- Other: 3%

Pharmaceutical: 66%
Chemical: 11%
Consumer Product: 8%
Food: 3%
Petroleum: 1%
Medical Devices: 6%
Other: 4%

84% have PhDs

10th Toxicology Salary Survey, data from 2017.
Where Do Toxicologists Work?
Salary Range by Degree in Toxicology

10th Toxicology Salary Survey, data from 2017.
Creating a safer and healthier world by advancing the science and increasing the impact of toxicology

www.toxicology.org
SOT Undergraduate Diversity Program

• Here you are!!
• Special program at SOT Annual Meeting
  ▪ Nationally competitive
  ▪ Travel support provided (Saturday–Monday)
  ▪ Three-day program includes:
    o Special toxicology presentations
    o How to prepare for graduate school
    o Time with academic toxicology program directors
    o Mentor circles with SOT toxicologists, postdocs, and graduate students

• Application deadline: October 9 each year
Additional SOT Undergraduate Awards

SOT Undergraduate Research Award
For undergraduate students who have research abstracts accepted for the Annual Meeting
• Travel funding for the full meeting

Perry J. Gehring Diversity Student Travel Award
For Undergraduate Diversity Program alumni who are presenting abstracts at a meeting within four years of participation

Diversity Initiatives Endowment Career Development Award
For undergraduate or graduate student professional development

Regional Chapters, Special Interest Groups, and Specialty Sections
Various awards
SOT Undergraduate Affiliates

• Connect with SOT
• Receive information from SOT
• Participate in the ToXchange network
  ▪ Community of peers
  ▪ Exchange information
Information for Undergraduates

- Career information
- Tips for graduate school
- Travel award programs
- Internships
SOT Pathway into Toxicology Programs

- Undergraduates interested in the Sciences
- Undergraduates aware of toxicology
- Undergrads able to act on awareness by applying for tox activities
- Undergraduates engaged in tox programs such as Internships
- Applicants to Tox Graduate Programs and ongoing relationships facilitated by SOT

Tox Scholar Visits
AM Undergrad Programming
Regional Chapter Meetings
NCABR Network

AM Undergrad Student Affiliate
SOT Undergrad Research Award

Matching Internship funds
Mentoring
Internship Hosts
ToxMSDT

SOT Graduate and Postdoc Activities
Regional Chapter Meetings

• Most SOT Regional Chapters have Fall Meetings
• Many have Poster Sessions including undergraduates
• SOT event calendar provides dates
• Travel funding may be available
• Mentoring and highlight career opportunities
Future SOT Annual Meetings

- 62nd Annual Meeting, March 19–23, 2023
  Nashville, TN
- 63rd Annual Meeting, March 10–14, 2024
  Salt Lake City, UT

Undergraduates receive complimentary registration
Summary

• Toxicology provides an interesting and exciting way to apply science to important problems of social, environmental, and public health significance

• Toxicologists help create a safer world

• Understanding how something produces a toxic effect can lead to new ways of preventing or treating chemically related diseases

• The Society of Toxicology offers networking and engagement in career-building
Questions???

Alexandra Noël, PhD
Email: anoel@lsu.edu