

ENV H 505 A Sp 19: Fundamentals Of Environmental And Occupational Toxicology

[Jump to Today](#)

 [Edit](#)

Syllabus: ENV H 505 – Fundamentals of Environmental and Occupational Toxicology

Spring quarter, 2019; 4 credits

Lectures: Mon Wed Fri, 11:30 - 12:20 am in HSB RR134

Graduate Student Presentations: Tue 1:30 – 2:20 pm in HSB T530

Instructors:

Dr. Terry Kavanagh; email: tjkav@uw.edu (<mailto:tjkav@uw.edu>)

Guest lecturers:

Ms. Rebekah Petroff; email: petroffr@uw.edu (<mailto:petroffr@uw.edu>)

Dr. Julia Cui; email: juliacui@uw.edu (<mailto:juliacui@uw.edu>) (<mailto:juliacui@uw.edu>)

Dr. Lucio Costa; email: lgcosta@uw.edu (<mailto:lgcosta@uw.edu>)

Dr. Marilyn Roberts; email: marilynr@u.washington.edu (<mailto:marilynr@u.washington.edu>)

Dr. David Scoville; email: dkscov@ue.edu (<mailto:dkscov@ue.edu>)

Appointments with Dr. Kavanagh by arrangement only.

Course Description

Basic principles governing the behavior and effects of environmental contaminants on biological systems, including: toxicity testing; disposition of environmental contaminants in the body; modifiers of response; fate and health effects of environmental contaminants, including damage to major organs (liver, gastrointestinal system, kidney, respiratory system, immune system); neurodegenerative diseases, cancer, birth defects; and risk assessment and government regulation of environmental contaminants in the home, the workplace and the general environment. The focus is on human health impacts of environmental contaminants in a public health context. Additional readings and presentations/discussions provide graduate - level coverage of related issues. Designed for non-toxicology majors.

Learning objectives for ENV H 505

The learning objectives for this course are based on fundamental concepts in the science and practice of toxicology. After having taken this course students will be able to:

- Identify significant figures and seminal events important in the history of toxicology, and the professional disciplines, job classifications and scientific fields occupied by toxicologists.
- Explain the principles of dose-response, including quantal vs. continuous measures of response and the descriptors used to define individual susceptibility to environmental contaminants.
- Discuss the different types of testing paradigms used to evaluate the adverse health effects of contaminants, including tests for acute, subacute and chronic toxicity; the various biochemical and molecular assays used to investigate mechanisms by which they cause injury; and the ethical principles surrounding *in vitro* and *in vivo* testing.
- Explain the concepts of absorption, distribution, metabolism and excretion, and their integral roles as determinants of adverse health outcomes.
- Explain the biochemical basis of contaminant biotransformation including the key enzymes systems involved, phases of metabolism, and their consequences for contaminant disposition.
- Discuss the impact of genetic variation, diet, age, gender, and infectious disease status on contaminant disposition and dose-response relationships.
- Discuss the consequences of contaminant exposure for different organs, especially the liver, the kidneys, the brain, the cardiovascular and respiratory systems, and the immune system, and why some contaminants target these organs.
- Identify susceptible periods of embryonic/fetal development that predispose to various kinds of contaminant-induced birth defects, and explain the value of comparative animal approaches for understanding mechanism of action for developmental toxicants.
- Describe the basic processes of chemical carcinogenesis, including initiation, promotion and progression, and the types of contaminant -induced genetic, molecular and cellular changes that lead to cancer.
- Discuss occupational practices and regulations designed to limit exposures and toxicity in the workplace, biomonitoring, and the roles of occupational health professionals in workplace safety.
- Categorize contaminant with respect to chemical class, mode of action, and potency, including pesticides, heavy metals, solvents, gases, halogenated hydrocarbons, polycyclic aromatic hydrocarbons, food additives and contaminants, solvents and vapors, and toxins produced by bacteria, plants and animals.
- Identify contaminants commonly found in the home environment, discuss the design of consumer products that limit contaminant exposures and explain how the Poison Control System works.
- Describe the major sources of pollution in air, water and soil, the contaminants of concern in the environment, and the distribution, fate and ecological effects of various pollutants.
- Integrate the concepts of exposure and hazard as they relate to risk, distinguish between risk assessment scenarios that assume threshold vs. non-threshold responses, and discuss various risk management strategies used to limit contaminant exposures.
- Define the statutory authority governmental agencies use to control contaminant releases to the environment, exposures in the workplace, and clean-up of contaminants; describe the means by which exposure criteria and standards are established, and discuss the economic, political, and ethical dilemmas associated with the regulation of contaminants.
- Lead discussion and effectively interpret and communicate the findings of current research papers in the field.

Required Textbook:

Casarett & Doull's Essentials of Toxicology, 3rd Edition, Curtis D. Klaassen & John B Watkins III, McGraw Hill, 2015

The text is available as an eBook through the UW Libraries. Or go directly to this website:

<http://accesspharmacy.mhmedical.com/book.aspx?bookid=1540>

[\(http://accesspharmacy.mhmedical.com/book.aspx?bookid=1540\)](http://accesspharmacy.mhmedical.com/book.aspx?bookid=1540)

ENVH 505 Website

Canvas Website is:

<https://canvas.uw.edu/courses/1139039>

Prerequisites

Prerequisite: 2 quarters of biology and 2 quarters of chemistry, or permission of instructor.

Grading*

Exam I	25%
Exam II	25%
Exam III	25%
Class Presentation	25%

Exams will be worth a total of 100 points each.

**(There will be an optional comprehensive final exam. Note that if you turn in the final exam, it will replace the lowest score of your previous three exams, even if it is lower! Thus, turn in the final exam only if you feel confident that you did better on it than your previous worst exam).*

Class presentations (25% of grade): Each student, as part of a group, will have the responsibility of presenting/discussing one presentation during the quarter. There will typically be 2-3 students assigned to that week's topic. The presentation will focus upon a current chemical (or group of chemicals) for which there is controversy regarding a major aspect of its human or environmental health risk. See below for suggested topics; however, feel free to suggest other topics of interest. The students have considerable freedom in how they approach the topic. One approach would be for one of the students to provide a 10 to 12 minute introduction to the compound in controversy, including background, sources and magnitude of toxicant exposure, and modes of toxicity. Following the introduction to the compound and topic, student 2 may present an argument supporting that the compound is of low health risk, and a third student provide a case for potentially banning the compound due to an unacceptable level of risk. All students should present a succinct but high-level discussion of these issues based upon the most current scientific literature and allow 5 to 10 minutes for class discussion. The presentation will be evaluated based on the knowledge of the topic and the discussion of points/questions related to journal articles published on this topic. Each presentation will be evaluated by Dr. Kavanagh (or a designated instructor when he is unavailable). Other students in the class are encouraged to submit constructive comments/feedback to Dr. Kavanagh (or the designated instructor) who

will then forward them to the presenters. **Students will be required to e-mail electronic copies of their presentation (generally in MS Power Point or PDF format) to Dr. Kavanagh the evening before the presentation. Similarly, if there is a key paper for discussion the student should send PDF files the evening before to Dr. Kavanagh so that he can copy/provide these before class.** The student presentations should be no more than 35 minutes to allow for class discussion. Dr. Kavanagh and/or Guest Lecturers will foster discussion and provide additional context to the issues raised, as needed. All students should participate in weekly discussions of the presented topics.

It is important when citing scientific papers to critically evaluate the methods used for testing any hypothesis associated with a paper, and to be critical of potential artifacts or shortfalls to the best of your ability. You may want to discuss in detail one or two tables or figures in a paper that you feel are particularly crucial to the topic, but it is not necessary to discuss in detail every table or figure. A list of some current toxicology-oriented journals is provided below.

Some Suggested Topics for ENV H 505:

1. Phthalate ester exposure in utero and developmental outcomes in infants.
2. Bis-phenol A vs. Bis-phenol S: A case of unfortunate substitution?
3. Does Triclosan exposure really lead to diabetes/metabolic syndrome/obesity?
4. Air pollution has been associated with Alzheimer's Disease – what could be the mechanism(s)?
5. Systems/computational toxicology – the use of “Big Data” in toxicological evaluations and risk assessments.
6. Are prescription drugs released into the environment through wastewater treatment plants an ecological and/or human health hazard? Puget Sound as a local issue?
7. The 2016 Frank Lautenberg Act: Chemical Safety for the 21st Century (Amends the Toxic Substances Control **Act**(TSCA); costs/benefits of the precautionary principle.
8. Nanotechnology and health; risk/benefit analyses
9. Genetics and epigenetics in toxicology; transgenerational effects of chemical exposures, etc...
10. The role of the microbiome in toxicology; influences on human and animal xenobiotic metabolism.
11. Organs-On-a-Chip technology and the 3 Rs (replace, reduce, refine) animal use
12. Woodsmoke/wildland fires – occupational and community health effects.
13. Community health effects of farming (especially NH₄ and asthma).

SOME TYPICAL JOURNALS THAT MAY INCLUDE ARTICLES RELEVANT FOR ENVH 505:

Am J Physiol

Am J Pathol

Arch Biochem Biophysics

Arch Environ Contam Toxicol

Arch Toxicol

Aquat Toxicol

Biochem Pharmacol

Biochem Biophys Res Comm

Biochim Biophys Acta

Birth Defects Res A and B

Bull Env Cont Toxicol

Carcinogenesis

Cardiovasc Toxicol

Cancer Research

Cell Biol Toxicol

Chem Res Toxicol

Comp Biochem Physiol C Toxicol Pharmacol

Crit Rev Toxicol

Drug Chem Toxicol

Drug Metab Disp

Ecotoxic Environ Saf

Environ Mol Mutagen

Env Sci Technol

Environ Toxicol Chem

Free Radic Biol Med

Hepatology

Human Exp Toxicol

Immunopharmacol Immunotoxicol

Inhal Toxicol

Int J Toxicol

In Vitr Mol Toxicol

J Anal Toxicol

J Appl Toxicol

J Biochem Mol Toxicol

J Biol Chem

J Environ Pathol Toxicol Oncol

J Pharmacol Exp Therap

Mol Pharmacol

Mutat Res

Nanotoxicology

Part Fibre Toxicol

Pharmacogenetics

Redox Biol

Reprod Toxicol

Toxicol Pathol

Toxicol Sci

Toxicology

Toxicol Appl Pharmacol

Toxicol Ind Health

Toxicol In Vitro

Toxicol Lett

Toxicon

Vet Human Toxicol

Xenobiotica

Note: This list is not meant to be exhaustive and you may find interesting articles in other journals.

Some general literature review guidelines and suggestions

1. Examine papers with the perspective of the level of the current journal, e.g. don't hold a paper in the *Bulletin of Environ Contam* to the same standards as a paper submitted to *Biological Chemistry*.
2. Is the topic of the paper current and relevant to the field of toxicology? Has this work been accomplished elsewhere (i.e. is it original)? This point is critical and may require some diving into the literature to answer the question.
3. Does the paper address a mechanism of toxicity?
4. Is it hypothesis driven? If not, is there an implied hypothesis or an objective stated in the paper early on that is clearly evaluated later in the paper?
5. Are the methods current and appropriate to test the hypotheses /objective(s) presented? Can you suggest better experimental approaches?

6. Do the authors indeed measure what they say they're measuring (e.g. is the sample prep and handling appropriate, are the assays optimized and specific for the endpoints of interest, etc.)? What are the chances that the results obtained are due to artifacts (statistical or otherwise)? Do you "believe" the data?
7. Are the statistical analyses appropriate?
8. Are the figures of high quality? Are there excess figures in the manuscript, i.e., can the data be better presented in a table? Should certain figures or tables be omitted from the manuscript or perhaps placed in supplementary files?
9. Are the references current or out of date?
10. Does the paper make a significant contribution to the field of toxicology?

Course Absence Policies

- It is your responsibility to notify the instructors **by the end of the first week** of any conflicts you may have with the exam schedule.
- There will be no make-up examinations unless approved by the instructor in advance. If a test is missed because of an unexcused absence, it will not be rescheduled. Contact your instructor **prior to or same day** to notify them that you are unable to take the exam.
- Your instructor will then set a date for a makeup exam contingent on the student showing **as soon as possible** a valid medical note issued by a medical professional on the original exam date. For other reasons (car accident, death in the family etc.), arrange to speak with the instructors to explain the circumstances. Within reason we expect to be notified prior to or the day of the exam for such instances.
- If you have any concerns about the class, you may contact Dr. Kavanagh by phone or email to arrange a meeting. If you are still not satisfied with the response that you receive, you may contact the DEOHS Department Chair. You may also contact the Graduate School at G -1 Communications Bldg, by phone at (206) 543-5139 or by email at [raan@uw.edu \(mailto:raan@uw.edu\)](mailto:raan@uw.edu).

The University of Washington and Academic Integrity

All written work you submit will be your own. Plagiarism is a serious offense that will be met with an appropriate penalty and the possibility of disciplinary action. Remember to cite your references and do not paraphrase any references you use for writing assignments. Directly quoting a source is acceptable provided that the source is properly attributed.

The University of Washington expects its students "to maintain the highest standards of academic conduct," as per its Statement of Academic Responsibility. Students who plagiarize are not only jeopardizing their grade and losing the opportunity to really learn, but they also are devaluing the work of their fellow classmates and diminishing the reputation of the University of Washington--which can make your degree less valuable.

University of Washington general policy statement

"Admission to the University carries with it the presumption that students will conduct themselves as responsible members of the academic community. As a condition of enrollment, all students assume responsibility to observe standards of conduct that will contribute to the pursuit of academic goals and to the welfare of the academic community. That responsibility includes but is not limited to: practicing high standards of academic and professional honesty and integrity."

[Reference: <https://www.washington.edu/cssc/for-students/academic-misconduct/>]

For SPH web-resources on understanding and avoiding plagiarism, go to:

<https://sph.washington.edu/sites/default/files/2019-03/AcademicIntegrity.pdf>

Accommodations for Students with Disabilities

Disability Resources for Students (DRS) offers resources and coordinates reasonable accommodations for students with disabilities. Reasonable accommodations are established through an interactive process between you, your instructor(s) and DRS. If you have not yet established services through DRS, but have a temporary or permanent disability that requires accommodations (this can include but not limited to; mental health, attention-related, learning, vision, hearing, physical or health impacts), you are welcome to contact DRS at 206-543-8924 or uwdrs@uw.edu (<mailto:uwdrs@uw.edu>) or disability.uw.edu

Lecture Schedule:

<u>Date</u>	<u>Topic</u>	<u>Reading Assignment</u>
April 1	Introduction/History of Toxicology (Petroff)	Chapter 1
April 2	No Class (Dr. Kavanagh out of town)	
April 3	Basic Principles of Toxicology (Cui)	Chapter 2
April 5	Biological Disposition I-absorption, distribution (Petroff)	Chapters 5 - 7
April 8	Biological Disposition II - biotransformation (Costa)	Chapters 5 - 7
April 9	Topic Assignments for Group Presentations	
April 10	Biological Disposition III - excretion (Kavanagh)	Chapters 5 - 7
April 12	Mechanisms/Factors that Modify Toxic Responses (Kavanagh)	Chapter 3
April 15	Toxicity Testing Procedures (Kavanagh)	Chapter 2
April 16	Group 1 Presentation	

April 17	Toxicity in Liver, Kidney and Immune System (Kavanagh)	Chapters 12, 13 & 14
April 19	Developmental and Reproductive Toxicology (Kavanagh)	Chapters 10, 20 & 21
April 22	Toxicity in the Nervous System (Kavanagh)	Chapter 16
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April 23	Group 2 Presentation	
April 24	Genetic Toxicology (Kavanagh)	Chapter 9
April 26	<i>Exam I (covers material from April 1 through April 22)</i>	
April 29	Basic Processes of Carcinogenesis (Cui)	Chapter 8
April 30	Group 3 Presentation	
May 1	Occupational Toxicology (Petroff)	Chapter 34
May 3	Toxic Metals I (Kavanagh)	Chapter 23
May 6	Toxic metals II (Kavanagh)	Chapter 23
May 7	Group 4 Presentation	
May 8	Drugs as Toxic Substances/Clinical Toxicology (Kavanagh)	Chapter 33
May 10	Microbial toxins I (Roberts)	Chapter 26, Handout
May 13	Ecotoxicology (Kavanagh)	Chapter 30
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May 14	Group 5 Presentation	

May 15	Microbial toxins II (Roberts)	Chapter 26, Handout
May 17	Exam II - (Covers material from April 23 - May 13)	
May 20	Air pollution/respiratory system toxicology (Scoville)	Chapters 15 & 29
May 21	Group 6 Presentation	
May 22	Household Products (Kavanagh)	Handout
May 24	Pesticides I (Kavanagh)	Chapter 22
May 27	Memorial Day – no classes	
May 28	Group 7 Presentation	
May 29	Pesticides II (Kavanagh)	Chapter 22
May 31	Risk Assessment / Risk Management I (Kavanagh)	Chapter 4
June 3	Risk Assessment / Risk Management II (Kavanagh)	Chapter 4
June 4	Group 8 Presentation	
June 5	Regulation of Toxic Chemicals (Kavanagh)	Handout
June 7	Review, summary, course evaluation (Kavanagh)	
June 12	#Exam III – (Covers material from May 15 - June 7), and Optional Final Exam*	

**(There will be an optional comprehensive final exam. Note that if you turn in the final exam, it will replace the lowest score of your previous three exams, even if it is lower! Thus, turn in the final exam only if you feel confident that you did better on it than your previous worst exam).*

#Time for Exam III and Optional Final Exam is Wednesday June 12th from 2:30 – 4:20 am, as determined by UW Spring 2019 Final Exam Schedule

(<http://www.washington.edu/students/reg/S2019exam.html>)

Schedule for Group Presentations

Date	Group#	Suggested Presenters and Topics (TBD)
April 16	1.	Carmona, Conery, Melendez Topic: Animal Testing and Organs-on-a-Chip
April 23	2.	Dostal, Doubleday, Kline Topic: PFOA and PFOS in drinking water
April 30	3.	Hyatt, Kelly Topic: Microbial resistance to antibiotics in wastewater
May 7	4.	Echt, Felder, Ghodsian, Aeluro Topic: 4
May 14	5.	Dickens, Nachtigal Topic: Human microbiome, microbial toxins and mental health disorders
May 21	6.	Pendergrast, Perkins, Philo Topic: Health effects of wildfire smoke
May 28	7.	Taing, Vandergeest, Weber Topic: Chlorpyrifos (CP) - proposed mechanisms of toxicity outside of AChE inhibition/regulatory
June 4	8.	Reimann, Robinson, Tadlock Topic: Risk assessment of PSP from Domoic Acid

Course Summary:

Date	Details
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