

Draft syllabus: ENV H 505 – Fundamentals of Environmental and Occupational Toxicology

Spring quarter, 2016; 4 credits

Lectures: Mon Wed Fri 10:30 - 11:20 am in HST \_\_\_\_\_

Graduate Student Presentations: Tue 12:30 – 1:20 pm in HST \_\_\_\_\_

Instructors: Dr. Terry Kavanagh; email: [tjkav@uw.edu](mailto:tjkav@uw.edu)

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Guest lecturers: Mr. Andrew Yeh; email: [ayeh3@uw.edu](mailto:ayeh3@uw.edu)

Mr. Christopher Schaupp; email: [cschaupp@uw.edu](mailto:cschaupp@uw.edu)

Appointments with Drs. Kavanagh and Gallagher by arrangement only.

**Course Description**

Basic principles governing the behavior and effects of toxic chemicals on biological systems, including: toxicity testing; the disposition of chemicals in the body; modifiers of toxic response; fate and effects of chemicals in the environment; chemicals and cancer; chemicals and birth defects; toxicity risk assessment and government regulation of chemical hazards in the home, the workplace and the general environment. Focus is on human health impacts of chemicals as it relates to public health. Additional readings and presentations/discussions provide graduate - level coverage of public health toxicology. 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 chemical dose-response, including quantal vs. continuous measures of response and the descriptors used to define individual susceptibility to toxicants.
- Discuss the different types of testing paradigms used to evaluate the toxicity of chemicals, including tests for acute, subacute and chronic toxicity; the various biochemical assays used to investigate mechanisms by which chemicals 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 toxicity.
- Explain the biochemical basis of toxicant biotransformation including the key enzymes systems involved, phases of metabolism, and their consequences for toxicant disposition.
- Discuss the impact of genetic variation, diet, age, gender, and infectious disease status on toxicant disposition and dose-response relationships.
- Discuss the consequences of toxicant exposure for different organs, especially the liver, the kidneys, the brain, and the cardiovascular and respiratory systems, and why some toxicants target these organs.
- Identify susceptible periods of embryonic/fetal development that predispose to various kinds of chemically-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 chemically-induced genetic, molecular and cellular changes that lead to cancer.
- Discuss occupational practices and regulations designed to limit chemical exposures and toxicity in the workplace, biomonitoring and the roles of occupational health professionals in workplace safety.
- Categorize toxicants with respect to chemical class, mode of action, and potency, including pesticides, heavy metals, solvents, gases, halogenated hydrocarbons, polycyclic aromatic hydrocarbons, drugs, food additives and contaminants, solvents and vapors, and toxins produced by bacteria, plants and animals.
- Identify toxicants commonly found in the home environment, discuss the design of consumer products that limit chemical exposures and explain how the Poison Control System works.

## **ENVH 505 Spring 2016 (Continued)**

- Describe the major sources of pollution in air, water and soil, the chemicals of concern in the environment, and the distribution, fate and ecological effects of various pollutants.
- Integrate the concepts of chemical 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 toxicant exposures.
- Define the statutory authority governmental agencies use to control toxicant releases to the environment, exposures in the workplace, and clean-up of chemical contamination; describe the means by which exposure criteria and standards are established, and discuss the economic, political, and ethical dilemmas associated with the regulation of toxicants.
- Lead discussion and effectively interpret and communicate the findings of current research papers in the field of toxicology.

### **Required Textbook:**

*Casarett & Doull's Essentials of Toxicology, 2<sup>nd</sup> Edition*, Curtis D. Klaassen & John B Watkins III, McGraw Hill, 2010

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

<http://accesspharmacy.mhmedical.com.offcampus.lib.washington.edu/book.aspx?bookid=449>

### **ENVH 505 Website**

Canvas Website is:

<https://canvas.uw.edu/courses/1040362/>

### **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 public or environmental health risk. The instructor will provide a suggested list of topics during the first class day of the course. 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

## **ENVH 505 Spring 2016 (Continued)**

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 the instructors. Other students in the class are encouraged to submit constructive comments/feedback to the instructors 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 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 the 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 the paper that you feel are particularly crucial to the conclusions of the paper, but is not necessary to discuss in detail every table or figure. A list of some current toxicology journals is provided below.

### **Some Suggested Topics for ENV H 505**

1. Phthalate ester exposure in utero and developmental outcomes in infants.
2. Polybrominated diphenyl ether fire retardants: Should these have been banned given the availability of alternative compounds and their risks?
3. Does Triclosan exposure exacerbate allergies?
4. Should atrazine be banned based upon its endocrine disrupting aspects in the environment or humans?
5. Should we be concerned regarding health effects of residual DDT exposures (or other banned organochlorine pesticides) in the US or developing countries?
6. Are prescription drugs released into the environment through wastewater treatment plants an ecological and/or human health hazard?
7. Toxic Substance Control Act (TSCA) reform by the US Congress; costs/benefits of the precautionary principle
8. Nanotechnology and health; risk/benefit analyses
9. Genetics and epigenetics in toxicology; transgenerational effects of chemical exposures
10. The role of the microbiome in toxicology; influences on human and animal xenobiotic metabolism.

### **SOME TYPICAL JOURNALS THAT MAY INCLUDE ARTICLES RELEVANT FOR ENV H 505**

*Am J Physiol*

*Am J Pathol*

*Arch Biochem Biophys*

*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*

## **ENVH 505 Spring 2016 (Continued)**

*Env Sci Technol*  
*Environ Toxicol Chem*  
*Free Radic Biol Med*  
*Hepatology*  
*Human Exp Toxicol*  
*Immunopharmacol Immunotoxicol*  
*Inhal Toxicol*  
*Int J Toxicol*  
*In Vitro 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. Review the paper 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 *J. 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 the paper clearly written, well organized and presented? Does it need re-editing?
5. 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?
6. Are the methods current and appropriate to test the hypotheses /objective(s) presented? Can you suggest better experimental approaches?
7. 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?
8. Are the statistical analyses appropriate?
9. Are the results presented in a clear and concise manner?
10. Is the discussion section appropriate to the strength of results, or is there too much conjecture?
11. 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?
12. Are the references current or out of date?
13. Does the paper make a significant contribution to the field of toxicology?

### **Course Absence Policies**

## **ENVH 505 Spring 2016 (Continued)**

- 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 instructors **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 will expect to be notified prior to or the day of the exam for these 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 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).

### **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.

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: WAC 478-120-020 Standards of Conduct

(2a),<http://www.washington.edu/students/handbook/conduct.html#020>]

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

<http://courses.washington.edu/hsstudev/studev/plagiarism.htm>

### **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](http://disability.uw.edu)

## ENVH 505 Spring 2016 (Continued)

### Lecture Schedule:

<u>Date</u>	<u>Topic</u>	<u>Reading Assignment</u>
March 28	Introduction/History of Toxicology (Kavanagh)	Chapter 1
<b>March 29</b>	<b>Topic Assignments for Group Presentations</b>	
March 30	Basic Principles of Toxicology (Gallagher)	Chapter 2
April 1	Biological Disposition I-absorption, distribution (Gallagher)	Chapters 5 - 7
April 4	Biological Disposition II - excretion (Kavanagh)	Chapters 5 - 7
<b>April 5</b>	<b>Group 1 Presentation</b>	
April 6	Biological Disposition III - biotransformation (Gallagher)	Chapters 5 - 7
April 8	Factors that Modify Toxic Responses (Kavanagh)	Chapter 3
April 11	Testing Procedures/Types and Routes of Exposure (Yeh)	Chapter 2
<b>April 12</b>	<b>Group 2 Presentation</b>	
April 13	Toxicity in the Liver and Kidney (Kavanagh)	Chapters 13 & 14
April 15	Developmental and Reproductive Toxicology (Kavanagh)	Chapters 10, 20 & 21
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April 18	Toxicity in the Nervous System (Kavanagh)	Chapter 16
<b>April 19</b>	<b>Group 3 Presentation</b>	
April 20	Basic Processes of Carcinogenesis (Gallagher)	Chapter 8
<b><u>April 22</u></b>	<b><i>Exam I (covers material through April 15)</i></b>	
April 25	Genetic Toxicology (Kavanagh)	Chapter 9
<b>April 26</b>	<b>Group 4 Presentation</b>	
April 27	Toxic metals 1 (Kavanagh)	Chapter 23
April 29	Toxic Metals II (Kavanagh)	Chapter 23
May 2	Industrial Chemicals; Occupational Toxicology (Kavanagh)	Chapters 24 & 33
<b>May 3</b>	<b>Group 5 Presentation</b>	
May 4	Household Products (Gallagher)	Handout
May 6	Drugs as Toxic Substances/Clinical Toxicology (Schaupp)	Chapter 32

## ENVH 505 Spring 2016 (Continued)

May 9	Air pollution /respiratory system toxicology (Kavanagh)	Chapters 15 & 28
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**May 10**      **Group 6 Presentation**

May 11	Ecotoxicology (Gallagher)	Chapter 29
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**May 13**      *Exam II - (Covers material from April 18 through May 9)*

May 16	Pesticides I (Gallagher)	Chapter 22
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**May 17**      **Group 7 Presentation**

May 18	Pesticides II (Gallagher)	Chapter 22
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May 20	Natural Toxins (Yeh)	Chapters 26 & 27
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May 23	Food Additives & Contaminants (Kavanagh)	Chapter 30
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**May 24**      **Group 8 Presentation**

May 25	Regulation of Toxic Chemicals (Kavanagh)	Handout
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May 27	Risk Assessment / Risk Management I (Kavanagh)	Chapter 4
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**May 30**      **Memorial Day**

**May 31**      **Group 8 Presentation**

June 1	Risk Assessment / Risk Management II (Gallagher)	Chapter 4
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June 3	Review, summary, course evaluation (Schaupp)	
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**June 6**      *#Exam III – (Covers material from May 11 through June 3), 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 Monday June 6<sup>th</sup> from 8:30 – 10:20 am, as determined by UW Spring 2016 Final Exam Schedule (<http://www.washington.edu/students/reg/S2016exam.html>)**

## **ENVH 505 Spring 2016 (Continued)**

### **Schedule for Presentations**

<b>Date</b>	<b>Group#</b>	<b>Presenters/Topic</b>
April 5	1.	SB, MB Topic: Organophosphorus insecticides
April 12	2.	MD, AD Topic: Tox21 - Toxicology Testing in the 21st Century
April 19	3.	DD, KD Topic: Flint H2O Crisis
April 26	4.	SH, CH Topic: PCBs in the Duwamish
May 3	5.	SK, CM, MN Topic: Hazards of Silica Exposure in the Workplace
May 10	6.	EN, AO Topic: Genetic Predisposition to Doxorubicin-induced Cardiomyopathy
May 17	7.	BR, DR Topic: Bisphenol-A vs. Bisphenol-S
May 24	8.	FR, JS Topic: Ecological Effects of Pharmaceuticals in Wastewater
May 31	9.	RS, EZ Topic: Occupational Hazards in Nail Salons