Environmental Exposure Assessment: ENVR 640

Fall semester, 2016. (3 credit hours)
Tuesday/Thursday 11:00 – 12:15 pm

Instructor: Joachim D. Pleil, Ph.D. U.S. EPA

Prerequisites: permission of instructor for non-majors; familiarity with MS-Excel and basic statistical concepts (descriptive statistics, graphs, distributions, etc.). It is expected that students have access to the UNC on-line library system.

Basic concepts: Accurate and complete exposure data provide the independent variables against which adverse health outcomes are measured. Time trends in exposure measures provide the means to test the effect of implemented prevention strategies. Regrettably, the development of such data is also considered the most difficult and most often overlooked component of environmental health research. Furthermore, exposure assessment often does not provide relevant toxicological data. This class will provide the tools for turning exposure assessment into exposure science.

The course material introduces the general concepts of assessing environmental exposures to chemicals in human populations. The underlying concepts are put into context with respect to occupational exposures from which much of environmental study is derived. This includes the design of ecologic and personal monitoring studies, the techniques and equipment used for sampling and analysis, and interpretation of data. The linkages among external concentrations, spatial and temporal parameters, exposure pathways (ingestion, inhalation, and dermal contact), internal dose, and biomarker expression are developed within the context of environmental exposure and risk assessment. Lectures include examples from actual EPA studies to illustrate the utility of exposure measurements in the broader public health framework.

Course description: This course is intended to develop an understanding and appreciation of environmental exposure assessment and its role in providing the tools and information for toxicology, epidemiology, and risk management. The target audience includes ENVR and EPID MS and PhD graduate students, as well as students pursuing MPH, MSPH, and other public health, medical, or health related graduate degrees. In addition to the sampling, analytical, and mathematical fundamentals, the lectures incorporate real-world examples drawn from the instructor's 25^{+} years of experience in exposure methods development in the National Exposure Research Laboratory of U.S. Environmental Protection Agency. The statistical concepts are limited to calculations that can be performed on standard spreadsheet software (e.g. Excel).

The textbook is "***Exposure Assessment in Occupational and Environmental Epidemiology***" by M.J. Nieuwenhuijsen. Additional readings will be assigned from the peer reviewed literature to serve as a basis for discussions. There will be one "take home" mid-term exam and one "take home" final exam that will provide 40% of the grade (each), the remaining 20% will be based on class participation and weekly homework assignments.

All work is expected to be independent; there are no group efforts or collaborations allowed. Class attendance and participation are highly recommended for successful performance because tests will rely heavily on concepts developed during lectures. I will use Blackboard to provide all class documents and lectures. There will be some guest lectures to address specific contemporary subjects.

Class lecture topics: The following is list that is subject to change to accommodate potential guest lectures, current environmental events, and late breaking exposure assessment research. If logistics permit, we will have two field trips, one to the EPA Human Studies Facility on campus, the other to the EPA research campus at RTP, NC.

1 Overview – class and air pollution.

2 Introduction to exposure assessment class: logistics, expectations, tests, attendance, homework, grades; exposure linkages, swing diagram, environmental media, sampling, analysis, classes of stressors, exogenous compounds, biomarkers

3 Occupational and environmental exposures: air, water, soil, food, dust, radiation. Differences among single component, aggregate, and cumulative exposure assessments.

4 Measurements and models: differences and complementary issues in exposure assessments – use of biomarkers

5 Discuss concepts of exposure, susceptibility, and disease relationships; environmental influences, stochastic events, rare events, association vs cause/effect, effect of politics, costs, public alarm.

5 Air sampling: methods for volatile organic compounds (VOCs), environmental effects – carcinogenicity, acute effects, latency, influence on secondary pollutants, EPA studies. Methods for aerosols and particulates, PM10 and PM2.5 FRMs, AQS data base, inorganic and organic constituents.

7 Sample preparation - matrices, storage/integrity, handling, safety, interferences and trace analysis, internal standards; assign readings in analytical methods.

8 Analysis 1: instrumentation for organics - GC-MS, LC-MS; applications to various analytes – focus on volatile organic compounds (VOCs) and polycyclic aromatic hydrocarbons (PAHs)

9 Analysis 2: sensitivity, specificity, LOQ, LOD, QA, calibration, regression curves, confidence bands, internal/external standards. Assign readings in factor analysis/PCA.

10 Data interpretation: discuss patterns, source apportionment, surrogates, internal standards, cumulative effects, congeners.

11 Data reduction 1: use of replicates, independence, repeat measures, normal distributions, log transforms. Introduce summary statistics concepts - 95%CI, mean, median, fold ratio. Assign exercise in frequency distributions.

12 Data reduction 2: discuss frequency distribution exercise - log vs normal space: geometric mean, geometric standard deviation. Assign WTC readings.

13 Midterm exam assigned; review and discussion

14 Midterm exam help session - general explanations and discussions

15 Midterm exam turned in beginning of class. Discuss WTC exposures, occupational vs environmental, acute vs long term, health effects: IUGR, pulmonary, long term risks.

16 WTC exposures source apportionment: PAHs, dioxins, PM, dusts; residual contamination, risk assessment, public perception, stake holders.

17 Midterm exam debriefing. Introduction to biomarker measurements - general discussion of blood, breath, urine, measurements. Systems biology and exposure to health linkage.

18 Exposure and effects markers, exposure timing, biological damping, proteins, adducts, chemical biomarkers, metabolites. Biomarker sampling and analyses - native compounds, phase-1 metabolites, non-invasive and invasive, small detailed study vs. population based study, IRBs.

19 Breath sampling and analysis: clinical and environmental applications. Collection, processing, GC-MS analysis, data interpretation, examples.

20 Blood and urine sampling and analysis: clinical and environmental applications. Collection, processing, GC-MS analysis, LC-MS, data interpretation, examples.

21 Overview of modeling: classical pharmacokinetic models - examples from chamber studies, contrast to PBPK models.

22 Introduction to PBPK modeling: relationships between animal and humans, differences among exposure routes, target organ dose, parameter estimation, sensitivity analysis.

23 Exposure reconstruction from PK and PBPK models; application to susceptible sub-populations, incremental risk assessment calculations, Cumulative exposure: endogenous biomarkers, medical test analogs.

24 Tour of EPA Human Studies facility (on campus). Visit environmental exposure chambers.

25 Application example: Evidentiary breath analyzers – possibility of false positives from environmental pollutants when tested for driving under the influence of alcohol.

26 Cumulative review. Assign Final exam – 1 week duration

27 Final exam help session - general explanations and discussions

28 Test due at beginning of class. General discussions about exposure assessment, questions about career opportunities, EPA research, linkage of exposure assessment to other epidemiology, ENVR, and toxicology classes. Class evaluations.

29 Review Test questions: Final discussions and questions.

Additional Contemporary Topics:

- Human inflammatory response (cytokines) from air pollutants
- Toxicity testing – high throughput applications and adverse outcome pathways
- Linkage of *in vivo* and *in vitro* testing in exposure diagnosis
- Brain chemistry pathways activation by exogenous chemicals
- Human systems interface: Root cause analysis of F-22 Raptor hypoxic incidents
- NASA: artificial atmosphere management (CO_2, O_2), microgravity fire-fighting technology, and environmental chemical instrumentation for space-flight
- Liver steatosis: exogenous chemical effects on human homeostasis
- Pragmatic statistics tools: Intra-Class Correlation (ICC), QQ-plots, left-censored data imputation, heatmap visualization
- High-resolution mass spectrometry: non-targeted (discovery) analysis of complex biological fluids (blood, breath, urine)