

Syllabus Module 234

N°	Titre
Coordinator	Aurore Gely-Pernot and Robert Barouki
Dates	January 14 th to 18 th 2019
Credits/ECTS	3 ECTS
Duration	5 days of 6 hours face to face, and personal or group work (estimation 30h)
Location	Université Paris Descartes, Inserm unit 1124, 45 rue des Saints Pères, Paris , room 473, 4 th floor
Description	The toxicity of chemicals or of other environmental stressors is highly dependent on exposure conditions and on the particular vulnerability of the exposed individual or group of persons. The module will address these issues with some emphasis on vulnerability during development and growth and on occupational exposures. The module is essentially multidisciplinary with epidemiological, toxicological and social sciences perspectives. The following items will be discussed: importance of windows of exposure to carcinogens or reprotoxic agents during pregnancy, in early life and at the workplace; vulnerability of children to physical agents; transgenerational epigenetic effects both in experimental animals and in humans; examples of gene-environment interaction and mechanistic basis of vulnerability, notably during development
Prerequisites	Basic knowledge on biological mechanisms of disease and molecular biology. Such background is provided in the M1 EOHS modules (for example module 118).
Course learning objectives	<ul style="list-style-type: none"> • Describe the hypothesis of the developmental origin of adult health and disease (DOHaD) • Identify the role of parental exposure at work or in the general environment in developmental toxicity Describe gene-environment interactions in fetal development and disease
Structure (details of sessions title/speaker/date /duration)	<ul style="list-style-type: none"> - Toxicological basis of vulnerability. Xavier Coumoul - Environmental exposure and genetic susceptibility in Parkinson Disease. Alexis Elbaz - Epigenetics in Health and Disease. Jonathan Weitzman - Gene-environment interaction in fetal development and disease. Michel Vekemans - Children exposure to electromagnetic waves. Joe Wiart - Social vulnerability. Yorghos Remvikos - Is adulthood fertility affected by prenatal or childhood exposure to environmental hazards? Epidemiological and toxicological evidence. Aurore Gely-Pernot - Reprotoxic agents at the workplace or as drugs. Paper discussion. Aurore Gely-Pernot - Developmental vulnerability to neurotoxicity. Philippe Grandjean -'Precautionary assessment of critical windows'. Philippe Grandjean -Use of Databases for Chemical Safety Assessment and Prediction of Potential Endocrine Disruptors. Thomas Darde
Resources	Books All readings and materials will be posted on REAL. Readings are available below for each session. Website, online library
Course requirement	Students are expected to attend all lectures and seminars. Class attendance will be checked accordingly. Students are expected to read and analyse selected papers for the group work before the courses.
Grading and assessment	1) Group work : paper will be read, Presentation made by groups (30% of final grade)

	<p>2) On table test of 2 hours: scientific paper reading and answers to a set of questions (critical analysis of the study design, writing of the hidden summary...). Grade on 20 at least equal to 10</p> <p>Note also that students will complete a questionnaire that assesses their own and their teammates' contributions to group work. All team members will receive the same grade except if it is clear that a student has not participated effectively (attended and contributed to meetings; made timely, helpful contributions; been constructive, etc.). In that case, the student's grade will be lowered accordingly.</p>
<p>Course policy</p>	<p>Attendance & punctuality Regular and punctual class attendance is a prerequisite for receiving credit in a course. Students are expected to attend each class. Attendance will be taken at each class. The obligations of attendance and punctuality cover every aspect of the course: - lectures, conferences, group projects, assessments, examinations, as described in EHESP Academic Regulations http://mph.ehesp.fr EHESP Academic Regulation Article. 3). If students are not able to make it to class, they are required to send an email to the instructor and to the MPH program coordinating team explaining their absence prior to the scheduled class date. All supporting documents are provided to the end-of-year panel.</p> <p>Students who miss class are responsible for content. Any student who misses a class has the responsibility for obtaining copies of notes, handouts and assignments. If additional assistance is still necessary, an appointment should be scheduled with the instructor. Class time is not to be used to go over material with students who have missed class.</p> <p>Lateness: Students who are more than 10 minutes late may be denied access to a class. Repeated late arrivals may be counted as absences (See http://mph.ehesp.fr EHESP Academic Regulation Article. 3 Attendance & Punctuality)</p> <p>Maximum absences authorized & penalty otherwise Above 20% of absences will be designated a fail for a given class. The students will be entitled to be reassessed in any failed component(s). If they undertake a reassessment or they retake a module this means that they cannot normally obtain more than the minimum pass mark (i.e. 10 out of 20)</p> <p>Exceptional circumstances Absence from any examination or test, or late submission of assignments due to illness, psychological problems, or exceptional personal reasons must be justified; otherwise, students will be penalized, as above mentioned. Students must directly notify their professor or the MPH academic secretariat before the exam or before the assignment deadline. Before accepting the student's justification, the professor or the MPH academic secretariat has the right to request either a certificate from the attending physician or from a psychologist, or from any other relevant person (See http://mph.ehesp.fr EHESP Academic Regulation Article 4 Examinations).</p> <p>Courtesy: <u>All cell phones/pages MUST be turned off during class time.</u> Students are required to conduct themselves according to professional standards, eating during class time is not permitted during class time, such as course or group work.</p>
<p>Valuing diversity</p>	<p>Diversity enriches learning. It requires an atmosphere of inclusion and tolerance, which oftentimes challenges our own closely-held ideas, as well as our personal comfort zones. The results, however, create a sense of community and promote excellence in the learning environment. This class will follow principles of inclusion, respect, tolerance, and acceptance that support the values of diversity. Diversity includes consideration of: (1) life experiences, including type, variety, uniqueness, duration, personal values, political viewpoints, and intensity; and (2) factors related to "diversity of presence," including, among others, age, economic circumstances, ethnic identification, family educational attainment, disability, gender, geographic origin, maturity, race, religion, sexual orientation and social position.</p>
<p>Course evaluation</p>	<p>EHESP requests that you complete a course evaluation at the end of the school year. Your</p>

	responses will be anonymous, with feedback provided in the aggregate. Open-ended comments will be shared with instructors, but not identified with individual students. Your participation in course evaluation is an expectation, since providing constructive feedback is a professional obligation. Feedback is critical, moreover, to improving the quality of our courses, as well as for instructor assessment.
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Session 1	Toxicological and critical windows
Speakers	Xavier Coumoul and Philippe Granjean
Session Outline	The first course will focus on some basic concept of toxicology and give some examples of vulnerable states of exposition. We will see the case of dioxin and polycyclic aromatic hydrocarbon (gene/environment interaction and developmental disruption) and the case of alcohol (genetic and epigenetic mechanism). The second course will focus on the precautionary assessment of critical windows.
Learning Objectives	<ul style="list-style-type: none"> - Introduce the module - Understand some basic concept of toxicology - Understand the notion on “windows of vulnerability” - Indicate precautionary assessment of critical windows
Duration	5,5 hours
Training methods	Lecture and Case Study
Reading	<p>-EEA. Science and the Precautionary Principle, 2013 (www.eea.europa.eu)</p> <p>-Grandjean P. Science for precautionary decision-making. In: Late Lessons from Early Warnings, volume II. European Environment Agency, 2013, pp. 517-35.</p> <p>-Grandjean P. Seven deadly sins of environmental epidemiology and the virtues of precaution. <i>Epidemiology</i> 2008; 19: 158-62.</p>

Session 2	Epigenetics in Health and Disease
Speakers	Jonathan Weitzman and Aurore Gely-Pernot
Session Outline	Courses will focus in a first time on the history and the basic concept of genetic and epigenetic. Students will see here the different kinds of epigenetics modifications, how epigenetics marks can affect gene expression and finally the link between epigenetic and disease. A specific focus will be done on how endocrine disruptors can affect the next generation after exposition (transgenerational impact).
Learning Objectives	<ul style="list-style-type: none"> - Understand the concept of epigenetic - Understand how environment can affect next generation
Duration	7 Hours
Training methods	Lecture
Reading	<p>-Environmentally induced epigenetic transgenerational inheritance of male infertility. <i>Curr Opin Genet Dev.</i> 2014 Jun;26:79-88. doi: 10.1016/j.gde.2014.06.005. Epub 2014 Aug 11</p> <p>Guerrero-Bosagna C¹, Skinner MK².</p> <p>-Epigenetic transgenerational actions of endocrine disruptors and male fertility. <i>Science.</i> 2005 Jun 3;308(5727):1466-9. Anway MD¹, Cupp AS, Uzumcu M, Skinner MK</p>

	<p>-Alterations in the developing testis transcriptome following embryonic vinclozolin exposure. <i>Reprod Toxicol.</i> 2010 Nov;30(3):353-64. doi: 10.1016/j.reprotox.2010.05.086. Epub 2010 Jun 8. Clement TM¹, Savenkova MI, Settles M, Anway MD, Skinner MK.</p> <p>- Epigenetic modulators, modifiers and mediators in cancer aetiology and progression. <i>Nat Rev Genet.</i> 2016 May;17(5):284-99. doi: 10.1038/nrg.2016.13. Epub 2016 Mar 14. Feinberg AP¹, Koldobskiy MA¹, Göndör A².</p>
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Session 3	Windows of vulnerability of reproduction biology
Speakers	Aurore Gely-Pernot
Session Outline	This course will focus on how prenatal or childhood exposure can affect fertility using toxicological et epidemiological evidence. First, we will see why fetal and childhood period are consider as period of vulnerability and some example of the effect of some pesticides (atrazine, chlordecone) or some drug on genital tracts development and fertility.
Learning Objectives	<ul style="list-style-type: none"> - Understand how adult fertility can be affect by pre-pubertal exposure - Work on scientific paper to see some specific case and to prepare exam of the module
Duration	6 hours
Training methods	Lecture and group word on article
Reading	Paper will be send and have to be read before course

Session 4	Children exposure to electromagnetic waves
Speakers	Joe Wiart
Session Outline	The aim of this course is to give some concepts to appreciate the exposition to electromagnetic waves and wireless technologies. It will focus on human exposition and absorption of electromagnetic wave, the protection limits and the exposure assessment. A specific focus will be done on children exposition during childhood or development.
Learning Objectives	<ul style="list-style-type: none"> - Understand how we can be exposed to electromagnetic waves - Understand how and why this exposition have to be take into account in public health
Duration	2,5 hours
Training methods	Lecture and Case Study
Reading	<p>-Wiart, J. (2016) Stochastic Dosimetry, in <i>Radio-Frequency Human Exposure Assessment</i>, John Wiley & Sons, Inc., Hoboken, NJ, USA. doi: 10.1002/9781119285137.ch3 Liorni, M Parazzini, N Varsier, A Hadjem, P Ravazzani and J Wiart</p> <p>-Exposure assessment of one-year-old child to 3G tablet in uplink mode and to 3G femtocell in downlink mode using polynomial chaos decomposition <i>Phy Med Bio</i> 2016 S Dahdouh, N Varsier, M. Ochoa, J Wiart, A Peyman, I Bloch</p> <p>-Infants and young children modeling method for numerical dosimetry studies: application to plane wave exposure <i>Physics in medicine and biology</i> 61 (4), 1500 (2016)</p> <p>- Analysis of RF exposure in the head tissues of children and adults J Wiart, A Hadjem, M F Wong and I Bloch, 2008 <i>Physics in Medicine and Biology</i>, Volume 53, Number 13</p>

Session 5	Environmental exposures and neurotoxicity
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Speakers	Alexis Elbaz and Philippe Grandjean
Session Outline	The presentation of Alexi Elbaz will provides an update on the epidemiology of Parkinson's disease, with a focus on the interplay between environmental factors and genetic susceptibility. The lecture of Philippe Grandjean will show how developmental vulnerability can induce neurotoxicity.
Learning Objectives	-understand how environmental factors during development can generate disease after birth - discuss issues related to epidemiologic studies of ageing-related disorders with a long prodromal phase.
Duration	5 hours
Training methods	Lecture
Readings	-Only One Chance: How Environmental Pollution Impairs Brain Development — and How to Protect the Brains of the Next Generation, Philippe Grandjean -Environmental risk factors and Parkinson's disease: An umbrella review of meta-analyses. Vanessa Bellou et al., 2016. -Epidemiology of Parkinson's disease. Alexis Elbaz et al, 2016.

Session 6	Social-economical vulnerability
Speakers	Yorghos Remvikos
Session Outline	The course will focus on the social determinants of health, the socio-economic environment and health outcome... Social vulnerability: Facts, mechanisms and consequences for action In Public Health vulnerability considerations tend to focus on differential sensitivity or susceptibility to a given physical exposure, typically to toxic substances. In this course we shall try to go beyond physiologically-based vulnerability and explore whether social factors, such as poverty, deprivation, or more generally low social status, that are generally acknowledged as confounding factors in epidemiological studies, could in fact be construed as causes of loss of health and, under which conditions.
Learning Objectives	We shall try to go beyond the evidence of the existence of social inequalities of health, by proposing models and mechanisms about how our social experience can impact health status, through a process of embodiment, i.e. the psychosocial connection. A sociological interpretative model of the social determinants of health will also be presented, thus uncovering new areas and means of intervention, for a more equitable health approach.
Duration	3 hours
Training methods	Lecture
Reading	

Session 7	Wokshop on databases use in toxicology
Speakers	Thomas Darde

Session Outline	<p>Use of Databases for Chemical Safety Assessment and Prediction of Potential Endocrine Disruptors</p> <p>The multidisciplinary nature of toxicology involves a wide variety of types of data, which are typically dispersed in numerous distinct databases. Over recent years new tools and repositories have therefore emerged with the aim of centralizing heterogeneous information on chemicals and their respective toxicity. Such structuring is indeed essential to improve interpretation and make full use of available data. It is also a compulsory prerequisite to predictive toxicology, i.e. to alternative methods that integrate existing knowledge in order to predict toxicity and prioritize chemicals for further testing.</p>
Learning Objectives	<p>The purpose of this workshop will be to learn how to navigate through relevant databases and collect useful information for predictive toxicology purposes. We will further discuss the benefits and goals of such approaches, and we will illustrate these by a case study for the identification of new endocrine disruptors.</p>
Duration	5,5 hours
Training methods	Lab work
Reading	