

Syllabus Module 234

N°234	Critical windows of exposures and vulnerability
Coordinator	Aurore Gely-Pernot and Robert Barouki
Dates	December 13 th to December 17 th 2021
Credits/ECTS	3 ECTS
Duration	5 days of 6 hours face to face, and personal or group work (estimation 30h)
Location	EHESP 20 Avenue George Sand 93210 LA PLAINE ST DENIS
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
Contributes to the development of the following competences	Competences : Uses vital statistics and health indicators effectively to increase knowledge and generate evidence about population health, including within at-risk and vulnerable groups
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. Aurore Gely-Pernot - 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 -Prenatal exposure to mixture of xenobiotics: challenges and perspectives to identify the chemical exposome and its effect on the development. Arthur David
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.

<p>Grading and assessment</p>	<p>1) Group work : paper will be read, Presentation made by groups (30% of final grade)</p> <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>

Course evaluation	EHESP requests that you complete a course evaluation at the end of the school year. Your 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	<ul style="list-style-type: none"> -EEA. Science and the Precautionary Principle, 2013 (www.eea.europa.eu) -Grandjean P. Science for precautionary decision-making. In: Late Lessons from Early Warnings, volume II. European Environment Agency, 2013, pp. 517-35. -Grandjean P. Seven deadly sins of environmental epidemiology and the virtues of precaution. <i>Epidemiology</i> 2008; 19: 158-62.

Session 2	Epigenetics in Health and Disease
Speakers	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	3 Hours
Training methods	Lecture
Reading	<ul style="list-style-type: none"> -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 Guerrero-Bosagna C¹, Skinner MK². -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 -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.

	- Epigenetic modulators, modifiers and mediators in cancer aetiology and progression. Nat Rev Genet. 2016 May;17(5):284-99. doi: 10.1038/nrg.2016.13. Epub 2016 Mar 14. Feinberg AP ¹ , Koldobskiy MA ¹ , Góndör A ² .
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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	7 hours
Training methods	Lecture and group word on article
Reading	Paper will be send and have to be read before course

Session 4	Environmental exposures and neurotoxicity
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	<ul style="list-style-type: none"> -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	6 hours
Training methods	Lecture
Readings	<p>-Only One Chance: How Environmental Pollution Impairs Brain Development — and How to Protect the Brains of the Next Generation, Philippe Grandjean</p> <p>-Environmental risk factors and Parkinson's disease: An umbrella review of meta-analyses. Vanessa Bellou et al., 2016.</p> <p>-Epidemiology of Parkinson's disease. Alexis Elbaz et al, 2016.</p>

Session 5	Social-economical vulnerability
Speakers	Yorghos Remvikos

Session Outline	<p>The course will focus on the social determinants of health, the socio-economic environment and health outcome...</p> <p>Social vulnerability: Facts, mechanisms and consequences for action</p> <p>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.</p>
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 6	Prenatal exposure to mixture of xenobiotics: challenges and perspectives to identify the chemical exposome and its effect on the development
Speakers	Arthur David
Session Outline	The concept of exposome will first be presented and then discussed to explain how it can be applied to study exposure to complex xenobiotic mixtures during the prenatal period. The lecture will then focus on the omics approach and in particular on metabolomics to explain how this technique can be used to improve exposure assessment and at the same study biological changes at a comprehensive level. Finally, challenges that we are currently facing to apply metabolomics in a high-throughput manner at the population level will be discussed.
Learning Objectives	<ul style="list-style-type: none"> - Understand the concept of "chemical exposome" - Understand how the omics approach can be used to characterize the exposure and study associated health effects
Duration	3 Hours
Training methods	Lecture
Reading	<ul style="list-style-type: none"> - Dennis KK, Marder E, Balshaw DM, Cui Y, Lynes MA, Patti GJ, Rappaport SM, Shaughnessy DT, Vrijheid M, Barr DB, 2017. Biomonitoring in the Era of the Exposome. Environ Health Perspect; 125: 502-510. 10.1289/EHP474 - Rappaport SM, 2011. Implications of the exposome for exposure science. J Expo Sci Environ Epidemiol; 21: 5-9. 10.1038/jes.2010.50 - Rappaport SM, Barupal DK, Wishart D, Vineis P, Scalbert A, 2014. The blood exposome and its role in discovering causes of disease. Environ Health Perspect; 122: 769-74. 10.1289/ehp.1308015 - Wild CP, 2005. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol Biomarkers Prev; 14: 1847-50. 10.1158/1055-9965.EPI-05-0456