

Syllabus Module 234

N°234	Critical windows of exposures and vulnerability
Coordinator	Aurore Gely-Pernot
Dates	October 24 th to October 28 th 2022
Credits/ECTS	3 ECTS
Duration	5 days of 6 hours face to face, and group work (estimation 30h)
Location	EHESP Paris
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. As common thread, we will approach the question of endocrine disruptors (EDs). We will see how some population are vulnerable to these compounds and why it is important to consider it. The regulation, the management and the risk assessment of endocrine disruptors will be also discuss.
Prerequisites	Basic knowledge on biological mechanisms of disease. 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 vulnerable population to environmental exposure • Knows and where needed applies the International Health Regulations to coordinate and develop strategic partnerships and resources in key sectors and disciplines for health security purposes • Identifies and describes the environmental determinants of health and the connections between environmental protection and public health policy • Critically analyses the take into account EDs at the local and international level
Structure (details of sessions title/speaker/date /duration)	<ul style="list-style-type: none"> - Prenatal exposure to mixture of xenobiotics: challenges and perspectives to identify the chemical exposome and its effect on the development. Arthur David - Toxicological basis of vulnerability. Xavier Coumoul - Reprotoxicity and transgenerational effect. Aurore Gely-Pernot - Developmental vulnerability to neurotoxicity. Philippe Grandjean - Social vulnerability. Yorghos Remvikos - Management of the issue of endocrine disruptors by public institutions. Annabelle Demy - Risk assessment of EDs. ANSES
Resources	<p>Books</p> <p>All readings and materials will be posted on REAL. Readings are available below for each session. Website, online library</p>
Course requirement	<p>Students are expected to attend all lectures and seminars. Class attendance will be checked accordingly.</p> <p>Students are expected to read and analyse selected papers for the group work before the courses.</p>
Grading and assessment	<ol style="list-style-type: none"> 1) Group work : paper will be read, Presentation made by groups (30% of final grade) 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>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</p>

	<p>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 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.</p>

Session 1	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.
Competency	<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. <i>Environ Health Perspect</i>; 125: 502-510. 10.1289/EHP474 - Rappaport SM, 2011. Implications of the exposome for exposure science. <i>J Expo Sci Environ Epidemiol</i>; 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. <i>Environ Health Perspect</i>; 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. <i>Cancer Epidemiol Biomarkers Prev</i>; 14: 1847-50. 10.1158/1055-9965.EPI-05-0456

Session 2	How chemicals including EDs affect health
Speakers	Xavier Coumoul, Philippe Grandjean and Aurore Gely-Pernot
Session Outline	<p>Xavier Coumoul 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).</p> <p>The lecture of Philippe Grandjean will show how developmental vulnerability can induce neurotoxicity.</p> <p>This course of Aurore Gely-Pernot will focus on how prenatal or childhood exposure can affect fertility using toxicological et epidemiological evidence. A specific focus will be done on how endocrine disruptors can affect the next generation after exposition (transgenerational impact).</p>
Competency	Analyze sources, pathways, and routes of exposure to these environmental and occupational hazards and safety, and determine the populations with a high risk of exposure
Duration	9 hours (Lecture) and Group works
Training methods	Lecture and Case Study
Reading	<ul style="list-style-type: none"> -Only One Chance: How Environmental Pollution Impairs Brain Development — and How to Protect the Brains of the Next Generation, Philippe Grandjean -The epigenetic impacts of endocrine disruptors on female reproduction across generations, <i>Biology of Reproduction</i>, 2019, 101(3), 635–644Saniya Rattan and Jodi A. Flaws. -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 MK.

Session 3	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>
Competency	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	2 hours (Lecture)
Training methods	Lecture and discussion
Reading	

Session 4	Management of the issue of endocrine disruptors by public institutions
Speakers	Anabelle Demy
Session Outline	This session aims to give a global understanding of the regulation of endocrine disruptors in the European Union (EU) today. After a brief history of how endocrine disruptors have come to be considered by the regulatory authorities of the United States, the EU and international organizations like the WHO and the OECD from the 1990s onwards, we will focus on the different European sectoral regulations dealing with endocrine disrupting chemicals and the actors involved to implement those.
Competency	<ul style="list-style-type: none"> -Critically analyses the take into account EDs at the local and international level -Knows and where needed applies the International Health Regulations to coordinate and develop strategic partnerships and resources in key sectors and disciplines for health security purposes
Duration	3 hours (Lecture) and Group work
Training methods	Lecture, Group work and Questions & Answers sessions
Reading	

Session 5	Risk assessment of EDs
Speakers	ANSES
Session Outline	
Learning Objectives	Identifies the connections between environmental protection and public health policy
Duration	3 hours
Training methods	Lecture
Readings	