Environmental Health Sciences 214
Winter Quarter 2018
Children's environmental health: prenatal and postnatal
Instructor: Michael Collins (CHS 71-297; mdc@ucla.edu)

The goal of this course will be to examine how environmental exposures to chemical, physical and biological agents during the period of maturation (from fertilization to adulthood) cause pathophysiological perturbations in homeostasis at any stage during life.

Lectures 1 and 2: Organism Development
-The environment as a determinant of phenotype: developmental plasticity
-How agents in the environment effect molecular changes in development
-Epigenetics
-Embryonic defenses: survival in a hostile world.

Learning objectives (LO):

LO 1: To gain an appreciation for the importance of the environment in determining phenotype via the presentation of examples from the biological kingdoms.

LO 2: To enumerate and discuss the relevance of various biological protection mechanisms for minimizing environmental impacts on developing organisms.

References:

Arias AM, Nichols J, Schroter C. 2013. A molecular basis for developmental plasticity in early mammalian embryos. Development 140(17): 3499-3510.

Bahari-Javan S, Varbanov H, Halder R, …… Sananbenesi F, Fischer A. HDAC1 links early life stress to schizophrenia-like phenotypes. Proc. Natl. Acad. Sci. USA 114(23): E4686-E4694 (2017).

Feil R, Fraga MF. 2012. Epigenetics and the environment: emerging patterns and implications. Nat. Rev. Genet. 13(2): 97-109.

Gilbert SF, Bosch TCG, Ledòn-Rettig C. 2015. Eco-evo-devo: developmental symbiosis and developmental plasticity as evolutionary agents. Nat. Rev. Genet. 16(10): 611-622.

Gilbert SF, Bosch TCG, Ledón-Rettig C. Eco-evo-devo: developmental symbiosis and developmental plasticity as evolutionary agents. Nat. Rev. Genet. 16: 611-622 (2015).

Hashimoto H, Zhang X, Vertino PM, Cheng X. 2015. The mechanisms of generation, recognition, and erasure of DNA 5-methylcytosine and thymine oxidations. J. Biol. Chem. 290(34): 20723-20733.

Heard E, Martienssen RA. 2014. Transgenerational epigenetic inheritance: myths and mechanisms. Cell 157(1): 95-109.

Kaelin WG Jr, McKnight SL. 2013. Influence of metabolism on epigenetics and disease. Cell 153(1): 56-69.

Peña CJ, Kronman HG, Walker DM, ……, Shen L, Nestler EJ. Early life stress confers lifelong stress susceptibility in mice via ventral tegmental area OTX2. Science 356: 1185-1188 (2017).

Perino M, Veenstra GJC. Chromatin control of developmental dynamics and plasticity. Dev. Cell 38: 610-620 (2016).

Siklenka K, Erkek S, Godmann M ……. Peters AHFM, Kimmins S. 2015. Disruption of histone methylation in developing sperm impairs offspring health transgenerationally. Science 350(6261): pii aab2006 1-12.

Stavrou S, Nicolaides NC, Critselis E, ……., Chrousos GP. Pediatric stress: from neuroendocrinology to contemporary disorders. Eur. J. Clin. Invest. 47(3): 262-269 (2017).

Lectures 3, 4, 5: Teratogenesis and related developmental outcomes (stillbirths/fetal deaths, spontaneous abortions, fetal growth retardation, functional deficits, prematurity)

-Aspects of gestational embryology
-Specific chemical teratogens: cyclopamine, retinoids, thalidomide, TCDD, ethanol, mercury
-Radiation as a physical teratogenic agent -Infectious agents as teratogens
-Maternal conditions in teratogenesis
-Behavioral teratogenesis
-Male-mediated teratogenesis
-Antagonism of teratogenesis by folates

LO 3: To evaluate Wilson's principles of teratology from a modern context.

LO 4: To provide examples of each of the major categories of human teratogens and the extent of mechanistic understanding of how these agents cause dysmorphogenesis.

LO 5: To scientifically assess the role of folic acid in antagonism of teratogenesis.

LO 6: To enumerate the principles of behavioral teratology as differentiated from classical teratology.

LO 7: Be able to describe how genes and the environment may interact to induce congenital malformations.

LO 8: Conceptualize the similarities and differences between neoplasia and embryogenesis.

References:

Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J. 2014. The placenta harbors a unique microbiome. Science Transl Med 6(237): 1-11.

Adibi JJ, Marques Jr. ETA, Cartus A, Beigi RH. 2016 (Mar 4). Teratogenic effects of the Zika virus and the role of the placenta. Lancet [Epub].

Hachisuga M, Oki S, Kitajima K …….. Wake N, Meno C. Hyperglycemia impairs left-right axis formation and thereby disturbs heart morphogenesis in mouse embryos. Proc. Natl. Acad. Sci. USA 112(38): E5300-E5307.

Ito T, Handa H. 2012. Deciphering the mystery of thalidomide teratogenicity. Cong Anom 52: 1-7.

Morishita H, Arora M. 2017. Tooth-matrix biomarkers to reconstruct critical periods of brain plasticity. Trends Neurosci 40(1): 1-3

Padmanabhan N, Jia D, Geary-Joo C, Wu X, Ferguson-Smith AC et al. 2013. Mutation in folate metabolism causes epigenetic instability and transgenerational effects on development. Cell 155(1): 81-93.

Rydeen A, Voisin N, D'Aniello, Ravisankar P, Devignes C-S, Waxman JS. 2015. Excessive feedback of Cyp26a1 promotes cell non-autonomous loss of retinoic acid signaling. Dev. Biol. 405: 47-55.

Shi H, Enriquez A, Rapadas M, ……., Dunwoodie SL. NAD deficiency, congenital malformations, and niacin supplementation. N. Eng. J. Med. 377(6): 544-552 (2017).

Sparrow DB, Chapman G, Smith AJ, Mattar MZ, Major JA, O'Reilly VC et al. 2012. A mechanism for gene-environment interaction in the etiology of congenital scoliosis. Cell 149(2): 295-306.

Tang H, Hammack C, Ogden SC …… Jin P, Song H, Ming G-l. 2016. Zika virus infects human cortical neural progenitors and attenuates their growth. Cell Stem Cell [Eub]

Vargesson N. 2015. Thalidomide-induced teratogenesis: history and mechanisms. Birth Defects Res C Embryo Today 105(2): 140-156.

Wallingford JB, Niswander LA, Shaw GM, Finnell RH. 2013. The continuing challenge of understanding, preventing, and treating neural tube defects. Science 339(6123): 1222002.

Wang F, Wu Y, Quon MJ, Li X, Yang P. 2015. ASK1 mediates the teratogenicity of diabetes in the developing heart by inducing ER stress and inhibiting critical factors essential for cardiac development. Am. J. Physiol Endocrinol. Metab. 309: E487-E499.

Wilde JJ, Petersen JR, Niswander L. 2014. Genetic, epigenetic, and environmental contributions to neural tube closure. Annu. Rev. Genet. 48: 583-611.

Yang P, Li X, Xu C, Eckert RL, Reece EA, Zielke HR, Wang F. 2013. Maternal hyperglycemia activates an ASK1-FoxO3a-Caspase 8 pathway that leads to embryonic neural tube defects. Sci Signal 6(290): ra74.

Yoon K-J, Song G, Qian X, …….., Zhu H, Song H, Ming GI. Zika-virus-encoded NS2A disrupts mammalian cortical neurogenesis by degrading adherans junction proteins. Cell Stem Cell 21: 349-358 (2017).

Zalc A, Rattenbach R, Auradé F, Cadot B, Relaix F. 2015. Pax3 and Pax7 play essential safeguard functions against environmental stress-induced birth defects. Dev Cell 33(1): 56-66.

Lectures 6, 7, 8: Developmental (fetal) basis of adult disease:

-Barker hypothesis
-Endpoints associated with fetal exposures
-Transplacental carcinogenesis
-Mechanisms of imprinted fetal perturbations

LO 9: To know what the Barker Hypothesis states and to have a conceptual understanding of the ramifications of the Hypothesis.

LO 10: To conceptualize the role of epigenetics in the fetal basis of adult disease.

LO 11: To be able to describe potential mechanisms of human pathogenesis induced during the fetal period. Have an awareness that the concept of mechanism is a continually evolving concept.

References:

Burton GJ, Fowden AL, Thornburg KL. Placental origins of chronic disease. Physiol. Rev. 96: 1509-1565 (2016).

Entringer S, Buss C, Wadhwa PD. 2012. Prenatal stress, telomere biology, and fetal programming of health and disease risk. Sci Signal 5(248): pt12.

Funkhouser LJ, Bordenstein SR. 2013. Mom knows best: the universality of maternal microbial transmission. PLoS Biol. 11(8): e1001631.

Kappil M, Wright RO, Sanders AP. Developmental origins of common disease: Epigenetic contributions to obesity. Annu. Rev. Genomics Hum. Genet. 17: 177-192 (2016).

Martinez D, Pentinat T, Ribó S, Daviaud C, Bloks VW et al. 2014. In utero undernutrition in male mice programs liver lipid metabolism in the second-generation offspring involving altered Lxra DNA methylation. Cell Metabolism 19: 941-951.

Öst A, Lempradl A, Casas E, Weigert M, Tiko T et al. 2014. Paternal diet defines offspring chromatin state and intergenerational obesity. Cell 159(6): 1352-1364.

Additional Fetal basis of adult disease references:

de la Torre-Ubieta L, Stein JL, Won H, Opland KG, ….. Geschwind DH. The dynamic landscape of open chromatin during human cortical neurogenesis. Cell 172: 289-304 (2018).

Lecoutre S, Pourpe C, Butruille L, Marousez L, Laborie C, Guinez C, Lesage J, Vieau D, Eeckhoute J, Gabory A, Oger F, Eberlé D, Breton C. Reduced PPARγ2 expression in adipose tissue of male rat offspring from obese dams is associated with epigenetic modifications. FASEB J. 2018 Jan 2. pii: fj.201700997R. doi: 10.1096/fj.201700997R

Thomas JD, Sznajder ŁJ, Bardhi O, Aslam FN, Anastasiadis ZP, Scotti MM, Nishino I, Nakamori M, Wang ET, Swanson MS. Disrupted prenatal RNA processing and myogenesis in congenital myotonic dystrophy. Genes Dev. 2017 Jun 1;31(11):1122-1133. doi: 10.1101/gad.300590.117. Epub 2017 Jul 11.

Madeen EP, Löhr CV, You H, Siddens LK, Krueger SK, Dashwood RH, Gonzalez FJ, Baird WM, Ho E, Bramer L, Waters KM, Williams DE. Dibenzo[def,p]chrysene

transplacental carcinogenesis in wild-type, Cyp1b1 knockout and CYP1B1 humanized mice. Mol Carcinog. 2017 Jan;56(1):163-171

Hanson MA, Gluckman PD. Early developmental conditioning of later health and disease: Physiology or pathophysiology. Physiol. Rev. 94: 1027-1076 (2014).

Mericq V, Martinez-Aguayo A, Uauy R, ……. Van der Steen M, Hokken-Koelega. Long-term metabolic risk among children born premature or small for gestational age. Nat. Rev. Endocrinol. 13(1): 50-62 (2017).

Sferruzzi-Perri AN, López-Tello J, Fowden AL, Constancia M. Maternal and fetal genomes interplay through phosphoinositol 3-kinase(PI3K)-p110 signaling to modify placental resource allocation. Proc. Natl. Acad. Sci. USA 113(40): 11255-11260 (2016).

Sieber MH, Thomsen MB, Spradling AC. Electron transport chain remodeling by GSK3 during oogenesis connects nutrient state to reproduction. Cell 164: 420-432 (2016).

Torii M, Sasaki M, Chang Y-W, Ishii S, ……., Hashimoto-Torii K. Detection of vulnerable neurons damaged by environmental insults in utero. Proc. Natl. Acad. Sci. USA 114(9): 2367-2372 (2017).

Todd N, Valleron A-J, Bougnères P. Prenatal loss of father during World War One is predictive of a reduced lifespan in adulthood. Proc. Natl. Acad. Sci. USA 114(16): 4201-4206 (2017).

Lin Q, Ponnusamy R, Widagdo J, …….., Ye K, Sun YE. MicroRNA-mediated disruption of dendritogenesis during a critical period of development influences cognitive capacity later in life. Proc. Natl. Acad. Sci. USA 114(34): 9188-9193 (2017).

Chawanthayatham S, Thiantanawat A, Egner PA, ……, Croy RG, Essigmann JM. Prenatal exposure of mice to the human liver carcinogen aflatoxin B_1 reveals a critical window of susceptibility to genetic change. Int. J. Cancer 136: 1254-1262 (2015).

Gilman SE, Hornig M, Ghassabian A, ……., Buka SL, Goldstein JM. Socioeconomic disadvantage, gestational immune activity, and neurodevelopment in early childhood. Proc. Natl. Acad. Sci. USA 114(25): 6728-6733 (2017).

Vallaster MP, Kukreja S, Bing XY, …….., Tapper AR, Rando OJ. Paternal nicotine exposure alters hepatic xenobiotic metabolism in offspring. eLife 6: e24771 (2017).

McDade TW, Ryan C, Jones MJ, ……., Kobor MS, Kuzawa CW. Social and physical environments early in development predict DNA methylation of inflammatory genes in young adulthood. Proc. Natl. Acad. Sci. USA 114(29): 7611-7616 (2017).

Veiga-Lopez A, Moeller J, Sreedharan R, ……., Pease A, Padmanabhan V. Developmental programming: interaction between prenatal BPA exposure and postnatal

adiposity on metabolic variables in female sheep. Am. J. Physiol. Endocrinol. Metab. 310: E238-E247 (2016).

Wyrwoll CS, Noble J, Thomson A, …….., Chapman KE, Holmes MC. Pravastatin ameliorates placental vascular defects, fetal growth, and cardiac function in a model of glucocorticoid excess. Proc. Natl. Acad. Sci. USA 113(22): 6265-6270 (2016).

Rogers JA, Mishra MK, Hahn J, ……., Metz LM, Yong VW. Gestational bisphenol-A exposure lowers the threshold for autoimmunity in a model of multiple sclerosis. Proc. Natl. Acad. Sci. USA 114(19): 4999-5004 (2017).

Baker TR, King-Heiden TC, Peterson RE, Heideman W. Dioxin induction of transgenerational inheritance of disease in zebrafish. Mol. Cell. Endocrinol. 398: 36-41 (2014).

Marchetto NM, Glynn RA, Ferry ML, Ostojic M, Wolff SM, Yao R, Haussmann MF. Prenatal stress and newborn telomere length. Am J Obstet Gynecol. 2016 Jul;215(1):94.e1-8

Lecture 9: The dynamic developmental physiology of infants and children as differentiated from adults

-Analysis of how various physiological parameters differ between children and adults and the impact of developmental dynamics on processes relevant to chemical exposures.

LO 12: To enumerate ways in which children physiologically and behaviorally differ from adults and to assess how the differences manifest as differential susceptibility to environmental factors.

LO 13: To conceptualize the differences between childhood and adult cancers, including how sequencing information contributes to an understanding of the differences.

LO 14: To have familiarity with the underlying assumptions for applying a lifestage approach to hazard and dose-response characterization.

References:

Charmandari E, Achermann JC, Carel J-C, Soder O, Chrousos GP. 2012. Stress response and child health. Science Signaling 5(248): 1-6.

Landrigan PJ, Miodovnik A. 2011. Children's health and the environment: An overview. Mount Sinai J Med 78: 1-10.

Subramanian S, Blanton LV, Frese SA, Charbonneau M, Mills DA, Gordon JI. 2015. Cultivating healthy growth and nutrition through the gut microbiota. Cell 161: 36-48.

Lectures 10, 11, 12: Endocrine disruption

-Holistic definition of the endocrine system
-Biochemistry, cell biology, physiology of normal endocrine function
-Role of endocrine system in reproductive function
-Chemical perturbations of endocrine function
-Mechanisms of endocrine disruption

LO 15: To develop an overall capacity to explain at the organ system level, anatomical and physiological aspects of the endocrine system.

LO 16: To be able to describe the scientific history of diethylstilbestrol with respect to carcinogenesis and teratogenesis.

LO 17: Enumerate the alternative pathways by which steroid hormone ligands may initiate biological effects in cells, including through nuclear receptors, via cell surface receptors, and through non-receptor impacts on cellular signaling. A further goal will be to be able to integrate from a systems biology perspective how these pathways may interact.

LO 18: Show a fundamental appreciation for what health effects may result from chemicals disrupting the endocrine system and how the chemical causes the outcome, and predict other health outcomes that may be due to endocrine disruption based on a synthesis of the information.

LO 19: Demonstrate an ability to explain the promiscuous nature of the steroid hormone receptors with respect to ligand variability.

References:

Caizzi L, Ferrero G, Cutrupi S, Cordero F, Ballaré C et al. 2014. Genome-wide activity of unliganded estrogen receptor-α in breast cancer cells. Proc. Natl. Acad. Sci. 111(3): 4892-4897.

Hu M, Richard JE, Maliqueo M …… Skibicka KP, Stener-Victorin E. 2015. Maternal testosterone exposure increases anxiety-like behavior and impacts the limbic system in the offspring. Proc. Natl. Acad. Sci. USA 112(46): 14348-14353.

Li W, Hu Y, Oh S ….. Zhang J, Liu W, Rosenfeld MG. 2015. Condensin I and II complexes license full estrogen receptor α-dependent enhancer activation. Mol Cell 59(2): 188-202.

Liu Z, Merkurjev D, Yang F, Li W, Oh S et al. 2014. Enhancer activation requires *trans*-recruitment of a mega transcription factor complex. Cell 159: 358-373.

Miyagawa S, Iguchi T. 2015. Epithelial estrogen receptor 1 intrinsically mediates squamous differentiation in the mouse vagina. Proc. Natl. Acad. Sci. USA 112(42): 12986-12991.

Van Os J, Kenis G, Rutten BPF. 2010. The environment and schizophrenia. Nature 468(7321): 203-212.

Wang Y, Zhu L, Kuokkanen S, Pollard JW. Activation of protein synthesis in mouse uterine epithelial cells by estradiol-17β is mediated by a PKC-ERK1/2-mTOR signaling pathway. Proc. Natl. Acad. Sci. USA 112(11): E1382-E1391.

Lecture 13 and 14: Postnatal contribution to the metabolic syndrome

-Role of postnatal factors (e.g. diet, weight gain) in the metabolic syndrome
-Interaction of nervous, endocrine and immune systems in the metabolic syndrome
-Role of the microbiome in the metabolic syndrome

LO 20: Be able to describe how postnatal environmental factors such as diet are involved in the metabolic syndrome.

LO 21: Be able to discuss the role of microbiome species diversification is associated with the metabolic syndrome.

LO 22: Be able to describe the role of hormones other than insulin in the metabolic syndrome.

References:

Bäckhed F, Roswall J …. Dahlgren J, Jun W. 2015. Dynamics and stabilization of the human gut microbiome during the first year of life. Cell Host Microbe 17(6): 690-703.

Blanton LV, Charbonneau MR, Salih T, Barratt MJ …….. Gordon JI. 2016. Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children. Science 351(6275): pii aad3311.

Cowley M, Garfield AS, Madon-Simon M, Charalambous M, Clarkson RW et al. 2014. Developmental programming mediated by complementary roles of imprinted *Grb10*in mother and pup. PLoS Biol 12(2): 1001799.

Cox LM, Yamanishi S, Sohn J, Alekseyenko AV, Leung JM et al. 2014. Altering the intestinal microbiota during a critical developmental window has lasting metabolic consequences. Cell 158: 705-721.

Dalgaard K, Landgraf K, Heyne S, Lempradl A, Longinotto J et al. 2016. Trim28 haploinsufficiency triggers bi-stable epigenetic obesity. Cell 164: 353-364

Garidou L, Pomié C, Klopp P, Waget A, Charpentier J et al. 2015. The gut microbiota regulates intestinal CD4 T cells expressing RORγt and controls metabolic disease. Cell Metabol. 22: 100-112.

Goran MI, Dumke K, Bouret SG, Kayser B, Walker RW, Blumberg B. The obesogenic effect of high fructose exposure during early development. Nat Rev Endocrinol 9: 494-500.

Hardikar A, Satoor SN, Karandikar MS, Joglekar MV, Puranik AS et al. 2015. .Multigenerational undernutrition increases susceptibility to obesity and diabetes that is not reversed after dietary recuperation. Cell Metabol 22: 312-319.

Schwarzer M, Makki K, Storelli G …….. Vidal H, Leulier F. 2015. *Lactobacillus plantarum* strain maintains growth of infant mice during chronic undernutrition. Science 351(6275): 854-857.

Wu L, Lu Y, Jiao Y, Liu B, Li S et al. Paternal psychological stress reprograms hepatic gluconeogenesis in offspring. Cell Metabol. 22: 1-9.

Lecture 15 and 16: Neurological dysfunction associated with environmental exposures in children

-Normal development of the nervous system and the blood-brain barrier
-Genetic versus environmental input to normal development
-Environmental chemical exposures and pathology
-Mechanisms of perturbation

LO 23: To realize that the nervous system is constantly developing from conception through adulthood, yet the goal is to be able to enumerate specific periods of sensitivity to perturbation that relate to specific events in the developmental pathway.

LO 24: To have an anatomical and functional understanding of the role of the blood-brain barrier.

LO 25: Using the effects of socioeconomic status on the nervous system as an example, develop a cognizance for how psychosocial variables will eventually be defined scientifically.

LO 26: Develop an appreciation for the tremendous complexity of the nervous system and be able to demonstrate this complexity at multiple levels of nervous system organization. Also, have an appreciation for how this complexity leads to vulnerability due the large number of targets for environmental perturbation.

References:

Chatterjee N, Lin Y, Santillan BA, Yotnda P, Wilson JH. 2015. Environmental stress induces trinucleotide repeat mutagenesis in human cells. Proc. Natl. Acad. Sci. USA 112(12): 3764-3769.

Goyal MS, Venkatesh S, Milbrandt J, Gordon JI, Raichle ME. 2015. Feeding the brain and nurturing the mind: Linking nutrition and the gut microbiota to brain development. Proc. Natl. Acad. Sci. USA 112(46): 14105-14112.

Hackman DA, Farah MJ, Meaney MJ. 2010. Socioeconomic status and the brain: mechanistic insights from human and animal research. Nature Rev Neuroscience 11:651-659.

Hunter RG, Gagnidze K, McEwen BS, Pfaff DW. 2014. Stress and the dynamic genome: Steroids, epigenetics and the transcriptome. Proc. Natl. Acad. Sci. USA [Epub 10 Nov 2014].

Klengel T, Binder EB. 2015. Epigenetics of stress-related psychiatric disorders and gene x environment interactions. Neuron 86(6): 1343-1357.

Mei Y, Monteiro P, Zhou Y, Kim J-A, Gao X, Fu Z, Feng G. 2016. Adult restoration of Shank3 expression rescues selective autistic-like phenotypes. Nature 530: 481-484. [Editorial: Burbach JPH. 2016. Unraveling a pathway to autism: A signaling pathway that controls protein synthesis may be a target for autism therapeutics. Science 351(6278): 1153-1154.

Mitchell C, Hobcraft J, McLanahan SS, Siegel SR, Berg A et al. 2014. Social disadvantage, genetic sensitivity, and children's telomere length. Proc. Natl. Acad. Sci. USA 111(16): 5944-5949.

Picard M, McManus MJ, Gray JD …….. McEwen BS, Wallace DC. 2015. Mitochondrial functions modulate neuroendocrine, metabolic, inflammatory and transcriptional responses to acute psychological stress. Proc. Natl. Acad. Sci. USA 112(48): E6614-E6623.

Lectures 17 and 18: Immune system dysfunction associated with environmental exposures in children

-Functional aspects of the cellular innate and acquired immune systems
-Development of the immune system in children
-Chemical and physical perturbations of the system

LO 27: To have an appreciation for the functional roles of the innate and acquired immune sytems, and the embryonic, fetal and postnatal development of the systems.

LO 28: To integrate information from the previous studied systems (neural and endocrine) to be able to explain how developmental perturbations of those systems could impact immunity and vice versa.

LO 29: To be able to enumerate classical agents that have been shown to perturb development of the immune system and the associated outcomes.

LO 30: To be capable of formulating hypotheses regarding the reasons for the increased incidence of asthma.

References:

Cahenzli J, Köller Y, Wyss M, Geuking MB, McCoy KD. 2013. Intestinal microbial diversity during early-life colonization shapes long-term IgE levels. Cell Host Microbe 14: 559-570.

Choi GB, Yim YS, Wong H …… Littman DR, Huh JR. 2016. The maternal interleukin-17a pathway in mice promotes autism-like phenotypes in offspring. Science 351(6276): 933-939. [Editorial: Estes ML, McAllister AK. 2016. Maternal T_H17 cells take a toll on baby's brain: Infection produces an immune molecule that interferes with brain development. Science 351(6276): 919-920.

De Agüero MG, Gamal-Vonarburg SC, Fuhrer T ……. McCoy KD, Macpherson AJ. 2016. The maternal microbiota drives early postnatal innate immune development. Science 351(6279): 1296-1302.

Du Y, Yang M, Lee S, Behrendt CL, Hooper LV et al. 2012. Maternal western diet causes inflammatory milk and TLR2/4-dependent neonatal toxicity. Genes Dev 26(12): 1306-1311.

Fujimura KE, Lynch SV. 2015. Microbiota in allergy and asthma and the emerging relationship with the gut microbiome. Cell Host Microbe 17(5): 592-602.

Julia V, Macia L, Dombrowicz D. 2015. The impact of diet on asthma and allergic diseases. Nat Rev Immunol 15(5): 308-322.

Kollmann TR, Kampmann B, Mazmanian SK, Marchant A, Levy O. Protecting the newborn and young infant from infectious diseases: Lessons from immune ontogeny. Immunity 46: 350-363 (2017).

Lewis JD, Chen EZ, Baldassano RN ….. Li H, Wu GD, Bushman FD. Inflammation, antibiotics, and diet as environmental stressors of the gut microbiome in pediatric Crohn's disease. Cell Host Microbe 18(4): 489-500.

McDade TW. 2012. Early environments and the ecology of inflammation. Proc Natl Acad Sci USA 109(Suppl 2): 17281-17288.

Raedler D, Schaub B. 2014. Immune mechanisms and development of childhood asthma. Lancet Respir. Med. 2: 647-656.

Rook GA, Lowry CA, Raison CL. 2014. Hygiene and other early childhood influences on the subsequent function of the immune system. Brain Res [Epub 13 April 2014].

Lectures 19 and 20: Respiratory system dysfunction associated with environmental exposures in children

-Development and function of the respiratory system in children
-Chemical and physical perturbations of the system during development

LO 31: To have a basic familiarity with the prenatal and postnatal development of the respiratory system from an anatomical and physiologic perspective.

LO 32: To be able to formulate hypotheses as to how various air pollutants may perturb lung development and function.

LO 33: Be able to delineate reasons for the differential susceptibility of the pulmonary system in children as compared to adults.

References:

Arrieta M-C, Stiemsma LT, Dimitriu PA ……. Turvey SE, Finlay BB. 2015. Early infancy microbial and metabolic alterations affect risk of childhood asthma. Science Transl. Med. 7(307): 307ra152 1-14.

Gauderman WJ, Urman R, Avol E, Berhane K, McConnell R et al. 2015. Association of improved air quality with lung development in children. N. Engl. J. Med. 372(10): 905-913.

Murphy SR, Oslund KL, Hyde DM, Miller LA, VanWinkle LS et al. 2014. Ozone-induced airway epithelial cell death, the neurokinin-1 receptor pathway, and the postnatal developing lung. Am. J. Physiol. Lung Cell, Mol. Physiol. 307(6): L471-481.

Teo SM, Mok D, Pham K, Kusel M, Serralha M et al. 2015. The infant nasopharyngeal microbiome impacts severity of lower respiratory infection and risk of asthma development. Cell Host Microbe 17: 1-12.

Weng T, Gao L, Bhaskaran M, Guo Y, Gou D, Narayanaperumal J, Chintagari NR, Zhang K, Liu L. 2009. Pleiotrophin regulates lung epithelial cell proliferation and differentiation during fetal lung development via beta-catenin and Dlk1.
J Biol Chem. 284(41):28021-32.

Course assignments:

Each student will be required to make one 10-20 minute presentation on papers from the syllabus or other papers that elucidate concepts that are critical to children's environmental health. These presentations will occur during the allotted time slots for the appropriate topics.. In addition, each student will be required to write two review papers on topics determined by the student in consultation with the instructor. These will be comprehensive review papers of specific topics in children's environmental health (no specific length but the topic must be covered extensively). Therefore, choose a narrow topic.

Grading:
Presentation: 30%
Class participation: 10%
First paper: 30%
Second paper 30%
Quizzes
Final examination
Oral examination

Competencies:

The Association of Schools of Public Health (ASPH) Environmental Health competencies that will be covered in this course are as follows:

2C. Describe the direct and indirect human, ecological and safety effects of major environmental and occupational agents.

3C. Specify current environmental risk assessment methods.

4C. Describe genetic, physiologic and psychosocial factors that affect susceptibility to adverse health outcomes following exposure to environmental hazards.

6C. Explain the general mechanisms of toxicity in eliciting a toxic response to various environmental exposures.