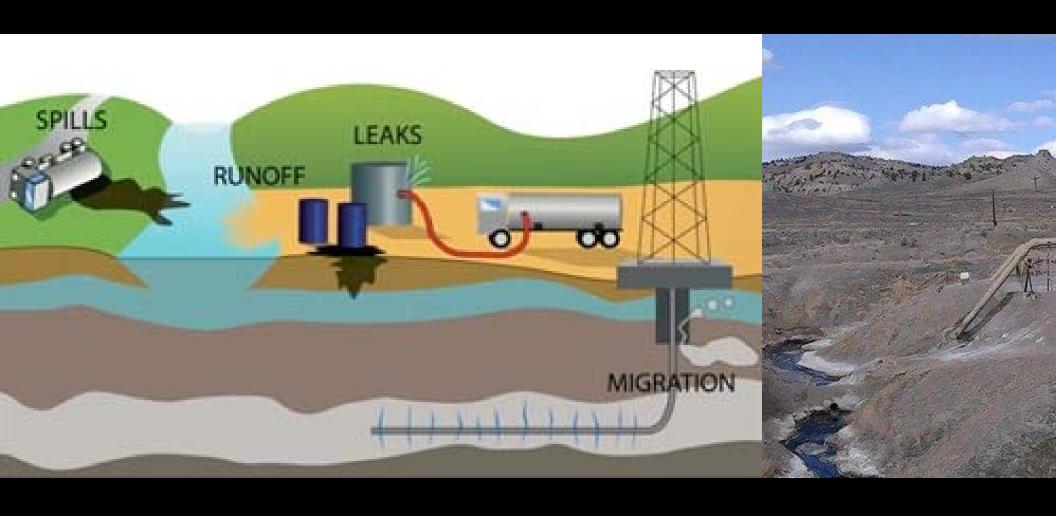
Endocrine Disrupting Activity Associated With Oil and Natural Gas Extraction

Susan C Nagel, PhD Associate Professor

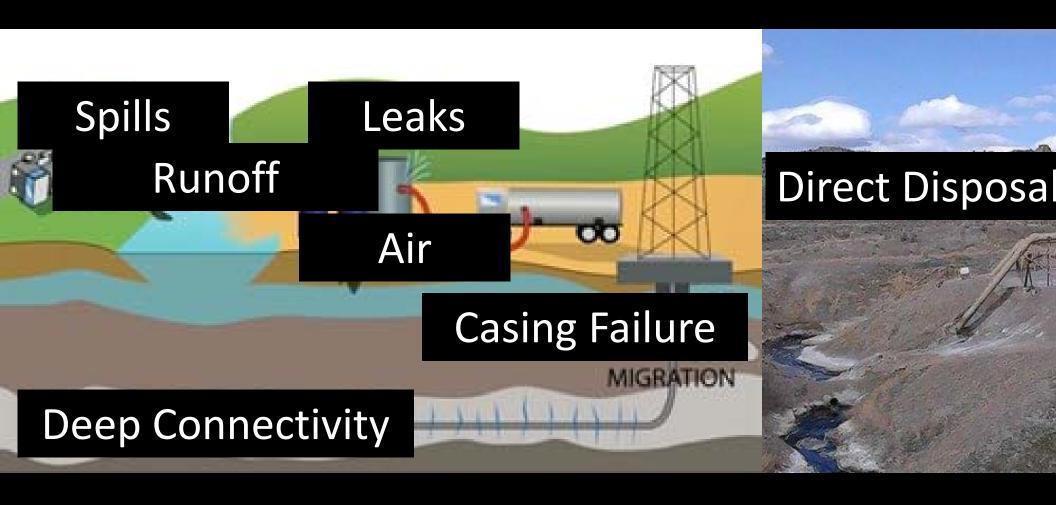
Obstetrics, Gynecology, and Women's Health
University of Missouri

NIH R21ES026395 and R01 ES021394, The University of Missouri, EPA STAR Fellowship (Kassotis)

Routes of contamination of surface and ground water with oil and gas wastewater



Routes of contamination of surface and ground water with oil and gas wastewater

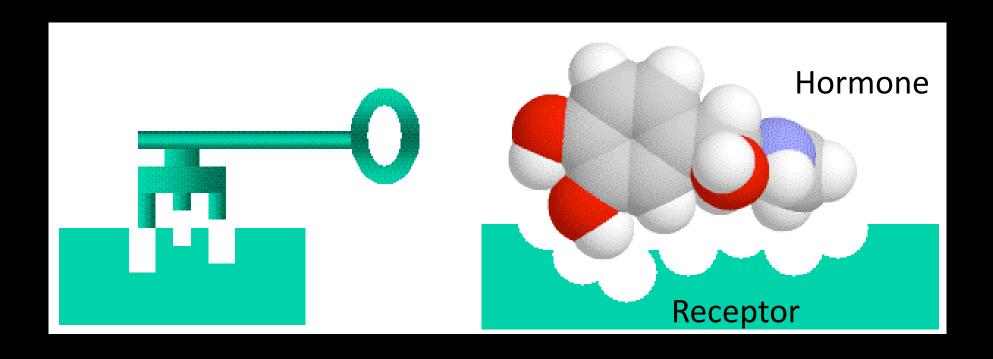


- 1. Can chemicals used in unconventional oil and gas (UOG) operations disrupt normal endocrine signals?
- 2. Is there evidence of an association between oil and gas activities and human reproduction?
- 3. Does perinatal exposure to a mixture of oil and gas chemicals alter adult health?

Hormones are chemical messages essential for normal health and development



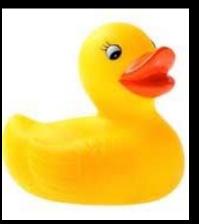
Hormone work by binding to specific receptors



Endocrine Disrupting Chemicals (EDC)

"A chemical, or mixture of chemicals, that interferes with any aspect of hormone action."











The Endocrine Society Statement on endocrine disrupting chemicals. Endocrinology 2012

Can chemicals used in unconventional oil and gas (UOG) disrupt normal hormone signals?

1,2,4-trimethylbenzene

2-(2-methoxyethoxy) ethanol

Fthv

Ethylene glycol

Ethylbenzene

2-ethylhexanol

Ethylene glycol butyl ether

Acrylamide

Methyl-4-isothiazolin

Benzene

Naphthalene

Bisphenol A

Phenol

Bronopol

Propylene glycol

Cumene

Sodium tetraborate decahydrate

Diethanolamine

Styrene

Dimethyl formamide

Toluene

Ethoxylated nonylphenol

Triethylene glycol

Ethoxylated octylphenol

Xylenes

EDC Activity of 23 UOG Chemicals

Receptor	Activation	Inhibition
Estrogen	0	21
Androgen	0	21
Progesterone	1	12
Glucocorticoid	0	10
Thyroid	2	7

Disruption of Hormones Is Associated with Human Disease

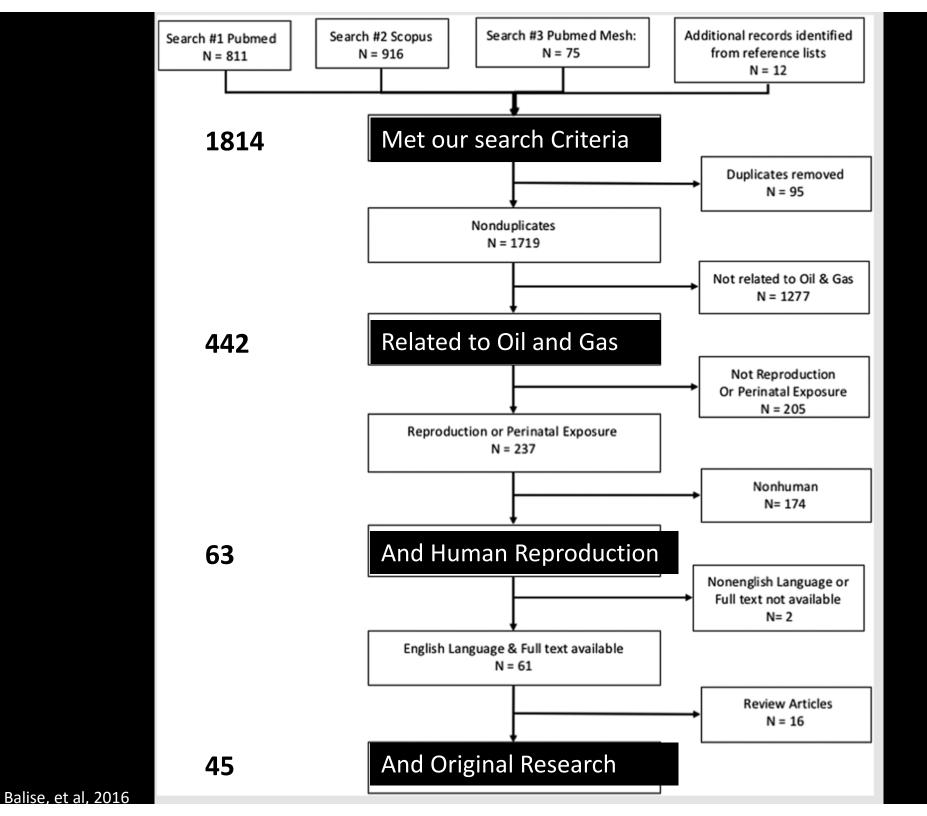
Cancer Estrogen Metabolic Syndrome **Immune Disorders** Androgen **Infertility** Glucocorticoids **Altered Puberty** Reproductive Problems Progesterone Neurological Issues **Behavioral Disorders** Thyroid **Organ Defects**

- 1. Can chemicals used in unconventional oil and gas (UOG) operations disrupt normal endocrine signals?
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Systematic review of the association between oil and natural gas extraction processes and human reproduction

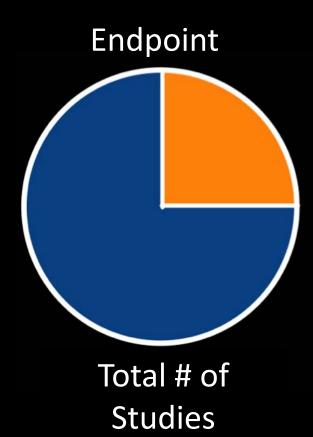
Victoria D. Balise, B.S., a,b Chun-Xia Meng, M.D., Ph.D., a Jennifer N. Cornelius-Green, M.S., Christopher D. Kassotis, Ph.D., Rana Kennedy, B.S., a,b and Susan C. Nagel, Ph.D.

^a Department of Obstetrics, Gynecology and Women's Health, and ^b Division of Biological Sciences, University of Missouri, Columbia, Missouri; and ^c Nicholas School of the Environment, Duke University, Durham, North Carolina

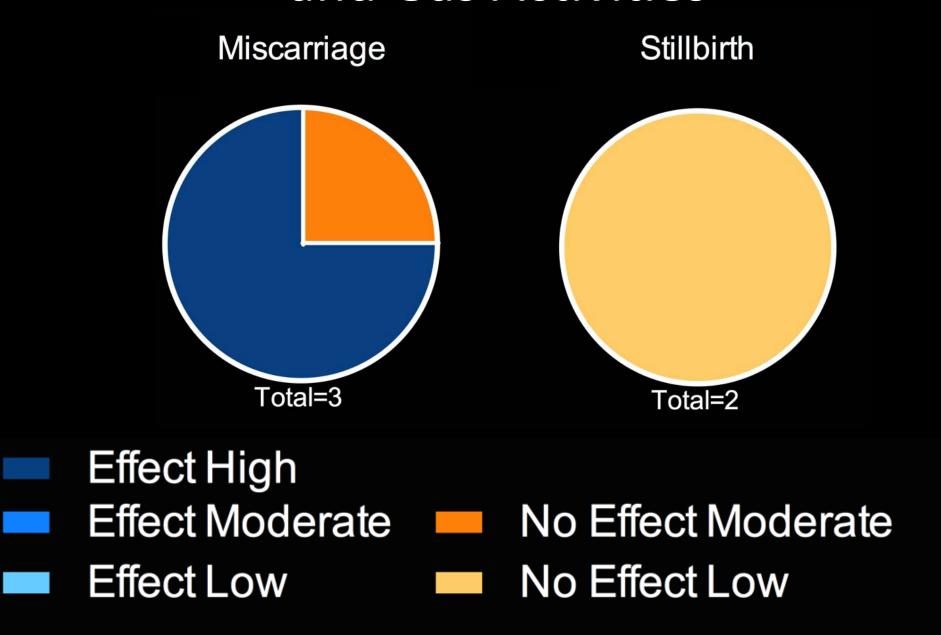


Studies were assessed for quality of evidence and risk of bias and then the evidence was integrated

- Effect High Number of Studies X 3
- Effect Moderate Number of Studies X 2
- Effect Low Number of Studies X 1
 - No Effect High Number of Studies X 3
- No Effect Moderate Number of Studies X 2
- No Effect Low Number of Studies X 1



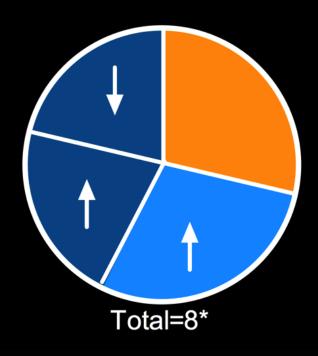
Birth Outcomes Associated with Oil and Gas Activities



Birth Outcomes Associated with Oil and Gas Activities

Preterm Birth

Low Birth Weight

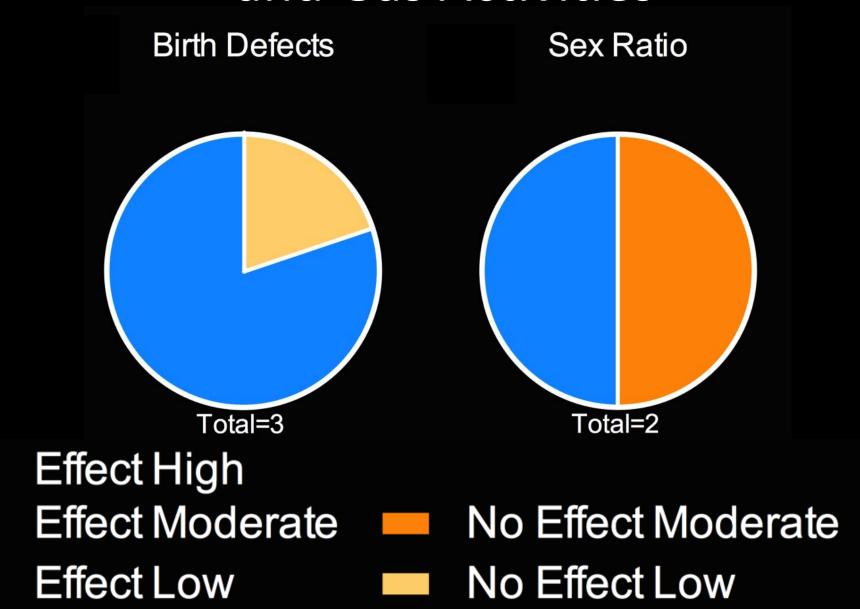




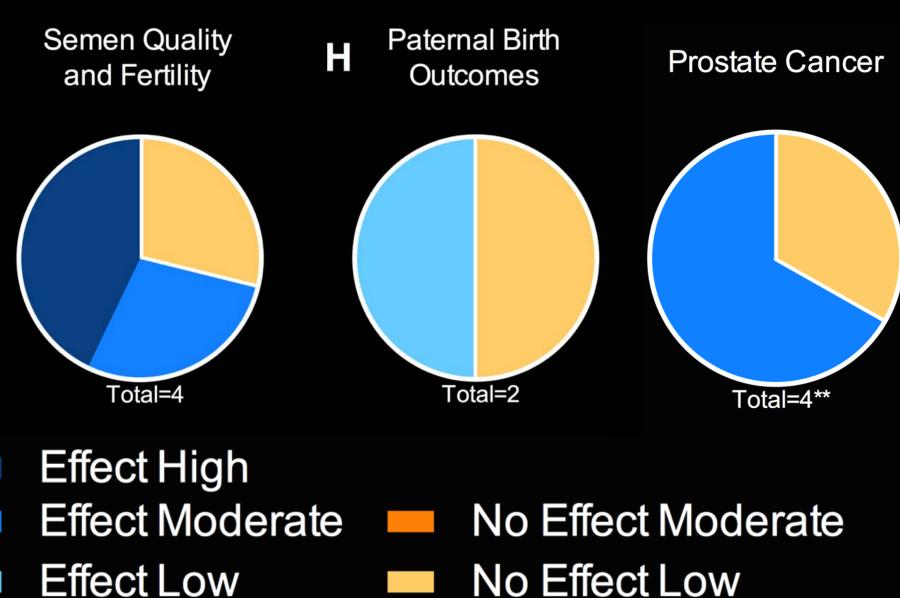
- Effect High
- Effect Moderate
 - Effect Low

- No Effect Moderate
- No Effect Low

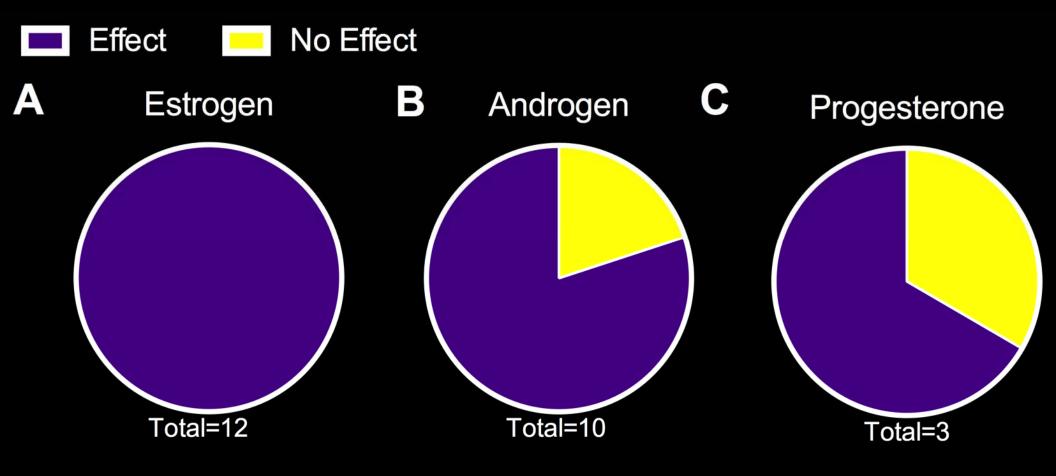
Birth Outcomes Associated with Oil and Gas Activities



Male Reproductive Health Associated with Oil and Gas Activities



Evidence from Systematic Review that UOG Chemicals can be Endocrine Disruptors



- 1. Can chemicals used in unconventional oil and gas (UOG) operations disrupt normal endocrine signals?
- 2. Is there evidence of an association between oil and gas activities and human reproduction?
- 3. What health effects may be associated with prenatal exposure to chemicals?

Fetal and early life exposure to EDCs is associated with adult disease

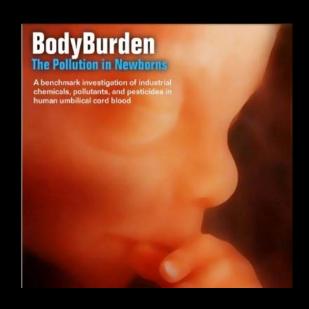
Pollutants



Nutrition



Maternal Health and Disease





Infertility Obesity **Heart Disease** Diabetes **Hypertension Hyperactivity Bone Health Endometriosis Breast Cancer Testicular Cancer**

Developmental exposure to a mixture of 23 UOG chemicals via drinking water

1,2,4-trimethylbenzene Ethylbenzene

2-(2-methoxyethoxy) ethanol Ethylene glycol

2-ethylhexanol Ethylene glycol butyl ether

Acrylamide Methyl-4-isothiazolin

Benzene Naphthalene

Bisphenol A Phenol

Bronopol Propylene glycol

Cumene Sodium tetraborate decahydrate

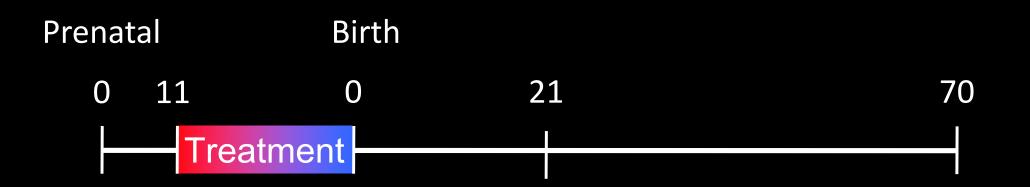
Diethanolamine Styrene

Dimethyl formamide Toluene

Ethoxylated nonylphenol Triethylene glycol

Ethoxylated octylphenol Xylenes

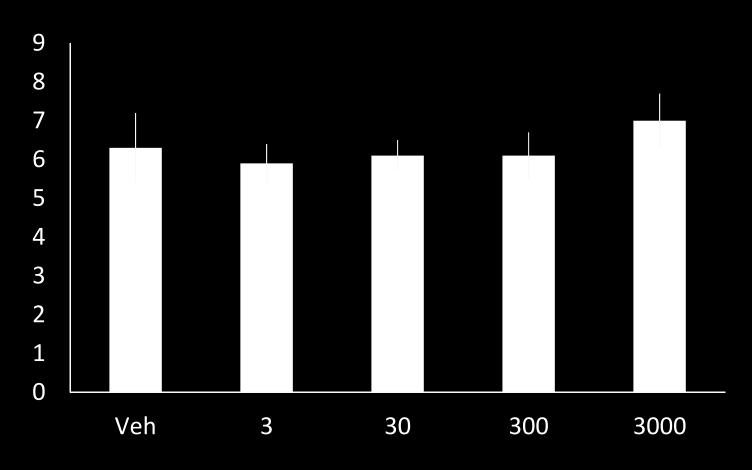
Developmental exposure to a mixture of 23 UOG chemicals via drinking water



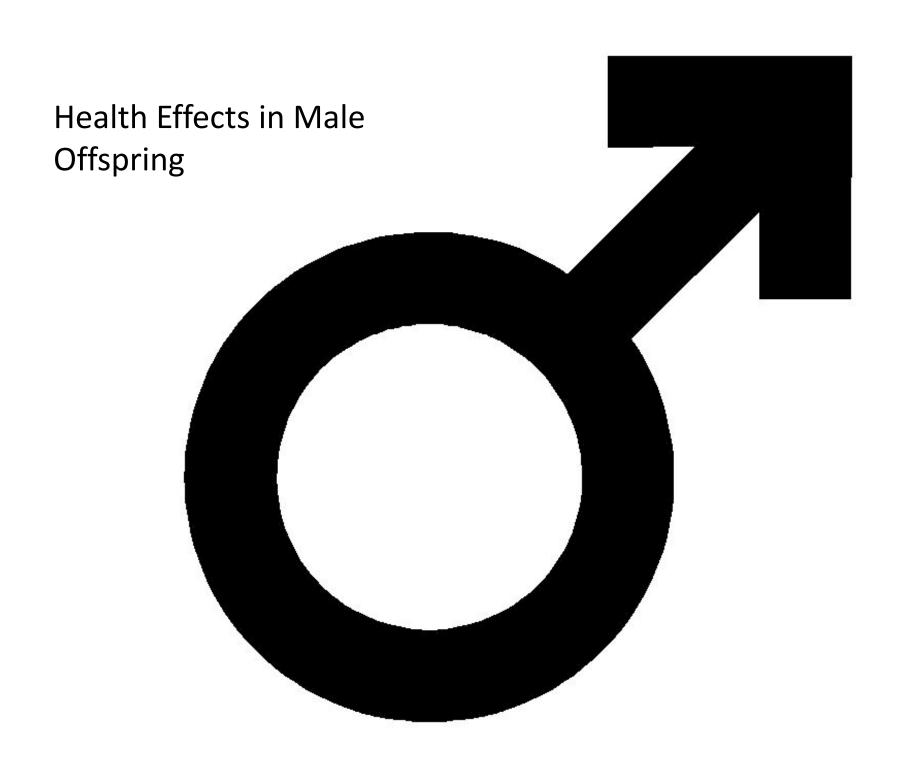
Vehicle 0.2% ethanol Mix 1 $3000 \mu g/kg$ Mix 2 $300 \mu g/kg$ Mix 3 $30 \mu g/kg$ Mix 4 $3 \mu g/kg$

Exposure was equivalent to roughly the second trimester of human pregnancy.

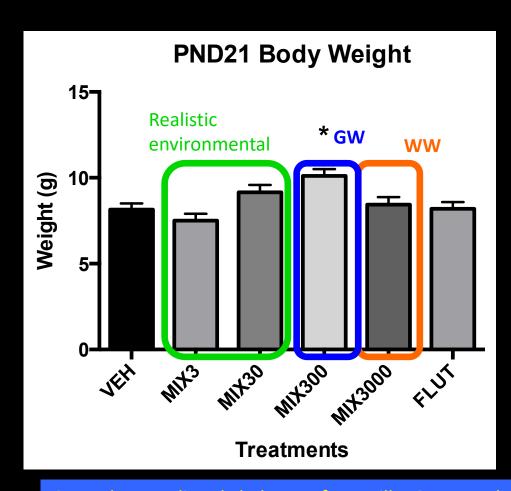
Prenatal exposure* to UOG mixture did not alter number of pups per litter

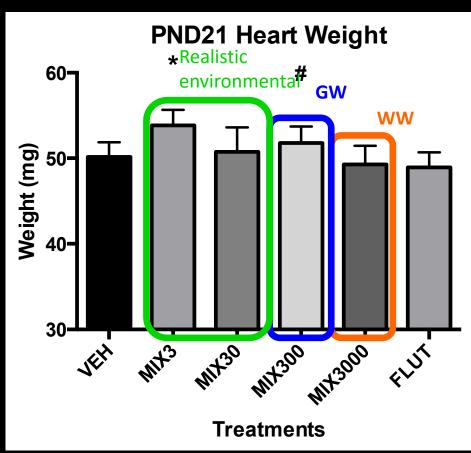


* Exposure equivalent to 2nd trimester of human pregnancy



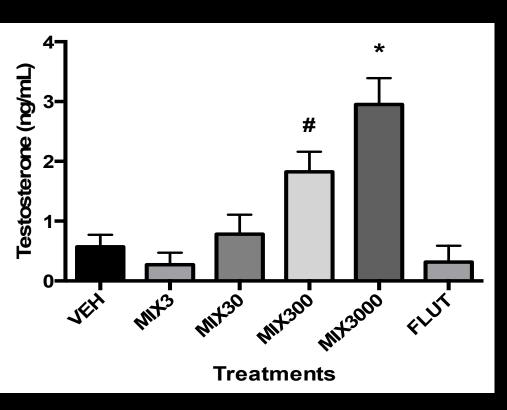
Prenatal exposure to UOG mixture altered body and organ weights in adult male mice

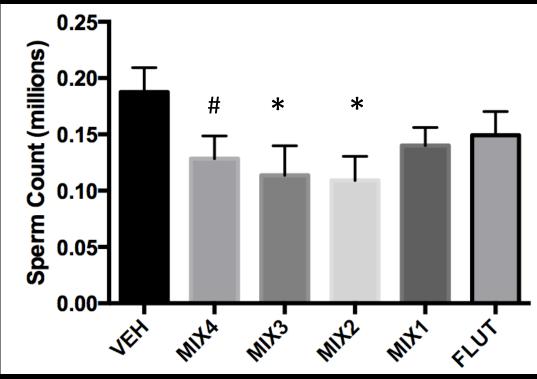




Ground water directly below surface spills, Gross et al

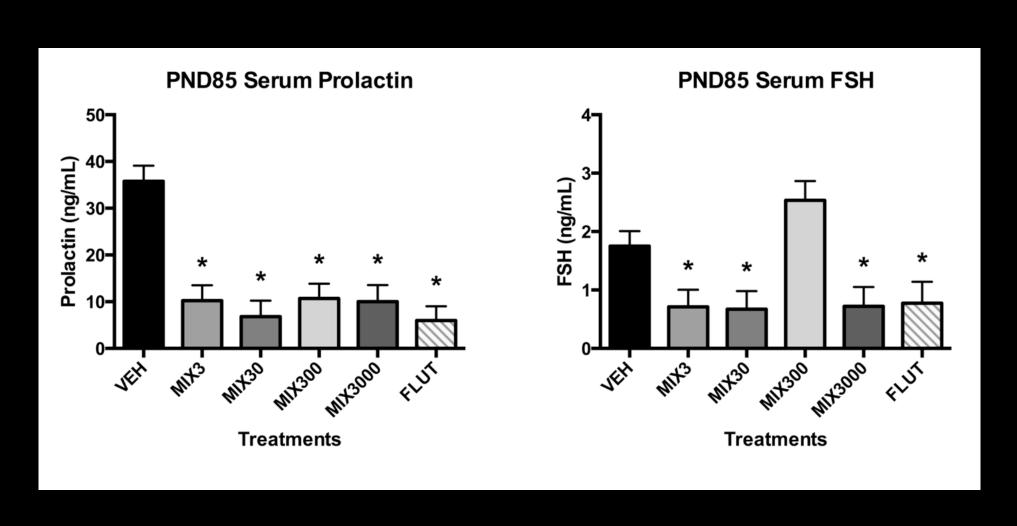
Prenatal exposure to UOG mixture increased adult testosterone and decreased sperm counts



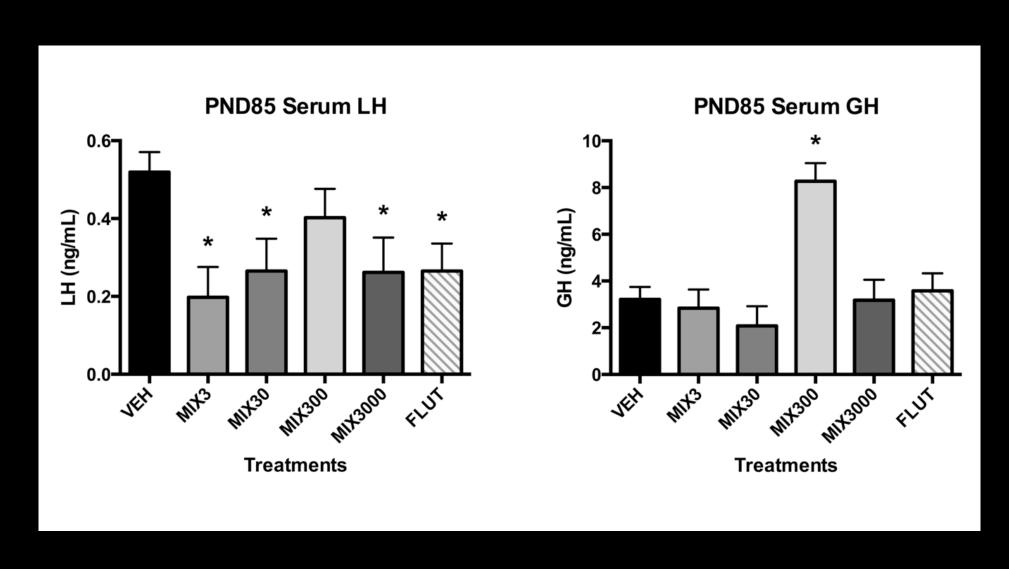




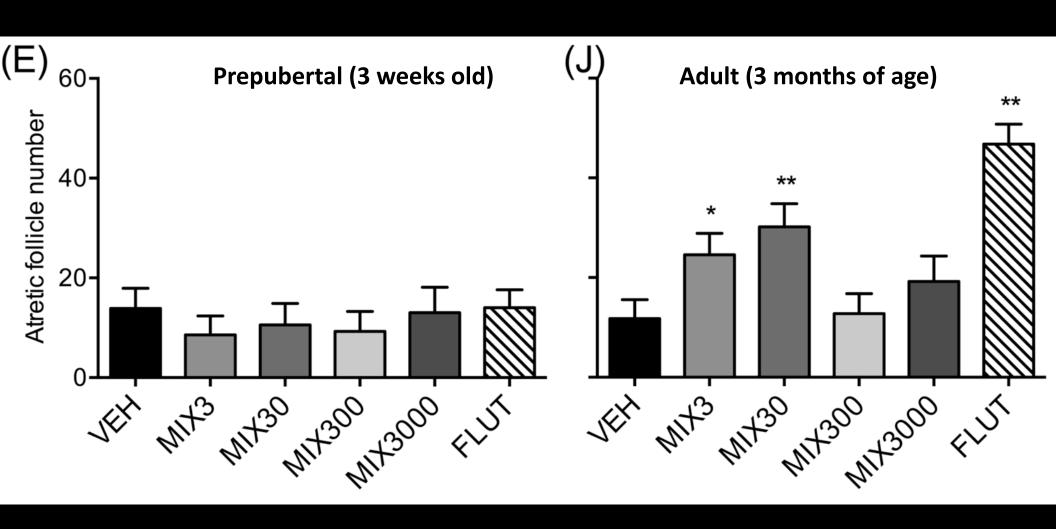
Prenatal Exposure Decreased Reproductive Hormones: Prolactin and FSH



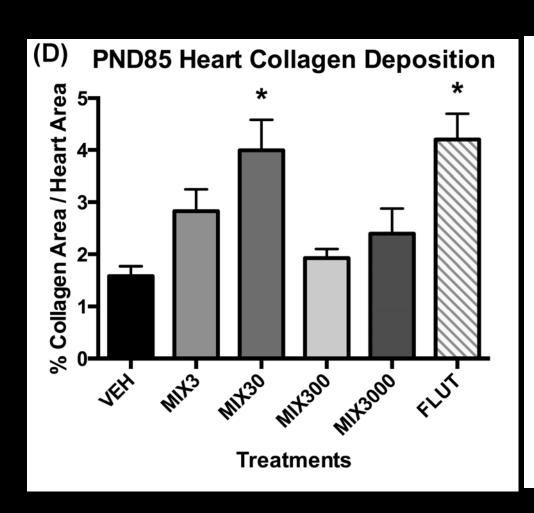
Prenatal Exposure Decreased LH and Increased GH

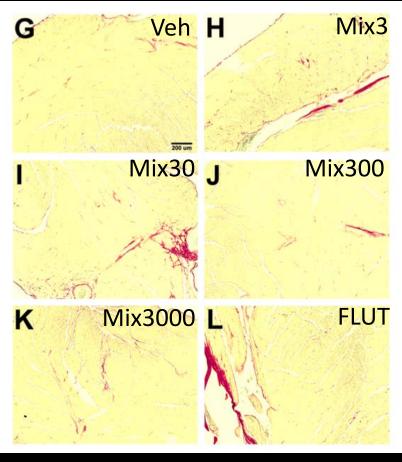


Prenatal Exposure Increased Number of Atretic Follicles at Low Doses



Collagen deposition was increased in the heart at low doses





Conclusions

- Many chemicals used in and produced by oil and gas activities can be EDCs
- A systematic review of published studies suggests there is evidence for an association between oil and gas activities and negative developmental and reproductive health effects in humans.
- Laboratory studies found an association between prenatal exposure to UOG chemicals and negative developmental and reproductive health outcomes.