ADJACENT
DIGITAL POLITICS LIMITED

Customer Statistical Information Pack

UCDAVIS
VETERINARY MEDICINE

Total Reach*

1,556,615

Total Engagement**

571,082

* Total Reach – combined reach of all products where your content appeared
** Total Engagement across all products where your content has appeared (digital editions, website and email newsletters)

EBOOK

SEPTEMBER 2018

Total Reach*

142,792

Total Engagement**

6,971

Email Opens

6,141

Edition Engagement

830

* Total Reach figure is the distribution for this edition of your ebook

** Total Engagement of the ebook content (email opens, PageSuite and HTML pageviews and Social Media activity (if applicable))

OPEN ACCESS **GOVERNMENT**

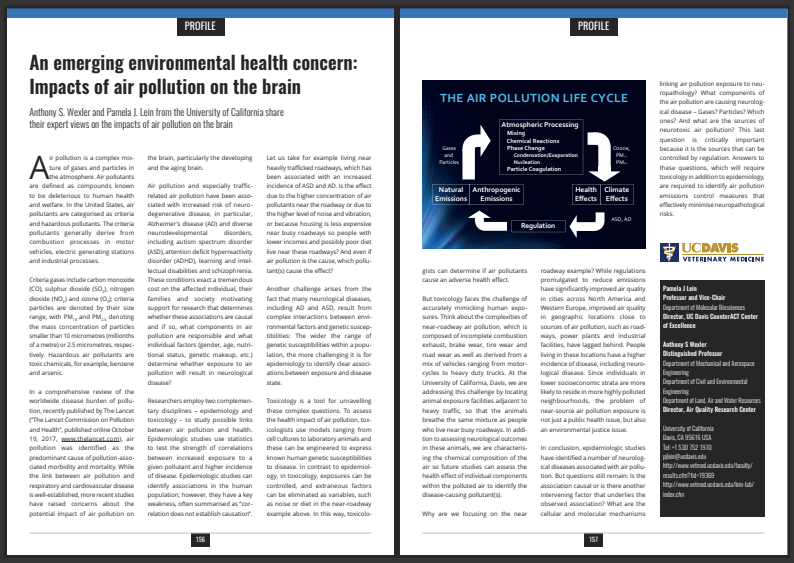
ISSUE 17 • FEBRUARY 2018

Total Reach*

280,505

Total Engagement**

171,645



PROFILE

An emerging environmental health concern: Impacts of air pollution on the brain

Anthony S. Wexler and Pamela J. Lein from the University of California share their expert views on the impacts of air pollution on the brain

Air pollution is a complex mixture of gases and particles in the atmosphere. Air pollutants are defined as compounds known to be deleterious to human health and welfare. In the United States, air pollutants are categorised as criteria and hazardous pollutants. The criteria pollutants generally derive from combustion processes in motor vehicles, electric generating stations and industrial processes.

Criteria gases include carbon monoxide (CO), sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3); criteria particles are denoted by their size range, with PM_{10} and $PM_{2.5}$ denoting the mass concentration of particles smaller than 10 micrometres (millionths of a metre) or 2.5 micrometres, respectively. Hazardous air pollutants are toxic chemicals, for example, benzene and arsenic.

In a comprehensive review of the worldwide disease burden of pollution, recently published by The Lancet ("The Lancet Commission on Pollution and Health", published online October 19, 2017, www.thelancet.com), air pollution was identified as the predominant cause of pollution-associated morbidity and mortality. While the link between air pollution and respiratory and cardiovascular disease is well-established, more recent studies have raised concerns about the potential impact of air pollution on the brain, particularly the developing and the aging brain.

Air pollution and especially traffic-related air pollution have been associated with increased risk of neurodegenerative disease, in particular, Alzheimer's disease (AD) and diverse neurodevelopmental disorders, including autism spectrum disorder (ASD), attention deficit hyperreactivity disorder (ADHD), learning and intellectual disabilities and schizophrenia. These conditions exact a tremendous cost on the affected individual, their families and society motivating support for research that determines whether these associations are causal and if so, what components in air pollution are responsible and what individual factors (gender, age, nutritional status, genetic makeup, etc.) determine whether exposure to air pollution will result in neurological disease?

Researchers employ two complementary disciplines – epidemiology and toxicology – to study possible links between air pollution and health. Epidemiologic studies use statistics to test the strength of correlations between increased exposure to a given pollutant and higher incidence of disease. Epidemiologic studies can identify associations in the human population; however, they have a key weakness, often summarised as "correlation does not establish causation". Let us take for example living near heavily trafficked roadways, which has been associated with an increased incidence of ASD and AD. Is the effect due to the higher concentration of air pollutants near the roadway or due to the higher level of noise and vibration, or because housing is less expensive near busy roadways so people with lower incomes and possibly poor diet live near these roadways? And even if air pollution is the cause, which pollutant(s) cause the effect?

Another challenge arises from the fact that many neurological diseases, including AD and ASD, result from complex interactions between environmental factors and genetic susceptibilities. The wider the range of genetic susceptibilities within a population, the more challenging it is for epidemiology to identify clear associations between exposure and disease state.

Toxicology is a tool for unravelling these complex questions. To assess the health impact of air pollution, toxicologists use models ranging from cell cultures to laboratory animals and these can be engineered to express known human genetic susceptibilities to disease. In contrast to epidemiology, in toxicology, exposures can be controlled, and extraneous factors can be eliminated as variables, such as noise or diet in the near-roadway example above. In this way, toxicologists can determine if air pollutants cause an adverse health effect.

But toxicology faces the challenge of accurately mimicking human exposures. Think about the complexities of near-roadway air pollution, which is composed of incomplete combustion exhaust, brake wear, tire wear and road wear as well as derived from a mix of vehicles ranging from motorcycles to heavy duty trucks. At the University of California, Davis, we are addressing this challenge by locating animal exposure facilities adjacent to heavy traffic, so that the animals breathe the same mixture as people who live near busy roadways. In addition to assessing neurological outcomes in these animals, we are characterising the chemical composition of the air so future studies can assess the health effect of individual components within the polluted air to identify the disease-causing pollutant(s).

Why are we focusing on the near roadway example? While regulations promulgated to reduce emissions have significantly improved air quality in cities across North America and Western Europe, improved air quality in geographic locations close to sources of air pollution, such as roadways, power plants and industrial facilities, have lagged behind. People living in these locations have a higher incidence of disease, including neurological disease. Since individuals in lower socioeconomic strata are more likely to reside in more highly-polluted neighbourhoods, the problem of near-source air pollution exposure is not just a public health issue, but also an environmental justice issue.

In conclusion, epidemiologic studies have identified a number of neurological diseases associated with air pollution. But questions still remain: Is the association causal or is there another intervening factor that underlies the observed association? What are the cellular and molecular mechanisms linking air pollution exposure to neuropathology? What components of the air pollution are causing neurological disease – Gases? Particles? Which ones? And what are the sources of neurotoxic air pollution? This last question is critically important because it is the sources that can be controlled by regulation. Answers to these questions, which will require toxicology in addition to epidemiology, are required to identify air pollution emissions control measures that effectively minimise neuropathological risks.

UC DAVIS VETERINARY MEDICINE

Pamela J Lein
Professor and Vice-Chair
Department of Molecular Biosciences
Director, UC Davis CounterACT Center of Excellence

Anthony S Wexler
Distinguished Professor
Department of Mechanical and Aerospace Engineering
Department of Civil and Environmental Engineering
Department of Land, Air and Water Resources
Director, Air Quality Research Center

University of California
Davis, CA 95616 USA
Tel: +1 530 752 1830
pjlein@ucdavis.edu
http://www.vetmed.ucdavis.edu/faculty/msalts.cfm?id=11530
http://www.vetmed.ucdavis.edu/lein-lab/index.cfm

An emerging environmental health concern: Impacts of air pollution on the brain

Email Opens

14,440

Edition Engagement

154,685

Client Pageviews

2,520

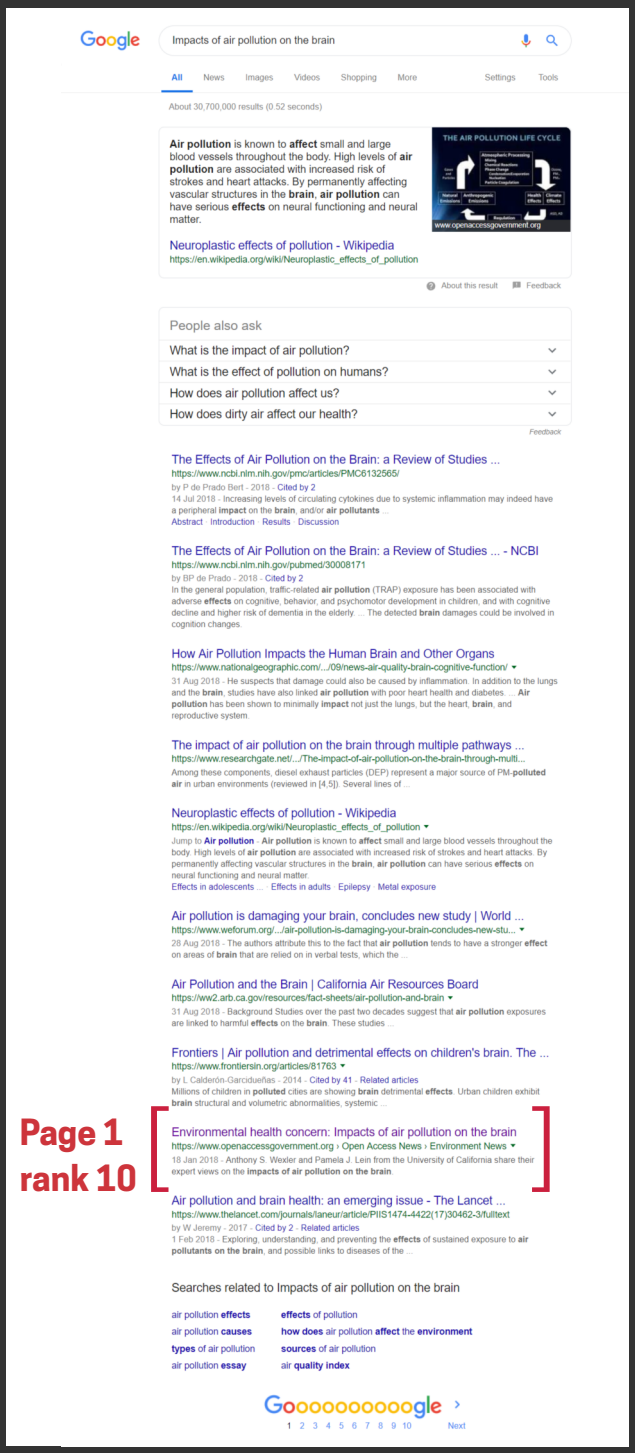
* Total Reach figure is the distribution for this edition of the publication

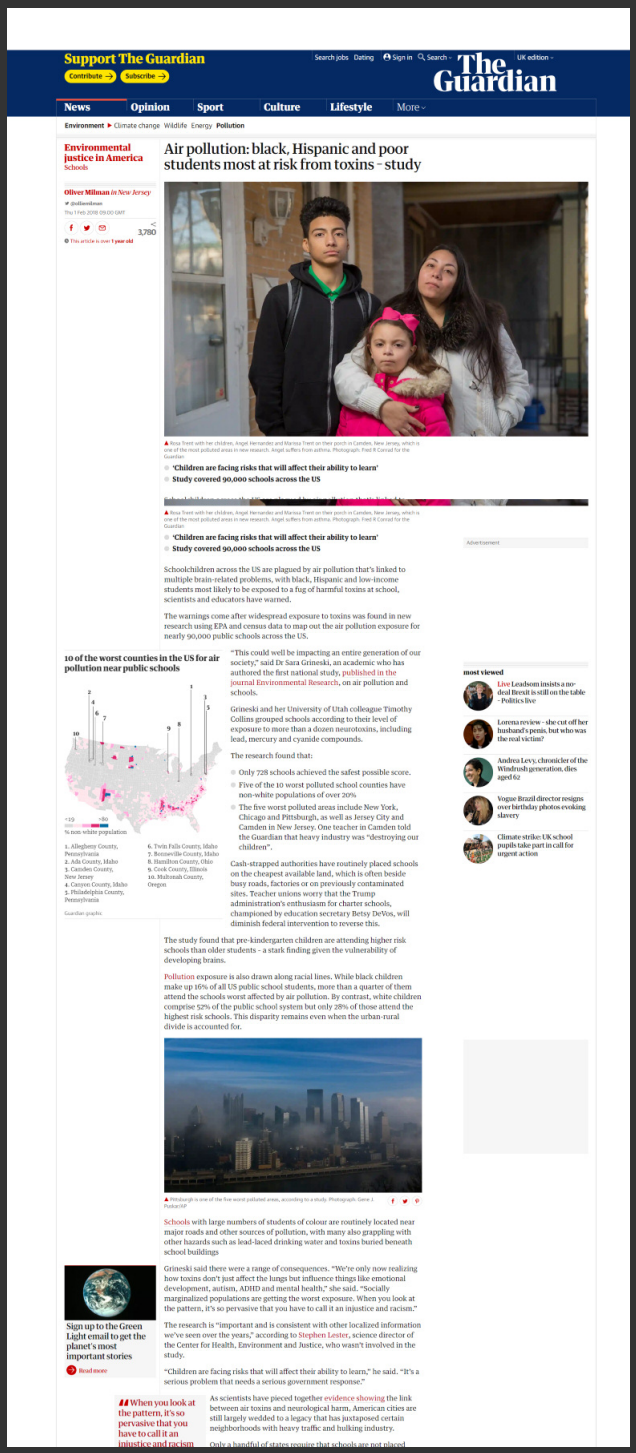
** Total Engagement of the publication content (email opens, PageSuite and HTML pageviews and Social Media activity)

SEARCH RESULTS:

IMPACTS OF AIR POLLUTION ON THE BRAIN

ORGANIC SEARCH





17 LINKING DOMAINS

23 LINKS (INCLUDING 2 FROM THE GUARDIAN UK)

OPEN ACCESS **GOVERNMENT**

ISSUE 18 • MAY 2018

Total Reach*

214,502

Total Engagement**

100,701

PROFILE

The potential long-term environmental health consequences of urban wildfire debris

Birgit Puschner and Pamela Lein from the University of California, Davis share their expert views on the impacts of urban wildfire on chemical contamination in small backyard agriculture

Worldwide, the frequency and severity of wildfires are increasing due to changes in temperature and precipitation patterns consistent with climate change and changes in land use, particularly at the rural-urban interface. The fire problem is particularly acute in Northern California, which has experienced a significant increase in wildfire frequency over the past few decades. In addition to the risk of injury, loss of life and destruction of property, there is increasing appreciation that wildfires pose significant environmental health threats.

Much of the research on adverse health impacts of wildfires has focused on wildfire smoke and recent reviews of this scientific literature conclude there is strong evidence that wildfire smoke exacerbates respiratory ailments, including asthma and chronic obstructive pulmonary disease and contributes to cardiovascular disease. What is less well understood, however, is the potential impacts of wildfire debris on human, animal and ecosystem health.

Debris from urban wildfires is particularly worrying because these fires involve the combustion of building materials, electronic equipment, chemicals and industrial equipment that contain toxic chemicals such as metals, pesticides and persistent organic pollutants (POPs).

POPs of concern include the polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs). PCBs are man-made chemicals that were widely produced for diverse industrial applications beginning in the 1930s until their production was banned in 1979 because of their carcinogenic potential and developmental neurotoxicity.

PCBs are found in older electrical transformers, capacitors and light ballasts still in use today and in caulking material, paints and sealants used to construct municipal buildings and homes prior to the 1979 ban. PBDEs are also man-made chemicals that were widely used as flame retardants in various consumer products including foam, plastics and textiles.

Due to health concerns, the state of California began prohibiting the manufacture, distribution and processing of flame-retardant products containing penta- and octa BDEs in 2006. However, human exposure continues because many households have products produced prior to the ban. Moreover, PBDEs are not chemically bound to materials and therefore, leach out of household products into the environment. Like PCBs, PBDEs persist in the environment and biomagnify up the food chain.

Pyrolysis results in the release of PCBs and PBDEs into the environment. Increased PCB concentrations have been documented in air masses associated with fires. The ash from the September 11th 2001 World Trade Center fire in New York City was found to contain excessive PBDE levels. The combustion of man-made materials, particularly electronic equipment, is also associated with the mobilisation of metals. For example, ash debris from the California wildfires from 2007 contained toxic metals, specifically, arsenic, cadmium, copper and lead, at levels associated with long-term health effects in animals and humans.

Urban wildfires not only release toxic chemicals, but also generate hazardous compounds, such as dioxins and dibenzofurans, which are formed by the combustion of organic matter, such as paper and wood. Once the burning has stopped, re-volatilised chemicals distribute out of the atmosphere onto soils, vegetation and surface water, while non-volatile chemicals are deposited as ash. The increased environmental availability of these chemicals increases the risk of groundwater contamination, the uptake by plants and ingestion by animals, culminating in increased risk of human exposure for months to years. Thus, a question of growing concern is whether urban wildfires pose a significant long-term environmental health risk via chemical contamination of home-grown produce or animal-derived foods.

PROFILE

Wildfire aftermath on Cobb Mountain during the Valley fire in northern California

This concern is heightened by lay articles in the New York Times and San Francisco Chronicle and peer-reviewed publications reporting increased human exposure to lead (Pb) through consumption of eggs produced by backyard chickens. Eggs and eggs products are one of the most consumed foods worldwide. In the United States, individuals consume an average of 24 grammes of eggs per day. Backyard chicken ownership has grown in the United States in part because the eggs from backyard hens are perceived to be healthier than commercially produced eggs.

However, recent studies have identified concerning levels of Pb in eggs produced by chickens raised in areas with significant Pb contamination of the soil, usually as the result of the weathering of older buildings with Pb-based paints. The consumption of one average size 50-60 grammme egg from Pb-contaminated environment can exceed the safe threshold dose of 6µg of Pb per day from all combined dietary sources. What about PCBs and PBDEs? These are very fat-soluble chemicals and egg yolk is rich in lipids resulting in an average fat content in an egg of 10%. Thus, the potential for significant contamination of eggs in regions with increased soil levels of these POPs is not unreasonable, as suggested by recent data reporting the detection of PCBs and PBDEs in milk from dairy cows of California.

The overwhelming majority of food safety research associated with backyard poultry and other home-produced food products has largely focused on microbial contamination. Human illness from most foodborne pathogens is limited to transient gastrointestinal symptoms; in contrast, human exposure to unsafe levels of PCBs, PBDEs or metals has the potential to cause long-term adverse health effects. Currently, urban and backyard farmers have no way of knowing whether eggs or other home-grown food products are contaminated with toxic chemicals unless they are lab tested. There is, therefore, an urgent need to study environmental chemicals in home-produced food in geographic regions that have experienced urban wildfires to assess the potential food safety risk and to generate information needed to inform rational risk management.

In conclusion, the increase in wildfires has potentially serious long-term health consequences for communities and ecosystems. One important concern is the generation or release of chemicals into the soil and water environment and the risk for chemical contamination of home-grown produce, eggs and other animal-derived food products. To more accurately predict the risk to humans, it will be necessary to obtain data regarding the actual levels of toxic chemicals of concern in the environment before and after urban wildfires and to model the transfer of these contaminants through the food chain.

UCDAVIS VETERINARY MEDICINE

Pamela J. Lein
Professor and Vice-Chair
Department of Molecular Biosciences
Director, UC Davis CounterACT Center of Excellence
plein@ucdavis.edu

Birgit Puschner
Professor and Chair
Department of Molecular Biosciences

University of California, Davis
Tel: +1 530 752 1930
http://www.vetmed.ucdavis.edu/bio-lab/

The potential long-term environmental health consequences of urban wildfire debris

Email Opens

18,139

Edition Engagement

82,350

Client Pageviews

212

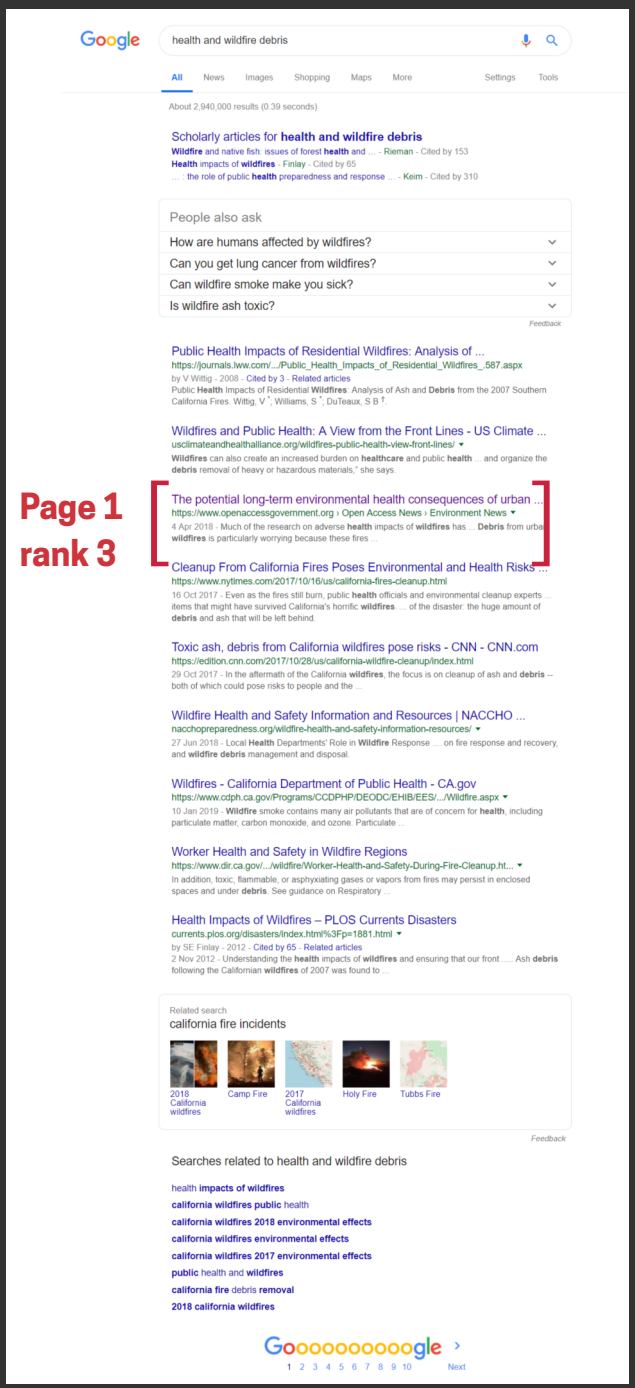
* Total Reach figure is the distribution for this edition of the publication

** Total Engagement of the publication content (email opens, PageSuite and HTML pageviews and Social Media activity)

SEARCH RESULTS:

HEALTH AND WILDFIRE DEBRIS

ORGANIC SEARCH



OPEN ACCESS **GOVERNMENT**

ISSUE 19 • JULY 2018

Total Reach*

154,366

Total Engagement**

117,180

PROFILE

Pesticides: A contributing factor to the increase in asthma?

Pamela J. Lein at the University of California, Davis discusses the evidence suggesting that pesticides are risk factors for asthma

Asthma is a chronic inflammatory lung disease, characterised by episodic and reversible bronchoconstriction (contraction of the smooth muscles that line the airways), excessive secretion of mucus in the airways and airway hyperreactivity (an exaggerated reaction of airway smooth muscle to contractile stimuli). All of these effects interfere with breathing.

Worldwide asthma prevalence and severity has increased markedly over the past two decades, especially in urban settings. Many hypotheses have been proposed to explain the increased asthma in urban residents, including exposure to allergens, air pollution, differences in healthcare and stress. However, an environmental factor associated with agricultural asthma that is beginning to receive increased attention in the context of urban asthma is exposure to organophosphorus pesticides (OPs).

OPs are the most widely used class of pesticides worldwide and are applied extensively in not only agricultural but also in suburban and urban settings to control insects. Although residential uses of OPs are being phased out in the United States and many European countries, OPs are still used heavily in agricultural, industrial and commercial settings and OPs are widely detected in the general human population in all countries in which this has been assessed.

Occupational exposures associated with the production, distribution and application of OPs occur primarily via dermal absorption, with more limited exposure via inhalation. The general population is exposed to OPs via ingestion of food and water contaminated with OPs and by dermal and inhalational exposure to pesticide drift and "overspray". The latter is not an insignificant source of exposure as extensive OP contamination has been documented in the air, homes and urine from pregnant women and children living in communities near agricultural fields sprayed with OPs.

OPs inhibit the enzyme acetylcholinesterase, which functions to inactivate the neurotransmitter acetylcholine. Acetylcholinesterase inhibition significantly increases acetylcholine levels at the synaptic junction between nerves that secrete acetylcholine and their target tissues, causing excessive stimulation of target tissues.

Acetylcholinesterase activity is functionally important in not only insects, but also humans. It is well established that OPs cause neurotoxicity in humans by inhibiting this enzyme, a medical condition referred to as the cholinergic crisis. Acute exposures to OPs that inhibit acetylcholinesterase by more than 80-90% of control levels can cause death in humans, typically by inhibiting the respiratory centres in the brain that control breathing. Thus, many regulatory agencies have identified safe levels of OPs as those that do not inhibit acetylcholinesterase.

Case reports published in the 1960's provided the first indication that exposures to OPs at levels that do not cause cholinergic crisis may trigger asthma in adults. Subsequent cross-sectional studies of farmers and their families, farmworkers and commercial pesticide applicators in multiple countries around the world provided further evidence that occupational exposures to OP pesticides are associated with adult-onset asthma.

More recent epidemiologic data suggest that not only occupational exposures, but also exposures to environmentally relevant levels of OPs, such as might be experienced by the general public, are associated with increased risk of asthma and asthmatic symptoms in adults and adolescents. OP-induced asthma may not be limited to these age groups, as indicated by emerging data from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), the longest-running longitudinal birth cohort study of pesticide effects on children's health, which has been studying children in a farmworker community in the Salinas Valley of northern California. Data from the CHAMACOS study suggests that OP exposures during pregnancy and the first year of life, as determined by analysis of urinary OP metabolites in pregnant women and their infants, are associated with respiratory symptoms in children at five and seven years of age.

212

PROFILE

Farm worker spraying pesticide treatment on fruit garden

While systematic reviews of the published epidemiologic literature generally support an association between OP pesticide exposure and asthma, it is difficult to establish a cause-effect relationship based on human data. This is due in large part to the fact that it is extremely challenging to accurately quantify OP exposure in humans. Thus, studies in animal models are critical for determining whether OPs are causally linked to asthma. The animal studies published to date support the hypothesis that OPs directly cause airway hyperreactivity, a key symptom of asthma.

Importantly, OP-induced airway hyperreactivity is observed at levels that do not inhibit acetylcholinesterase. Several different OPs, including chlorpyrifos, parathion and diazinon, can induce airway hyperreactivity in guinea pigs following subcutaneous injection, a route of exposure that mimics dermal exposure in humans. In contrast, pyrethroids, a class of pesticides structurally and mechanistically distinct from OPs, do not induce airway hyperreactivity in guinea pigs, suggesting that the airway response to OPs is not a generalised property of all pesticides.

Interestingly, the effect of OPs on airway hyperreactivity was not evident immediately after exposure, but rather were manifest 24 hours later and persisted for at least seven days after a single injection of the OP. Further studies in the guinea pig model suggest that OPs cause airway hyperreactivity by interfering with neural mechanisms that normally function to limit the release of acetylcholine from airway nerves onto airway smooth muscle. This effectively increases the amount of acetylcholine available to cause contraction of the airway smooth muscle.

How OPs cause dysfunction of airway nerves remains an outstanding question, although preliminary data suggest that the mechanism may vary depending on the allergic status of the individual. Answering this question will be critical for identifying susceptible subpopulations and for designing more effective therapeutic interventions for preventing or reversing OP-induced airway hyperreactivity. More immediately, these findings raise significant questions regarding the use of acetylcholinesterase activity as a point of departure for regulatory action. Furthermore, these findings suggest the possibility that the increased prevalence of asthma is related less to the insects that we live with than to the chemicals we use to kill them.

UCDAVIS VETERINARY MEDICINE

Pamela J. Lein
Professor
University of California, Davis
Tel: +1 530 752 1930
plein@ucdavis.edu
http://www.vetmed.ucdavis.edu/lein-lab/

213

Pesticides: A contributing factor to the increase in asthma?

Email Opens

13,293

Edition Engagement

103,485

Client Pageviews

402

* Total Reach figure is the distribution for this edition of the publication

** Total Engagement of the publication content (email opens, PageSuite and HTML pageviews and Social Media activity)

SEARCH RESULTS:

PESTICIDES AND ASTHMA

ORGANIC SEARCH

OPEN ACCESS **GOVERNMENT**

ISSUE 20 • OCTOBER 2018

Total Reach*

105,376

Total Engagement**

89,088

PROFILE

Polychlorinated biphenyls (PCBs): A persistent environmental health problem

Carolyn R. Klocke, Postdoctoral Scholar and Pamela J. Lein, Professor at University of California, Davis both argue that polychlorinated biphenyls (PCBs) are a persistent environmental health problem today

Polychlorinated biphenyls (PCBs) are a family of synthetic chemicals that were produced in large quantities for industrial and commercial applications beginning in the late 1920s through the late 1970s. PCB mixtures were synthesised globally and identified under several trade names, including Aroclor® (United States and United Kingdom), Clophen® (Germany), Phenclor® (France) and Kanechlor® (Japan). Chemically, PCBs are biphenyls with variable chlorine atoms substituted for the hydrogen atoms in the benzene rings. There are 209 possible PCB compounds – each of which is referred to as a congener – that are named according to the number and position of chlorine substitutions (i.e., lower-chlorinated congeners have lower number designations and higher-chlorinated congeners that have higher number designations).

PCB Cleanup site at Sheboygan Falls, Wisconsin, United States, circa 1990

Image: Wisconsin Department of Natural Resources

While concern regarding adverse health outcomes associated with occupational exposures to PCBs arose as early as the 1930s, by the 1960s and 1970s there was significant alarm about the human health risks of PCBs in the environment. The manufacturing, use and disposal of PCBs had resulted in widespread PCB contamination of air, water and soil, and because PCBs are highly resistant to degradation, they had accumulated in the human food chain and were readily detected in human tissues, including breast milk. These observations, coupled with emerging data linking environmental PCB levels to increased cancer risk in humans and animal models, impelled the United States Congress to institute a ban on PCB production in 1979. This was followed by a global ban on the production and use of PCBs by the Stockholm Convention on Persistent Organic Pollutants in 2001.

In the decades following the ban on PCB production, environmental PCB levels decreased significantly. During this time, basic research scientists identified the biological mechanisms by which PCBs cause cancer and regulatory scientists established "safe" exposure levels for PCBs in the environment and human food supplies based on attributable cancer risk. It was widely believed that the PCB problem was solved and that further research on PCBs was not warranted. However, emerging research on PCBs over the past decade has revealed a number of unexpected findings that suggest the mainstream understanding of PCB exposures and PCB toxicity may be too limited and that PCB regulations focused on cancer outcomes may not be protective of vulnerable populations.

One surprise from current research is that while environmental levels of PCBs are decreasing globally, levels have stabilised or may be increasing in some geographic regions. One explanation is the accelerated release of "legacy" PCBs from ageing products. For example, higher than expected

254

PROFILE

levels of PCBs in the air over the city of Chicago are thought to be due in part to the release of PCBs from ageing paints and caulking materials used to construct municipal buildings during the era when PCBs were intentionally added to these construction materials. The release of legacy PCBs from paints and caulking materials may also explain why PCB levels in the indoor air of elementary schools in the United States exceed the 2009 public health guidelines set by the United States Environmental Protection Agency. Additionally, novel PCBs that were not part of the original industrial mixtures have been detected in the environment and in human tissues. The toxic potential of most of these contemporary PCBs, many of which are lower chlorinated congeners, is largely unknown.

Historically, consumption of contaminated food was thought to be the primary source of PCB exposure in humans, with fish, meat and dairy products comprising the main dietary sources of PCBs. However, recent studies documenting PCB contaminants in the air of major cities and indoor air of municipal buildings, including schools, suggest that inhalation may be a significant and underappreciated source of human exposure. While sources of airborne PCBs, which include both legacy PCBs as well as the lower chlorinated contemporary PCBs, are not yet completely understood, some studies have demonstrated that PCBs can be unintentionally produced during the synthesis of yellow and green paint pigments. Once dried, volatile PCBs can be released into the air (a phenomenon also referred to as "off-gassing"), to be inhaled by humans. Whether the toxic effects of PCB are different if they are inhaled from the air vs. ingested with food remains to be determined.

Another evolution in our understanding of the environmental health impacts of PCBs is the realisation that the developing brain is a vulnerable target of PCBs. PCBs interfere with the growth and maturation of neurons in the developing brain, which shifts the developmental trajectory of the brain in a manner that disrupts normal patterns of connections between brain regions. The magnitude of this effect differs depending on the specific PCB congener involved and whether it is a higher- or lower-chlorinated congener. Interestingly, a pathological change that is common to many neurodevelopmental disorders, including autism and attention deficit hyperactivity disorder (ADHD), is altered connectivity in the brain, and recent studies report that elevated maternal PCB levels are associated with increased risk of having a child with autism or ADHD.

The recent discovery of PCB contamination in the indoor and outdoor air has also raised concern regarding the effects of exposure to airborne PCBs on the developing lung. Lung development continues long after birth, so there is the possibility that inhalation of PCBs interferes with lung development and growth. Since PCBs are known to interfere with neuronal development, it is hypothesized that the inhalation of airborne PCBs may interfere with innervation of the lung, resulting in increased airway hyperreactivity, a hallmark characteristic of asthma. It has been hypothesized that airborne PCBs contribute to the unexplained and perplexing increase in childhood asthma since the 1960s.

Collectively, epidemiologic studies and experimental data from animal models suggest that further investigation of PCBs is warranted to understand how the changing patterns of PCB exposure are contributing to non-cancer outcomes, specifically neurodevelopmental disorders and potentially pediatric asthma. Such work is required to ensure that regulatory policies targeting PCBs are protective of the most vulnerable members of society.

UCDAVIS VETERINARY MEDICINE

Carolyn R. Klocke
Postdoctoral Scholar
University of California, Davis
crklocke@ucdavis.edu
www.linkedin.com/in/carolyn-klocke

Pamela J. Lein
Professor
University of California, Davis
Tel: +1 530 752 1930
plein@ucdavis.edu
www.vetmed.ucdavis.edu/faculty/lein-lab/

255

Email Opens

16,583

Edition Engagement

72,217

Client Pageviews

228

Polychlorinated biphenyls (PCBs): A persistent environmental health problem

* Total Reach figure is the distribution for this edition of the publication

** Total Engagement of the publication content (email opens, PageSuite and HTML pageviews and Social Media activity)

SEARCH RESULTS:

POLYCHLORINATED BIPHENYLS (PCBS) AND HEALTH

ORGANIC SEARCH

Page 1 rank 7

OPEN ACCESS **GOVERNMENT**

ISSUE 21 • JANUARY 2019

Total Reach*

181,234

Total Engagement**

83,284

PROFILE

Are environmental chemicals contributing to the obesity epidemic?

A group of experts from the University of California, Davis and the University of Southern California explain the extent to which environmental chemicals are contributing to the obesity epidemic

Obesity is a metabolic disease characterised by excessive body fat that is defined clinically as having a body mass index (BMI) over 30. For the first time in human history, the number of obese and overweight people is greater than the number of those who are underweight. An estimated 1/3 of the world's population currently meet the clinical definition of obese, and it is predicted that approximately half the world's population will be obese by 2030.

Obesity is a major risk factor for numerous life-threatening diseases, including cardiovascular disease, cancer, and Type 2 diabetes, and in 2014, the global economic burden of obesity was estimated to be $2 trillion. Given the significant health and economic impacts of obesity, there is an urgent need to identify the risk factors involved in the development of obesity. While caloric excess and sedentary lifestyle are classically identified as the main drivers of obesity, these two factors do not explain the recent dramatic rise in the global incidence of obesity.

Factors that are receiving increased scrutiny as potential risk factors for obesity are chemicals that interfere with the action of hormones that regulate metabolism and weight gain. These chemicals, which are referred to as "environmental obesogens", are thought to promote obesity by interfering with metabolic homeostasis.

In support of the obesogen hypothesis, several human studies have demonstrated a positive association between exposure to environmental chemicals and obesity. For example, increased levels of dichlorodiphenyltrichloroethane (DDT), a pesticide once widely used to control mosquitoes, have been linked to higher BMI in both children and adults in multiple populations around the world. More recently, maternal smoking or exposure to near roadway air pollution have been reported to increase the risk of childhood obesity.

While human studies are essential for assessing the feasibility of the environmental obesogen hypothesis, they do not establish that exposure to DDT, air pollutants, or other environmental chemicals, actually cause obesity. This is because it is difficult to tease out whether other factors that coincide with environmental exposure, such as socioeconomic stressors, may be the actual cause. However, studies of laboratory animals maintained in a controlled environment on a fixed diet have confirmed that at least some environmental chemicals can increase the risk of obesity.

Studies of animal and cell culture models are also providing insight as to how environmental chemicals promote an obese phenotype. For example, environmental chemicals can increase fat storage capacity by increasing the number and/or size of fat cells, known as adipocytes. Cell culture experiments suggest that the industrial chemical tributyltin (TBT) increases the number of adipocytes by activating a receptor that promotes the differentiation of stem cells into adipocytes.

> **"Obesity is a global epidemic that affects adults, children and infants, and the rising incidence of obesity and its related diseases shows no signs of levelling off."**

Consistent with these observations, experimental animal models exposed to environmentally relevant concentrations of TBT during development have increased fat accumulation in adipose tissues and the liver compared to control animals. Of concern, these studies suggest that the obesogenic effect of TBT is transgenerational, meaning that TBT may influence obesity risk in not only the individual exposed during development but also in the children and even grandchildren of the exposed individual.

Obesogens have also been shown to affect adipocyte function. Healthy adipocytes not only store energy but also produce hormones that signal throughout the body to control

PROFILE

appetite and energy balance. Air pollutants can interfere with both of these processes, increasing the body's ability to store energy while also decreasing the production of hormones important for metabolic health. The body also contains a special type of adipose tissue called brown adipose, which burns energy to create heat to maintain body temperature. This process is known as thermogenesis, and decreased thermogenesis has been linked to obesity in humans. Developmental exposure to DDT hinders thermogenesis in mice and decreases the expression of genes involved in burning energy.

The hypothalamus is a region of the brain that monitors and responds to changes in the body's hormonal and nutritional status to maintain metabolic homeostasis, and disruption of hypothalamic function can lead to obese phenotypes in animal models. Recent studies in mice have shown that exposure to air pollutants increases inflammation in the hypothalamus, which can interfere with hypothalamic function, and this effect coincides with increased body weight. Another animal study of the obesogenic effects of air pollution linked increased obesity with decreased expression of hormone receptors involved in appetite regulation. Whether environmental chemicals alter the hypothalamus in other ways remains a critical data gap.

Obesity is a global epidemic that affects adults, children and infants, and the rising incidence of obesity and its related diseases shows no signs of levelling off. These alarming trends warrant research focused on understanding the relative contribution of environmental chemicals to the development of obesity, especially since exposures to environmental chemicals are modifiable risks. However, an effective public health strategy requires determining which of the tens of thousands of chemicals in the human environment have obesogenic activity. It may be possible to address this problem by leveraging cell culture models that express receptors that drive adipocyte differentiation or are implicated in controlling feeding behaviours. Chemicals found to activate these receptors in cell culture at environmentally relevant concentrations could then be studied in preclinical models to confirm obesogenic potential at the organism level. In addition, it will be important to educate the public – especially pregnant women – as to the effects of environmental exposures on the disease risk in their child. Given the increasing evidence linking chemical exposure in utero to increased risk of obesity, it will be important to educate parents on the approaches for mitigating or reducing their exposure to suspected environmental obesogens before, during and after pregnancy, with the goal of reducing the risk of obesity in their children.

References

1 Heindel, J. J. et al. Metabolism disrupting chemicals and metabolic disorders. Reprod. Toxicol. 68, 3-33, doi:10.1016/j.reprotox.2016.10.001 (2017).

2 Janesick, A. S. & Blumberg, B. Obesogens: an emerging threat to public health. Am. J. Obstet. Gynecol. 214, 559-565, doi:10.1016/j.ajog.2016.01.193 (2016).

UC DAVIS VETERINARY MEDICINE

Carolyn R. Klocke, PhD
Postdoctoral Scholar
University of California, Davis
crklocke@ucdavis.edu
www.linkedin.com/in/carolyn-klocke

Sanjay Sethi, PhD
Postdoctoral Scholar
University of Southern California
Tel: +1 323 671 1549
ssethi@chla.usc.edu

Pamela J. Lein, PhD
Professor
University of California, Davis
Tel: +1 530 752 1630
pjlein@ucdavis.edu
www.vetmed.ucdavis.edu/faculty-lab/pamela-lein
www.twitter.com/UCDAVISTEST1

Are environmental chemicals contributing to the obesity epidemic?

Email Opens

15,619

Edition Engagement

67,349

Client Pageviews

316

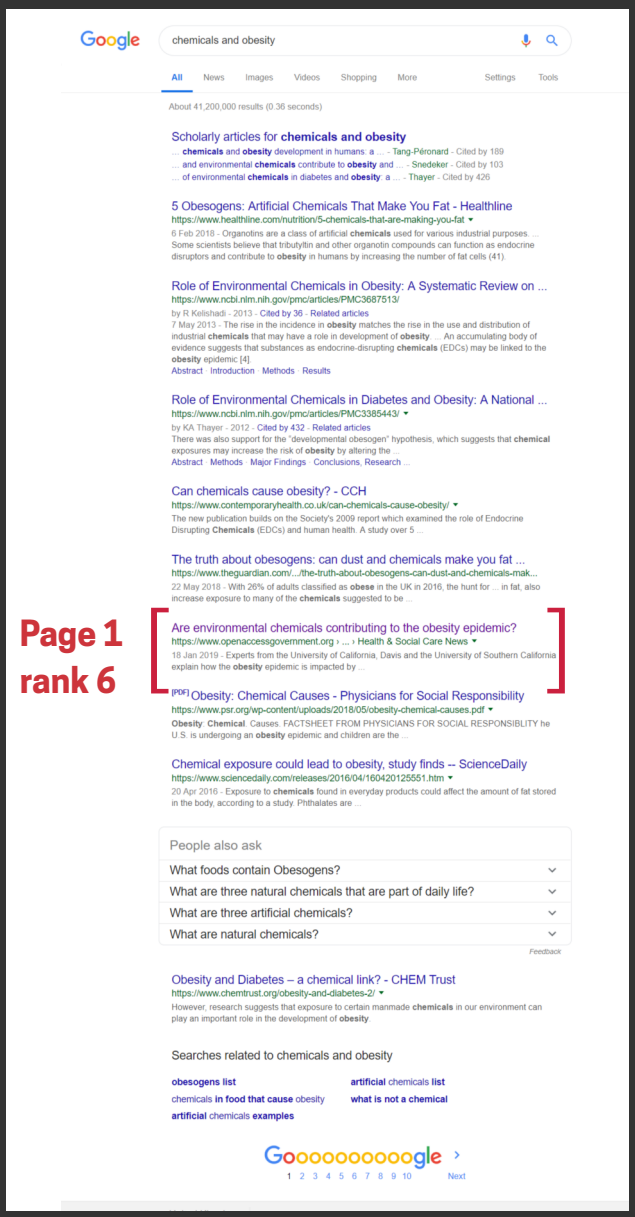
* Total Reach figure is the distribution for this edition of the publication

** Total Engagement of the publication content (email opens, PageSuite and HTML pageviews and Social Media activity)

SEARCH RESULTS:

CHEMICALS AND OBESITY

ORGANIC SEARCH



2 LINKING DOMAINS
4 INBOUND LINKS

DIGITAL CONTENT

Banner on Health page
from January 2018

Reach*
477,840

Engagement**
514

* Reach figure is the audience for the pages where your banner has appeared since it went live
** Engagement is the number of clicks your banner has received

Stakeholder page
from January 2018

Engagement**
91

** Engagement is the number of views your stakeholder page has received

Special Report – Developmental neurotoxicity testing – the need for a new approach
from June 2018

Engagement**
164

** Engagement is the number of views your special report page has received

Special Report – E-Cigarettes: Safer But Not Safe
from September 2018

Engagement**
1,444

** Engagement is the number of views your special report page has received

All viewing and visitor stats provided by Adjacent Digital Politics Limited are guaranteed and correct at the time of the report. They are compiled using industry leading organisations and aids such as PageSuite and Google Analytics. The company is strongly committed to under-promising and over-delivering on its distribution figures and has an anti-spamming policy complying with data protection advice and legislation. The company endeavours to ensure its distribution data is of the highest quality in relation to cleanliness and relevance – this is supported by its low bounce rates and low un-subscribes.

The company does not offer expected viewing or visitor numbers either at, or following, the point of sale and does not accept any responsibility for open rates or interaction between the recipient and the advertiser. The advertiser is strongly advised to monitor all visitor data to its website and social media profiles to ensure that the marketing exercises undertaken are not wasted. We also encourage the advertiser to work closely with the company's production and copy writing team to ensure the messages being distributed are written to their optimum level thereby maximising the chances of creating an impact.