Integral Ecology, Epigenetics and the Common Good, Reflections on *Laudato Si* and Flint, Michigan

published as: Butkus, Russell A and Steven A Kolmes (2017) Integral Ecology, Epigenetics and the Common Good, Reflections on Laudato Si and Flint, Michigan. Journal of Catholic Social Thought 14(2):291-320

Russell A. Butkus, PhD.
Department of Theology and Environmental Studies
University of Portland,
5000 N. Willamette Blvd, Portland, OR 97203
butkus@up.edu,
503-943-7370

Steven A. Kolmes, PhD.
Rev. John Molter C.S.C. Chair in Science
Chair Environmental Studies Department
University of Portland
5000 N Willamette Blvd, Portland, OR 97203
kolmes@up.edu
503-943-7291

Introduction

With the release of *Laudato Si* (2015) Pope Francis has introduced new conceptual language into Catholic social teaching (CST), what he has called "integral ecology." His intent appears to be grounded in the realization that "It is essential to seek comprehensive solutions which consider the interactions with natural systems themselves and with social systems" (*LS*, no. CXXXVIII). Pope Francis goes on to make the case that "We are faced not with two separate crises, one environmental and the other social, but rather with one complex crisis with is both social and environmental" (*LS*, no. CXXXVIII). Consequently, in order to solve this crisis we need to utilize "an integrated approach to combating poverty, restoring dignity to the excluded, and at the same time protecting nature" (*LS*, no. CXXXVIII). This perspective represents a major development in CST whereby the encyclical connects the dots between ecology/environment, economics and society, three essential aspects of what many in the environmental community and elsewhere see as indispensable for humanity to achieve a sustainable relationship with the Earth. While this is extremely important for articulating a Catholic vision of sustainability, that is not the direction we take in this article. Rather our intent is to use the concept of integral ecology to do three things: (1) examine a current case in the U.S. that has received significant media attention as well as notoriety—the water crisis in Flint, Michigan; (2) describe how our recent understanding of the epigenetic impacts of environmental toxins casts a new and ominous light on this crisis and on other instances of environmental toxin exposure, and (3) propose some ideas on how epigenetic research might enlarge our interpretation of basic aspects of CST highlighted in *Laudato Si* such as human dignity, justice and the common good.

The baseline of the situation in Flint is ecological insofar as it has to do with access to clean and safe drinking water for its residents—a basic ecological necessity for all humans. Consider for a moment the following observations on water from *Laudato Si*:

- "Fresh drinking water is an issue of primary importance, since it is indispensable for human life and for supporting terrestrial and aquatic systems" (*LS*, no. XXVIII).
- "One particular serious problem is the quality of water available to the poor. Every day, unsafe water results in many deaths and the spread of water-related diseases, including those caused by microorganisms and chemical substances" (*LS*, no. XXIX).
- "Even as the quality of available water is constantly diminishing, in some places there is a growing tendency, despite its scarcity, to privatize this resource, turning it into a commodity subject to the laws of the market. Yet *access to safe drinking water is a basic and universal human right, since it is essential to human survival and, as such, is a condition for the exercise of other human rights*" (*LS*, no. XXX).

From the perspective of CST the situation in Flint is alarming on two counts. First the right to safe drinking water was abrogated as a result of poor and perhaps criminal decisions by official and institutional authorities. Second, as a result of these poor decisions the municipal water source became contaminated with high levels of lead. While estimates vary somewhere between 8000-9000 children under the age of six were

exposed to lead—a developmental neurotoxin. This became a public health emergency that represents a serious breach to the right to health and bodily integrity.

Why did this occur? Primarily it was an economic decision to lower costs by switching to the Flint River rather than Lake Huron. While this is true, taken by itself it masks broader and deeper economic problems in Flint. Like many "rust belt" cities Flint has been in economic decline for years largely as a result of the loss of heavy industry, particularly the auto industry. A city with a population of a little over 100,000, 41.5% of Flint's residents are below the poverty line. This raises the need of what Pope Francis has called an "economic ecology." "Today" he states, "the analysis of environmental problems cannot be separated from the analysis of human, family, work-related and urban contexts, nor from how individuals relate to themselves, which leads in turn to how they relate to others and to the environment" (*LS*, no. CXLI). Unless the economic situation is adequately addressed, even if the problem of lead in their drinking water is solved, the wounds in Flint will continue to fester.

Fundamental for integral ecology is society, that is, social and human ecology. The debacle in Flint was propagated in large part by the failure of social institutions particularly the Michigan Department of Environmental Quality. The consequences of that dysfunctional entity are exacerbated by the fact that Flint is by and large predominantly African-American. Social ecology cannot overlook the very real possibility that underlying this tragedy is racial inequality and very likely an issue of social, racial and environmental justice. The social and human analysis does not end here. As noted above the situation in Flint became a public health event whereby thousands were exposed to lead. Human ecology requires an analysis of the biological impacts

including the immediate and long range, even generational, health consequences of toxic exposure. It is here that epigenetic impacts emerge as an instance of intergenerational injustice, and that the connections between the present, the future, and the impacts of poverty become clear, as *Laudato Si* states

- "Furthermore, our inability to think seriously about future generations is linked to our inability to broaden the scope of our present interests and to give consideration to those who remain excluded from development. Let us not only keep the poor of the future in mind, but also today's poor, whose life on this earth is brief and who cannot keep on waiting." (*LS*, no. CLXII)

What follows is a summary of the events that led to the debacle of Flint, Michigan, and a subsequent discussion of epigenetic impacts of environmental toxins connecting Flint to a broader set of examples.

Fiasco in Flint, Michigan

When the State of Michigan appointed an emergency manager to take over administration of the City of Flint, in November of 2011, it was supposed to help the financially struggling, primarily African-American community, maintain basic services in the face of insufficient local revenues. There was debate from the start about the loss of local control, and whether elected local officials ought to be left in control of their community, but the Governor of Michigan appointed what turned out to be a series of rapidly shifting emergency managers nonetheless. This action eventually led to thousands of young minority children suffering lead poisoning at levels that has the potential to diminish their future prospects, and as we will see below to even much worse than this.

Flint originally relied on water from the City of Detroit's water system, which might not sound appetizing on first glance since many people think of Detroit as a struggling rust-belt city itself, but Detroit draws its water from Lake Huron, the third largest body of freshwater on Earth and fed in considerable part by underground springs. Lake Huron water is easily treated to produce pure drinking water. In a cost-saving move, the emergency manager for Flint decided to disconnect from the existing water source and move Flint to join a new water source, the Karegnondi Water Authority, which would build a new pipeline to Lake Huron and supposedly supply drinking water less expensively to Flint and other communities. The problem with this plan was that the pipeline to Lake Huron did not in fact yet exist, and the emergency manager decided to draw Flint's drinking water from the highly polluted Flint River until the new pipeline could be eventually constructed. Other communities joining the Karegnondi Water Authority continued to use water from Detroit until the new pipeline could be built. The emergency manager's decision to use Flint River water, which is quite corrosive, combined with old lead pipelines the Flint water system relied upon, led to what can only be construed as a tragedy.

In April of 2014, with a permit from the Michigan environmental regulators in hand, the City of Flint was switched to Flint River water as a drinking water source. Citizens immediately began to complain about discoloration and foul tastes, and in short order advisories to boil the water due to fecal bacterial contamination begin to be issued. In October of 2014 a General Motors plant in Flint stopped using the City water because it was corroding car parts, and the State of Michigan spent $440,000 to provide a special connection to Lake Huron water for the factory while Flint residents continued to receive

substandard water. In this case the old saying “What is good for General Motors is good for the country” would have been true, but only GM got the noncorrosive water.

In January of 2015, aware of the injustice unfolding in Flint, the City of Detroit’s water system offered to waive a $4 million dollar reconnection fee and begin to provide safe drinking water to Flint again. The emergency manager declined, and the citizens of Flint were reassured by officials that their water was safe. In January and February of 2015 water tests showing high lead levels began to surface, with residential tests coming back as high as 397 parts per billion, well above any level that could conceivably be called safe. In October of 2015 there was a flurry of EPA warnings to an enigmatically inactive Michigan Department of Environmental Quality, but the State of Michigan, declaring the financial emergency over, dumped the crisis back on local officials. Subsequent developments included the following: the discovery of children with clinical lead poisoning according to blood tests, warnings from experts that it was the lack of an inexpensive corrosion control process that was making the water so dangerous, and month after month of toxic water coming out of faucets in the homes of poor people. From this point, with a public outcry in full voice, the State of Michigan began providing water filters to Flint residents; churches and other groups began a large scale donation of bottled water, and in general much attention began to be paid to what was an ignored crisis.

The true depth of this tragedy is not yet apparent from what we have discussed. Lead and other heavy metals produce epigenetic changes, explained below, that impact the health of not just one generation but at least three generations of people and perhaps

more.[1] Lead exposure is known to cause miscarriages, stillbirths, infertility, kidney damage, and developmental problems including eventual negative impacts on behavior and intelligence. Only recently are we beginning to learn the mechanisms of how epigenetic changes due to lead poisoning produce multigenerational impacts.[2] The Flint River water therefore was actually a generational curse that will reach across decades through the epigenome of those exposed to high levels of lead in Flint. Understanding the epigenetic process and the very real potential for epigenetic dysregulation and subsequent negative health consequences is crucial for any ethical analysis of what has occurred in Michigan.

This article will summarize the biological mechanisms involved in one type of epigenetic alteration that is caused by anthropogenic environmental toxins and discuss the known developmental and health impacts and inter-generational heritability of those epigenetic alterations. This analysis will also consider the ethical implications of the recent research by considering the question: What does the epigenetic research on toxic exposure mean for understanding and interpreting the basic characteristics of Catholic social teaching such as human dignity, the common good, human rights and justice? The

---

[1] J. Richard Pilsner, Howard Hu, Adrienne Ettinger, Brisa N. Sánchez, Robert O.Wright, David Cantonwine, Alicia Lazarus, Héctor Lamadrid-Figueroa, Adriana Mercado-García, Martha Maria Téllez-Rojo and Mauricio Hernández-AvilaSource, "Influence of Prenatal Lead Exposure on Genomic Methylation of Cord Blood DNA," *Environmental Health Perspectives* Vol. 117 (2009): 1466-1471; Arko Sen, Nicole Heredia, Senut, Marie-Claude, Pablo Cingolani, Arko Sen, Adele Kruger, Asra Shaik, Helmut Hirsch, Steven T Suhr, and Douglas Ruden, "Epigenetics of early-life lead exposure and effects on brain development," *Epigenomics* 4(6) (2012): 665–674.

[2] Marie-Claude Senut, Pablo Cingolani, Arko Sen, Adele Kruger, Asra Shaik, Helmut Hirsch, Steven T Suhr, and Douglas Ruden, "Epigenetics of early-life lead exposure and effects on brain development," *Epigenomics* 4(6) (2012): 665–674.

article concludes with an ethical reflection on the necessary remedial actions for justice in Flint, MI.

Epigenetics

There has been a longstanding idea that human physical characteristics are the result of an interplay between the genes encoded in our DNA and the environment in which we are raised, with the genes themselves passing unaltered through individuals from one generation to another. This idea credited physical attributes to genetic recombinations of maternal and paternal genes into new patterns. This seemed like settled science for many decades. The genes in our DNA, read rather like the words in a book of instructions by living cells, were themselves considered largely aloof from the fray of life. They were believed to remain unaltered, unless a one-in-a-million odds mutation in the genetic code occurred. We now know that this is only part of the story. While the DNA sequences of genes may show a remarkable degree of stability over generations, gene activity can be altered in heritable ways by interactions with the environment. We refer to the various changes that alter gene activity without actually changing the DNA sequence as epigenetic processes.

As scientists have worked recently to unravel the implications of this new understanding, it has become clear that there are environmental toxins that many people are exposed to on a daily basis that have epigenetic impacts. Moreover many of these toxins are the result of human activities, and the exposure of children to them has been previously discussed in terms of ethical implications and health impacts for the life of a

single growing individual.[3] Very specific timing of exposures may produce developmental windows of vulnerability for epigenetic distortions by materials like endocrine disruptors.[4] Other materials like Arsenic can cause epigenetic distortions at any point in a person's life cycle.[5] The new realization that there are heritable epigenetic alterations that cause various human diseases raises ethical concerns to a new and different level.

Types of Epigenetic Alterations

The DNA sequence of genes can be thought of in a simplified way as a series of letters that can be read like an instruction manual to provide information about how to build and operate a human being. There are several ways in which genetic expression can be changed without altering the DNA sequence of genes.[6] In the interest of achieving a reasonable length for this article, we will, using the best understood science, focus solely on DNA-methylation.[7] Other epigenetic distortions can also lead to disease, but DNA-

[3] Russell A. Butkus and Steven A. Kolmes, "Children in Jeopardy: Anthropogenic Toxins and Childhood Exposure," *The Journal of Catholic Social Thought* 7 (2010): 83-114.
[4] T. T. Schug, A. Janesick, B. Blumberg, J. J. Heindel, "Endocrine disrupting chemicals and disease susceptibility," *Journal of Steroid Biochemistry and Molecular Biology* 127(3-5) (2010) :204-15.
[5] X Ren, McHale CM, Skibola CF, Smith AH, Smith MT, Zhang L, "An emerging role for epigenetic dysregulation in arsenic toxicity and carcinogenesis," *Environmental Health Perspectives* 119(1) (2011) :11-9.
[6] Changes in the histone proteins surrounding the DNA can occur, and changes due to small non-coding RNAs are possible as well (Michael K. Skinner, "Role of epigenetics in developmental biology and transgenerational inheritance," *Birth Defects Research* (Part C) 93 (2011): 51-55.). However, neither of those processes are as well understood in terms of disease impacts and transgenerational heritability as is DNA-methylation, so we will focus in our limited space on DNA-methylation alone.
[7] It has recently been realized that hydroxymethyl groups, which are larger than methyl groups because they have an oxygen and hydrogen replacing one of the simple hydrogens of a methyl group, can also attach to DNA and have epigenetic impacts, but this is a recently recognized and hence less understood process that we will not delve into.

methylation provides so many examples that there is no reason for this article to go beyond one type of epigenetic change.

The code in which DNA is written has only four possible subcomponents, chemicals called adenine, guanine, cytosine, and thymine. Cellular biochemistry "reads" these subcomponents in "triplets" of three units at a time, so that the four subcomponents can occur in a number of patterns and code for different messages. There are 64 possible triplet combinations of the four subcomponents possible. In a simplified explanation we can think of a long sequence of triplets being read as a group comprising a gene that encodes for some physical trait.

Methylation means the attachment to another molecule of a methyl group, the latter is a carbon with three hydrogens attached to it, written $–CH_3$. DNA-methylation that impacts genetic activity takes place almost entirely at one type of specific DNA location, it is the addition of a methyl group at the number 5 carbon location on the 6-sided ring structure of cytosine, resulting in 5-methylcytosine being formed. This addition of a methyl group can change DNA activity at that site.[8] Our normal biochemistry provides our cells with the capacity to add or remove methyl groups from cytosine as needed to increase or decrease the activity of specific genes. Without the interference of environmental toxins, normal DNA-methylation acts rather like an "on/off" switch for normal and dynamic gene expression.

Some level of DNA-methylation is always a part of normal human biology and shifting patterns of DNA-methylation are part and parcel of typical developmental changes. In fact, regulatory changes in levels of DNA-methylation of specific genes are

[8] This typically occurs in DNA where a cytosine is located next to a guanine.

fundamental to normal human embryonic and adult biology. However, when an unusually high level of DNA-methylation occurs, it means that larger biochemicals called methyl-binding proteins can attach to the methyl groups (on the cytosines) and ultimately silence the activity of the methylated gene. The opposite can be true as well. If something in the environment prevents the normal level of DNA-methylation from taking place, the genes lacking their typical level of methyl groups (on their cytosines) are more accessible to the cellular machinery that "reads" the genetic sequences on the DNA to produce proteins, and this produces an excessive level of activity for those genes. Environmental toxins can produce levels of DNA-methylation that are either atypically high or atypically low, therefore leading to lowered or raised levels of gene activity, both of which can produce a variety of human diseases, depending on the gene(s) involved.

Toxin Exposure, DNA-methylation, and Disease

There are numerous examples of DNA-methylation changes in humans that have health impacts, and we know even more examples of environmental toxins altering DNA-methylation patterns in laboratory animals that damage health and development. The examples we describe below are illustrative rather than comprehensive. We have chosen only a few examples highlighting how exposure to an environmental toxin that produces DNA-methylation changes has a clear link to one or more diseases. For the interested reader, there are thorough reviews of a variety of epigenetic mechanisms, beyond what we can discuss in this article.[9]

[9] Lifang Hou, Xiao Zhang, Dong Wang and Andrea Baccarelli, "Environmental chemical exposures and human epigenetics," *International Journal of Epidemiology* Volume 41(1) (2012):79-105.

The human exposure examples cited here frequently have issues of social justice associated with them. Inner city dwellers or industrial workers or agricultural workers are often exposed to environmental toxins in a way people with more financial resources can avoid. When human activity results in toxin exposure that prevents a person from fulfilling their genetic potential, and this loss is passed on through generations, an arena of social responsibility, previously unaddressed, emerges. As Medawar and Medawar wrote[10], "genetics proposes, epigenetics disposes" but perhaps it is really other people who are causing exposure to epigenetic modifiers and therefore "disposing" part of the genetic potential for generations of disadvantaged humans.

Lead, Cadmium, Nickel and DNA-methylation

Exposures to heavy metals are associated with overall changes in DNA-methylation in cases where the metals are well known to have associations with specific diseases, but individual genetic regions linked to those diseases that are methylated have to date only occasionally been identified. Increasing levels of lead in a mother's patella (her knee cap) detected via special X-rays were accompanied by increased DNA-methylation in umbilical cord blood.[11] Lead exposure is linked to numerous health impacts, including poor pregnancy outcomes and problems with development and cognitive functions. Mothers in Detroit with high neonatal blood lead levels had altered DNA methylation at 564 loci in their children's neonatal blood, and it is therefore probable that lead exposure during pregnancy goes on to affect the DNA methylation of

[10] P.B. Medewar and J. S. Medewar, *Aristotle to Zoos: A Philosophical Dictionary of Biology* (Cambridge, Harvard University Press, 1983), 114.
[11] Pilsner et. al., "Influence of Prenatal Lead Exposure," 1466-1471.

the fetal germ cells and alter DNA methylation in their grandchildren.[12] Li *et al.* found that increased lead exposure in adults resulted in changes in ALAD gene methylation, that in turn produced less gene activity, and the ALAD gene is involved in producing an enzyme vital to the hemoglobin production needed for healthy red blood cells.[13] Increased cadmium exposure is associated with decreased DNA-methylation in several genetic regions for Andean women.[14] Researchers found that cadmium-induced transformation of human prostate cells to a malignant state involved tumor suppressor gene inactivation associated with significant increases of overall DNA-methylation levels.[15] Cadmium exposure is linked to cancer, kidney damage, brittle bones, and developmental problems. Prenatal mercury exposure altered methylation at ten genetic sites associated with a high-risk neurodevelopmental profile.[16]

---

[12] Arko Sen et. al., "Multigenerational epigenetic inheritance in humans: DNA methylation changes associated with maternal exposure to lead," *Nature, Science Reports* Sept 29;5 (2015):14466. doi: 10.1038/srep1446; Marie-Claude Senut, et. al., "Epigenetics of early-life lead exposure," *Epigenomics* 4(6): 665–674.

[13] Chungping Li, Ming Xu, Sumeng Wang, Xiaolin Yang, Shourong Zhou, Jingping Zhang, Qizhan Liu, Yujie Sun, "Lead exposure suppressed *ALAD* transcription by increasing methylation level of the promoter CpG islands," *Toxicology Letters* 203 (2011):48–53.

[14] Mohammad Bakhtiar Hossain, Marie Vahter, Gabriela Concha, and Karin Broberg, "Low-Level Environmental Cadmium Exposure Is Associated with DNA Hypomethylation in Argentinean Women," *Environmental Health Perspectives* June; 120(6) (2012): 879–884.

[15] L. Benbrahim-Talla, R.A. Waterland, A.L. Dill, M.M. Webber, M.P. Waalke, "Tumor suppressor gene inactivation during cadmium-induced malignant transformation of human prostate cells correlates with overexpression of de novo DNA methyltransferase," *Environmental Health Perspectives* 115(10) (2007):1454-9.

[16] Jennifer Z.J. Maccani, Devin C. Koestler, Barry Lester, E. Andrés Houseman, David A. Armstrong, Karl T. Kelsey, and Carmen J. Marsit, "Placental DNA Methylation Related to Both Infant Toenail Mercury and Adverse Neurobehavioral Outcomes," *Environmental Health Perspectives* 123(7) (2015):723-729.

Other metals producing altered DNA-methylation patterns in specific genes exist. Nickel exposure leads to DNA-methylation of the promoter region of the DNA repair gene *O6-methylguanine DNA methyltransferase (MGMT)* which silences the action of this gene in lung cancer cells[17] as well as other types of epigenetic changes involving micro-RNAs that are beyond the scope of the present article for brevity's sake.[18] Chronic exposure to chromium produces lung cancer specimens in which there is silencing of the tumor suppressor *p16INK4a* due to DNA-methylation of its' promoter region.[19] A recent review article provides a detailed discussion of possible mechanisms for these and other epigenetic impacts on humans of metal exposure.[20]

Polycyclic Aromatic Hydrocarbons and Asthma

Exposure to polycyclic aromatic hydrocarbons (PAHs) is associated with a number of human diseases. PAHs are a related group of over 200 compounds that come from sources as diverse as diesel or gasoline exhaust, wood smoke, coal burning, and even parking lot sealant. PAH exposure has been implicated by earlier studies in health

[17] W. Ji, L.Yang , L.Yu, J.Yuan, D. Hu, W. Zhang, Y. Pang, W. Li, J. Lu, J. Fu, J. Chen, Z. Lin, W. Chen, Z. Zhuang, "Epigenetic silencing of O6-methylguanine DNA methyltransferase gene in NiS-transformed cells," *Carcinogenesis* 29 (2008):1267-75.
[18] W. Ji, L. Yang, J. Yuan, L. Yang, M. Zhang, D. Qi, X. Duan, A. Xuan, W. Zhang, J. Lu, Z. Zhuang, G. Zeng, "MicroRNA-152 targets DNA methyltransferase 1 in NiS-transformed cells via a feedback mechanism," *Carcinogenesis* 34(2) (2013):446-53.
[19] K. Kondo,Y. Takahashi, Y. Hirose, T. Nagao, M. Tsuyuguchi, M. Hashimoto, A. Ochiai, Y. Monden, A. Tangoku, "The reduced expression and aberrant methylation of p16(INK4a) in chromate workers with lung cancer," *Lung Cancer* 53 (2006):295-302.
[20] Ricardo Martinez-Zamudioa and Hyo Chol Ha, "Environmental epigenetics in metal exposure, *Epigenetics* 6:7, 820-827, DOI: 10.4161/epi.6.7.16250.

risks as diverse as breast cancer,[21] cancers of the bladder and lungs,[22] fatal coronary artery disease,[23] developmental delay, reduced IQ at 5 years of age, symptoms of being anxious/depressed and attention problems.[24] Prenatal PAH exposure leads to lower overall DNA-methylation in umbilical cord blood white blood cells.[25]

Researchers looked at DNA-methylation of the *IFN-gamma* gene promoters, which are responsible for the ability of the body to produce Interferon. Loss of Interferon-production capacity in lymphocytes (white blood cells) as well as other cellular events, are biochemical changes associated with early asthma onset. Increased maternal exposure to PAHs (measured by personal maternal air monitoring during pregnancy) was associated with increased DNA-methylation in the *IFN-gamma* genetic

---

[21] Marilie D. Gammon, Regina M. Santella, Alfred I. Neugut, Sybil M. Eng, Susan L. Teitelbaum, Andrea Paykin, Bruce Levin, Mary Beth Terry, Tie Lan Young, Lian Wen Wang, Qiao Wang, Julie A. Britton, Mary S. Wolff, Steven D. Stellman, Maureen Hatch, Geoffrey C. Kabat, Ruby Senie, Gail Garbowski, Carla Maffeo, Pat Montalvan, Gertrud Berkowitz, Margaret Kemeny, Marc Citron, Freya Schnabel, Allan Schuss, Steven Hajdu, and Vincent Vinceguerra, "Environmental Toxins and Breast Cancer on Long Island. I. Polycyclic Aromatic Hydrocarbon DNA Adducts," *Cancer Epidemiology, Biomarkers and Prevention* 11 (2002): 677

[22] C. Bosetti, P. Boffetta, C. La Vecchia. Occupational exposures to polycyclic aromatic hydrocarbons, and respiratory and urinary tract cancers: a quantitative review to 2005. *Annals of Oncology* 2007 Mar.18(3) (2007): 431-46.

[23] I. Burstyn, H. Kromhout, T. Partanen, O. Svane, S. Langård, W. Ahrens, T. Kauppinen, I. Stücker, J. Shaham, D. Heederik, G. Ferro, P. Heikkilä, M. Hooiveld, C. Johansen, B.G. Randem, P. Boffetta, "Polycyclic aromatic hydrocarbons and fatal ischemic heart disease," *Epidemiology* Nov;16(6) (2005): 744-50.

[24] Frederica P. Perera, Deliang Tang, Shuang Wang, Julia Vishnevetsky, Bingzhi Zhang, Diurka Diaz, David Camann, and Virginia Rauh, "Prenatal polycyclic aromatic hydrocarbon (PAH) exposure and child behavior at age 6–7 years," *Environmental Health Perspectives* 120(6):921–926 (2012); http://dx.doi. org/10.1289/ehp.1104315.

[25] J.B. Herbstman, D. Tang, D. Zhu, L. Qu, A. Sjödin, Z. Li, D. Camann, F.P. Perera, "Prenatal exposure to polycyclic aromatic hydrocarbons, benzo[a]pyrene-DNA adducts, and genomic DNA methylation in cord blood," *Environmental Health Perspectives* 120(5) (2012): 733-8.

region of cord blood of their children.[26] An epigenetic change in a specific gene region known to be associated with the onset of asthma was therefore observed. For a gene (*FOXP3*) that impacts *IFN-gamma* levels, asthmatic children had both higher PAH exposure and higher DNA-methylation levels in the *FOXP3* gene region.[27] In a separate study of maternal exposure to PAHs, DNA-methylation of the *ACSL3* genetic region was significantly associated with both maternal airborne PAH exposure and with parental reports of asthma symptoms in children prior to age 5.[28] Therefore DNA-methylation of a third genetic sequence due to transplacental PAH exposure is also implicated in childhood asthma. Saudi children with asthma had higher levels of blood serum PAHs than did nonasthmatic controls.[29]

Arsenic and Cancer

Arsenic exposure is associated with increased rates of cancer, neurological diseases, cardiovascular and liver diseases, respiratory diseases, and other serious health

---

[26] Wan-Yee Tang, Linda Levin, Glenn Talaska, Yuk Yin Cheung, Julie Herbstman, Deliang Tang, Rachel L. Miller, Frederica Perera, Shuk-Mei Ho, " Maternal Exposure to Polycyclic Aromatic Hydrocarbons and 5′-CpG Methylation of Interferon-γ in Cord White Blood Cells," *Environmental Health Perspectives* 120 (2012):1195-1200.

[27] K.M. Hew, A. I. Walker, A. Kohli, M. Garcia, A. Syed, C. McDonald-Hyman, E. M. Noth, J. K. Mann, B. Pratt, J. Balmes, S. Katharine Hammond, E. A. Eisen and K. C. Nadeau, "Childhood exposure to ambient polycyclic aromatic hydrocarbons is linked to epigenetic modifications and impaired systemic immunity in T cells," *Clinical & Experimental Allergy* 45 (1) (2015): 238–248.

[28] Frederica Perera , Wan-yee Tang , Julie Herbstman, Deliang Tang, Linda Levin, Rachel Miller, Shuk-mei Ho, "Relation of DNA Methylation of 5′-CpG Island of *ACSL3* to Transplacental Exposure to Airborne Polycyclic Aromatic Hydrocarbons and Childhood Asthma," *PLoS ONE* 4(2) (2009): e4488.

[29] Nasser Al-Daghri, Majed S Alokail, Sherif H Abd-Alrahman, Hossam M Draz, "Polycyclic aromatic hydrocarbon distribution in serum of Saudi children using HPLC-FLD: marker elevations in children with asthma," *Environmenatl Science Pollution Research* 21 (2014):12085–12090 DOI 10.1007/s11356-014-3108-0.

issues.[30] The skin cancer basal cell carcinoma is linked to arsenic exposure.[31] Prenatal maternal arsenic exposure from water in Thailand altered gene expression in human newborns.[32] For most people exposure to arsenic comes mainly from ingesting contaminated food and water, although there are occupational exposures in the use of pesticides, wood preservatives, and other materials, and exposures associated with living in proximity to mining or smelting operations. Mouse experiments have shown that Arsenic does not cause many tumors when adult mice are exposed to it, but transplacental exposure of the mouse fetus during gestation produces a variety of tumors when the young have grown to adulthood. The most damaging circumstance is when both gestational and subsequent adult exposure takes place.[33]

---

[30] Marie Vahter, "Health Effects of Early Life Exposure to Arsenic," *Basic & Clinical Pharmacology & Toxicology* Vol. 102, Issue 2 (2008): 204–211.

[31] G. Leonardi, M. Vahter, F. Clemens, W. Goessler, E. Gurzau, K. Hemminki, R. Hough, K. Koppova, R. Kumar, P. Rudnai, S. Surdu, T. Fletcher, "Inorganic Arsenic and Basal Cell Carcinoma in Areas of Hungary, Romania, and Slovakia: A Case–Control Study," *Environmental Health Perspectives* 120 (2012):721–726; http://dx.doi.org/10.1289/ehp.1103534.

[32] R. C. Fry, P. Navasumrit, C. Valiathan, J.P. Svensson, B.J. Hogan, M. Luo, S. Bhattacharya, K. Kandjanapa, S. Soontararuks, S. Nookabkaew, C. Mahidol, M. Ruchirawat, L. D. Samson, "Activation of inflammation/NF-kappaB signaling in infants born to arsenic-exposed mothers," *PLoS Genetics* Nov. 3(11) (2007): e207. doi:10.1371/journal.pgen.0030207.

[33] M.P. Waalkes, J. M. Ward, B. A. Diwan, "Induction of tumors of the liver, lung, ovary and adrenal in adult mice after brief maternal gestational exposure to inorganic arsenic: promotional effects of postnatal phorbol ester exposure on hepatic and pulmonary, but not dermal cancers," *Carcinogenesis* 25(1) (2004):133–141; M. P. Waalkes, J. M. Ward, J. Liu, B. A. Diwan, "Transplacental carcinogenicity of inorganic arsenic in the drinking water: induction of hepatic, ovarian, pulmonary, and adrenal tumors in mice," *Toxicology and Applied Pharmacology* 186(1) (2003) :7–17; E. J. Tokar, B. A. Diwan, J. M. Ward, D. A. Delker, M. P. Waalkes, "Carcinogenic effects of "whole-life" exposure to inorganic arsenic in CD1 mice," *Toxicological Sciences* 119(1) (2011):73–83.

Animal studies have also shown that gestational Arsenic exposure changes DNA-methylation.[34] Low level *in utero* human exposure to arsenic has also been linked in umbilical cord blood studies to changes in DNA-methylation.[35] Low level chronic exposure in laboratory experiments on human skin cells (in HaCaT cells originally derived from adult skin cells) indicates that arsenic competes for methyl donors with various cellular processes, and represses the activity of the DNA methyltransferase genes, both of which would produce changes in DNA-methylation levels.[36] Laboratory exposure of human lung cancer cells to sodium arsenate resulted in significant increases in DNA-methylation within the promoter region of a tumor suppressor gene.[37] In a study of 64 people exposed to different levels of arsenic via drinking water, people with high levels of exposure showed signs of increased overall genomic DNA-methylation.[38] Prenatal Arsenic exposure is associated with overall DNA-methylation in cord blood DNA, and

---

[34] Yaxiong Xie, Jie Liu, Lamia Benbrahim-Tallaa, Jerry M. Ward, Daniel Logsdon, Bhalchandra A. Diwan, and Michael P. Waalkes, "Aberrant DNA methylation and gene expression in livers of newborn mice transplacentally exposed to a hepatocarcinogenic dose of inorganic arsenic," *Toxicology* 236(1–2) (2007): 7–15.

[35] Devin C. Koestler, Michele Avissar-Whiting, E. Andres Houseman, Margaret R. Karagas, and Carmen J. Marsit, "Differential DNA Methylation in Umbilical Cord Blood of Infants Exposed to Low Levels of Arsenic in Utero," *Environmental Health Perspectives* 121 (2013): 971–977

[36] John F. Reichard, Michael Schnekenburger, and Alvaro Puga, "Long term low-dose arsenic exposure induces loss of DNA methylation," *Biochemical Biophysical Research Communications.* 352(1) (2007): 188–192.

[37] M. J. Mass and L. Wang. Arsenic alters cytosine methylation patterns of the promoter of the tumor suppressor gene p53 in human lung cells: a model for a mechanism of carcinogenesis. *Mutation Research* 386(3) (1997): 263-277.

[38] S. Majumdar, S. Chanda, B. Ganguli, D. N. Mazumder, S. Lahiri, U. B. Dasgupta, "Arsenic exposure induces genomic hypermethylation," *Environmental Toxicology* Jun. 25(3) (2010) :315-8. doi: 10.1002/tox.20497.

this may occur in a sex-specific manner, which could potentially produce gender-differentiated disease outcomes later in life.[39]

There is a direct relationship between urinary Arsenic concentrations and DNA-methylation in both maternal and umbilical cord white blood cells from Bangladesh. Tens of millions of people there are exposed to Arsenic in their drinking water, in part because of misguided Western development efforts on their behalf,[40] but Chile, Argentina, and the United States and Mexico also have regions where the groundwater is contaminated with Arsenic. Both maternal and umbilical cord white blood cells show higher DNA-methylation values among the individuals demonstrating the highest urinary Arsenic levels compared to those with the lowest Arsenic levels.[41] Exposure to higher levels of Arsenic was positively associated with DNA-methylation at sites within the promoter region of the tumor suppressor gene *p16.* Associations were observed in both maternal and fetal leukocytes. The increased DNA-methylation in the promoter region of a tumor suppressor gene (which would reduce normal levels of tumor suppression) suggests that a heritable increase in susceptibility to cancers may be a consequence of increased Arsenic exposure. These results are consistent with those of other researchers who found that for

---

[39] J. Richard Pilsner, Megan N. Hall, Xinhua Liu, Vesna Ilievski, Vesna Slavkovich, Diane Levy, Pam Factor-Litvak, Mahammad Yunus, Mahfuzar Rahman, Joseph H. Graziano, Mary V. Gamble, "Influence of Prenatal Arsenic Exposure and Newborn Sex on Global Methylation of Cord Blood DNA," *PLoS ONE* 7(5) (2012): e37147. doi:10.1371/journal.pone.0037147

[40] Pallava Bagla, "Arsenic-Laced Well Water Poisoning Bangladeshis," *National Geographic News* June 5 (2003), available online at http://news.nationalgeographic.com/news/2003/06/0605_030605_arsenicwater.html (accessed 21 February, 2014).

[41] Molly L. Kile, Andrea Baccarelli, Elaine Hoffman, Letizia Tarantini, Quazi Quamruzzaman, Mahmuder Rahman, Golam Mahiuddin, Golam Mostofa, Yu-Mei Hsueh, Robert O. Wright, David C. Christiani, "Prenatal Arsenic Exposure and DNA Methylation in Maternal and Umbilical Cord Blood Leukocytes," *Environmenal Health Perspectives* 120 (2012): 1061-1066.

adults in Bangladesh, arsenic exposure was positively associated with white blood cell DNA-methylation in a dose-dependent manner.[42] These results are also consistent with other findings from studies of adult DNA-methylation levels and changes associated with bladder cancer, prostate cancer, and skin cancer.[43]

Particulate Matter, Cardiovascular and Respiratory Disease

High levels of Particulate Matter (PM) are associated with a variety of sources of air pollution including burning coal, diesel exhaust, wood smoke, and other combustions. Ambient PM has also been associated in adults with increased hospitalization and

---

[42] J Richard Pilsner, Xinhua Liu, Habibul Ahsan, Vesna Ilievski, Vesna Slavkovich, Diane Levy, Pam Factor-Litvak, Joseph H Graziano, and Mary V Gamble, "Genomic methylation of peripheral blood leukocyte DNA: influences of arsenic and folate in Bangladeshi adults, *American Journal Clinical Nutrition* 86 (2007): 1179-86; M. Argos, L. Chen, F. Jasmine, L. Tong, B. L. Pierce, S. Roy, R. Paul-Brutus, M. V. Gamble, K. N. Harper, F. Parvez, M. Rahman, M. Rakibuz-Zaman, V. Slavkovich, J. A. Baron, J. H. Graziano, M. G. Kibriya, H. Ahsan, "Gene-specific differential DNA methylation and chronic arsenic exposure in an epigenome-wide association study of adults in Bangladesh," *Environmental Health Perspectives* 123 (2015): 64–71; http://dx.doi.org/10.1289/ehp.1307884

[43] C. J. Marsit, M. R. Karagas, H. Danaee, M. Liu, A. Andrew, A. Schned, H. H. Nelson, K. T. Kelsey, "Carcinogen exposure and gene promoter hypermethylation in bladder cancer," *Carcinogenesis* 27(1) (2006) :112–116; Sarmishtha Chanda, Uma B. Dasgupta, Debendranath GuhaMazumder, Mausumi Gupta, Utpal Chaudhuri, Sarbari Lahiri, Subhankar Das, Nilima Ghosh, Debdutta Chatterjee, "DNA hypermethylation of promoter of gene*p53* and *p16* in arsenic-exposed people with and without malignancy," *Toxicology Science* 89(2) (2006): 431–437; W. T. Chen, W. C. Hung, W. Y. Kang, Y. C. Huang, C. Y. Chai, "Urothelial carcinomas arising in arsenic-contaminated areas are associated with hypermethylation of the gene promoter of the death-associated protein kinase," *Histopathology* 51(6) (2007) :785-92; Chee-Yin Chai, Ya-Chun Huang, Wen-Chun Hung, Wan-Yi Kang, Wan-Tzu Chen, "Arsenic salts induced autophagic cell death and hypermethylation of DAPK promoter in SV-40 immortalized human uroepithelial cells," *Toxicology Letters* 173 (1) (2007): 48–56; L. L. Benbrahim-Tallaa, R. A. Waterland, M. Styblo, W. E. Achanzar, M. M. Webber, M. P. Waalkes, "Molecular events associated with arsenic-induced malignant transformation of human prostatic epithelial cells: aberrant genomic DNA methylation and K-ras oncogene activation," *Toxicology and Applied Pharmacology* 206(3) (2005): 288-98.

mortality due to cardiopulmonary disease and lung cancer.[44] Overall anthropogenic particulate matter is estimated to be associated with roughly 3 ½ million premature human mortalities globally each year due to cardiopulmonary disease.[45] Increased levels of fine particulates are associated with increased post-neonatal mortality due to respiratory causes.[46]

For infants, high maternal exposure to particulates prior to birth results globally in low birth weights and therefore a wide array of subsequent health problems for the infant.[47] High prenatal exposure to particulate matter is also associated with an increased chance of autism spectrum disorder developing later in life.[48]

---

[44] A. Peters, "Particulate matter and heart disease: evidence from epidemiological studies," *Toxicology Applied Pharmacology* 207(suppl) (2005): 477–482; P. Vineis and K. Husgafvel-Pursiainen, "Air pollution and cancer: biomarker studies in human populations," *Carcinogenesis* 26 (2005): 1846–1855.

[45] Susan C. Anenberg, Larry W. Horowitz, Daniel Q. Tong, J. Jason West, "An Estimate of the Global Burden of Anthropogenic Ozone and Fine Particulate Matter on Premature Human Mortality Using Atmospheric Modeling," *Environmental Health Perspectives* 118 (2010): 1189-1195 http://dx.doi.org/10.1289/ehp.0901220.

[46] Tracey J. Woodruff, Jennifer D. Parker, and Kenneth C. Schoendorf, "Fine Particulate Matter (PM2.5) Air Pollution and Selected Causes of Postneonatal Infant Mortality in California," *Environmental Health Perspectives* 114(5) (2006): 786–790.

[47] P. Dadvand, J. Parker, M. L. Bell, M. Bonzini, M. Brauer, L. A. Darrow, U. Gehring, S. V. Glinianaia, N. Gouveia, E. Ha, J. H. Leem, E. H. van den Hooven, B. Jalaludin, B. M. Jesdale, J. Lepeule, R. Morello-Frosch, G. G. Morgan, A. C. Pesatori, F. H. Pierik, T. Pless-Mulloli, D. Q. Rich, S. Sathyanarayana, J. Seo, R. Slama, M. Strickland, L. Tamburic, D. Wartenberg, M. J. Nieuwenhuijsen, T. J. Woodruff, "Maternal Exposure to Particulate Air Pollution and Term Birth Weight: A Multi-Country Evaluation of Effect and Heterogeneity," *Environmental Health Perspectives* 121 (2013): 367–373; http://dx.doi.org/10.1289/ehp.1205575.

[48] R. Raz, A. L. Roberts, K. Lyall, J. E. Hart, A. C. Just, F. Laden, M. G. Weisskopf, "Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case–control analysis within the Nurses' Health Study II cohort," *Environmental Health Perspectives* 123 (2015): 264–270; http://dx.doi.org/10.1289/ehp.1408133.

A situation in which the relationship between exposure to airborne PM and epigenetic changes can be most readily investigated is in foundries. Foundry work is known to be associated with adverse health outcomes, including cardiovascular and respiratory disease and increased incidence of lung cancer.[49] In foundry facilities PM levels are well above the concentrations found in most ambient outdoor air.

The inducible nitric oxide synthase gene (*iNOS*) in foundry workers has been studied to look for DNA-methylation. Nitric oxide synthase activity is an important factor in normal regulation of human airways. Lower DNA-methylation in the *iNOS* gene promoter region corresponds to increased gene expression.[50] Increased *iNOS* expression is found in cases of diseases associated with PM exposure, such as cardiovascular disease and lung cancer.[51] Therefore changes in *iNOS* DNA-methylation due to PM exposure serve as a marker for an epigenetic cause of disease.

The data showed that *iNOS* methylation was significantly decreased after 3 successive days of foundary work when compared with measures taken before the first

[49] Z. Xu, L. M. Brown, G. W. Pan, T. F. Liu, G. S. Gao, B. J. Stone, R. M. Cao, D. X. Guan, J. H. Sheng, Z. S. Yan, M. Dosemeci, J. F. Fraumeni, Jr, W. J. Blot, "Cancer risks among iron and steel workers in Anshan, China, Part II: Case-control studies of lung and stomach cancer," *Amerian Journal of Industrial Medicine* 30 (1996): 7–15.

[50] G. C. Chan, J. E. Fish, I. A. Mawji, D. D. Leung, A. C. Rachlis, P. A. Marsden, "Epigenetic basis for the transcriptional hyporesponsiveness of the human inducible nitric oxide synthase gene in vascular endothelial cells," *Journal of Immunology* 175 (2005): 3846–3861.

[51] Laura Comini, Tiziana Bachetti, L. Agnoletti, G. Gaia, S. Curello, Bruno Milanesi, Maurizio Volterrani, Giovanni Parrinello, C. Ceconi, Anella Giordano, Angelo Corti, Roberto Ferrari, "Induction of functional inducible nitric oxide synthase in monocytes of patients with congestive heart failure. Link with tumour necrosis factor-alpha," *European Heart Journal* 20 (1999): 1503–1513: C. Y. Liu, C. H. Wang, T. C. Chen, H. C. Lin, C. T. Yu, H. P. Kuo, "Increased level of exhaled nitric oxide and up-regulation of inducible nitric oxide synthase in patients with primary lung cancer," *British Journal of Cancer* 78 (1998): 534–541.

day of the work week.[52] This occurred regardless of the exact level of PM exposure experienced by the workers. This suggests that PM exposure in a foundry setting, and perhaps in other areas with high levels of air pollution, may be resulting in decreased *iNOS* DNA-methylation and therefore producing adverse health impacts.

Children exposed to higher levels of particulate matter in the air they breathed had altered DNA-methylation levels at several gene regions associated with regulation of nitric oxide levels *(NOS1, NOS2A, and NOS3*).[53] The epigenetic impacts of particulates involve children exposed to polluted air because of where their parents live, in a way very similar to the known impacts on industrial workers. Elderly men exposed to air pollutants from traffic, in which particulates featured prominently, had significantly reduced lung function and they also showed DNA-methylation changes in a series of genes that were examined (*CRAT*, *IFN-* γ, *IL6, and ICAM1*) known to be related to inflammation and immunity.[54] It seems that the contemporary world is making all of us from infants to the elderly, into foundry workers of a kind.

Epigenetics and Autoimmune Disease

---

[52] Letizia Tarantini, Matteo Bonzini, Pietro Apostoli, Valeria Pegoraro, Valentina Bollati, Barbara Marinelli, Laura Cantone, Giovanna Rizzo, Lifang Hou, Joel Schwartz, Pier Alberto Bertazzi, and Andrea Baccarelli, "Effects of Particulate Matter on Genomic DNA Methylation Content and iNOS Promoter Methylation," *Environmental Health Perspectives* 117 (2009): 217-222.

[53] Carrie V. Breton, Muhammad T. Salam, Xinhui Wang, Hyang-Min Byun, Kimberly D. Siegmund, and Frank D. Gilliland, "Particulate Matter, DNA Methylation in Nitric Oxide Synthase, and Childhood Respiratory Disease," *Environ Health Perspectives* 120 (2012): 1320–1326.

[54] J. Lepeule, M. A. C. Bind, A. A. Baccarelli, P. Koutrakis, L. Tarantini, A. Litonjua, D. Sparrow, P. Vokonas, J. D. Schwartz, "Epigenetic influences on associations between air pollutants and lung function in elderly men: the Normative Aging Study," *Environmental Health Perspectives* 122 (2014): 566–572; http://dx.doi.org/10.1289/ehp.1206458.

Reduced T-cell DNA-methylation in specific genetic regions is found in lupus patients and T-cell DNA-methylation reduction appears to be a basic part of this destructive autoimmune disease. T-cells from patients with active lupus have diminished levels of an enzyme (DNA MTase) that helps carry out DNA-methylation, and decreased chemical signaling within the T-cells that leads to DNA-methylation.[55] Both of these processes seen in active lupus T-cells result in loss of DNA-methylation. Lupus patient T-cells act like ones with laboratory induced DNA-methylation reductions.[56] Because only women have inactive X chromosomes, reduction of DNA-methylation of specific genes (*CD40LG* and maybe other genes) on the inactive X chromosome could contribute to the disproportionate number of females who develop lupus.[57] Other characteristics in common between lupus patients and results of experiments reducing T-cell DNA-methylation have been reviewed.[58] Additional experiments done on T-cell DNA-methylation have supported the view that epigenetic causes are important in lupus[59] and that reduction in T-cell DNA-methylation is key to the development of lupus. A genetic

---

[55] Chun Deng, Mariana J. Kaplan, Jun Yang, Donna Ray, Zhiyong Zhang, W. Joseph McCune, Samir M. Hanash, Bruce C. Richardson, "Decreased ras–mitogen-activated protein kinase signaling may cause DNA hypomethylation in T lymphocytes from lupus patients," *Arthritis & Rheumatism* 44(2) (2001): 397–407.

[56] E. Ballestar, M. Esteller, B. C. Richardson, "The epigenetic face of systemic lupus erythematosus," *Journal of Immunology*. 176(12) (2006) :7143-7; Qianjin Lu, Ailing Wu, Laura Tesmer, Donna Ray, Neda Yousif and Bruce Richardson, "Demethylation of CD40LG on the Inactive X," *Journal of Immunology* 179 (2007) :6352-6358; Richardson B. Primer, "Epigenetics of autoimmunity," *Nature Clinical Practice Rheumatology* 3 (2007): 521-527.

[57] Lu et al., "Demethylation of CD40LG," 521-527.

[58] Glinda S. Cooper, Kathleen M. Gilbert, Eric L. Greidinger, Judith A. James, Jean C. Pfau, Leslie Reinlib, Bruce C. Richardson and Noel R. Rose, "Recent Advances and Opportunities in Research on Lupus: Environmental Influences and Mechanisms of Disease," *Environmental Health Perspectives* Vol. 116(6) (2008): 695-702.

[59] Faith M. Strickland and Bruce C. Richardson, "Epigenetics in human autoimmunity," *Autoimmunity* 41(4) (2008): 278.

predisposition may make some people more susceptible to lupus, but as indicated by the development of lupus in only one member of pairs of identical twins, environmental influences (such as toxins that produce epigenetic changes) are needed to initiate the disease in an individual.[60]

Rheumatoid arthritis (RA) is associated with epigenetic changes. There are two clusters of genes within the major histocompatibility complex region whose differential methylation was associated with the presence of RA.[61] The researchers found 10 genetic sites with different DNA-methylation in RA patients, the methylation seemed to alter risk for RA. Nine of the 10 sites were within a region of the genome known to play an important role in autoimmune diseases. The aggressive fibroblast cells from the joints of RA patients show lower levels of DNA-methylation than typical.[62] Inflammatory arthritis is associated with genomic DNA hypomethylation that is reversed with methotrexate, which is a drug often used to alleviate RA symptoms.[63] Environmental causes of RA are still in an early stage of investigation, but RA may be related to birth size and early

[60] D. R. Patel, B. C. Richardson, "Dissecting complex epigenetic alterations in human lupus," *Arthritis Research and Therapy* 15 (2013): 201.
[61] Yun Liu, Martin J Aryee, Leonid Padyukov, M Daniele Fallin, Espen Hesselberg, Arni Runarsson, Lovisa Reinius, Nathalie Acevedo, Margaret Taub, Marcus Ronninger, Klementy Shchetynsky, Annika Scheynius, Juha Kere, Lars Alfredsson, Lars Klareskog, Tomas J Ekström, Andrew P Feinberg, "Epigenome-wide association data implicate DNA methylation as an intermediary of genetic risk in rheumatoid arthritis," *Nature Biotechnology* 31, 142–147 (2013): doi:10.1038/nbt.2487.
[62] E. Karouzakis, R. E. Gay, B. A. Michel, S. Gay, M. Neidhart, "DNA hypomethylation in rheumatoid arthritis synovial fibroblasts," *Arthritis Rheumatology* 60(12) (2009): 3613-22. doi: 10.3389/fcell.2014.00049.
[63] Y. Kim, J. W. Logan, J.B. Mason, R. Roubenoff, "DNA hypomethylation in inflammatory arthritis: Reversal with methotrexate," *Journal of Laboratory and Clinical Medicine* 128 (2) (1996): 165-172.

growth rates[64] and changes in these attributes are known consequences of epigenetic changes seen in children who were conceived during periods of extremely poor maternal nutrition.

Other autoimmune diseases have early evidence collecting that suggests that DNA-methylation patterns are associated with the development of disease. These include relapsing-recurring multiple sclerosis (MS) being associated with a very different methylation pattern observed at *chr.6 p21*, with the strongest difference located at *HLA-DRB1* as well as at 55 *non-HLA CpG* sites with significantly modified methylation (and for many of the latter locations, they are associated with genes that have previously been linked to MS).[65] A recent review suggests that the list of autoimmune diseases that will eventually be found to have epigenetic associations with their onset will include systemic lupus erythematosus, progressive systemic sclerosis, psoriasis, Sjögren's syndrome, scleroderma, and ulcerative colitis.[66] Some evidence exists for relationships between environmental exposures and epigenetic changes in specific genes associated with autoimmune disease, but to date it has been difficult to establish causal relationships between specific environmental factors and disease onset.[67] Biochemical mechanisms

[64] C .J. Edwards and C. Cooper, "Early environmental factors and rheumatoid arthritis," *Clinical and Experimental Immunology* 143(1) (2006): 1-5.
[65] M. Graves, M. Benton, R. Lea, M. Boyle, L. Tajouri, D. Macartney-Coxson, R. Scott, J. Lechner-Scott, "Methylation differences at the HLA-DRB1 locus in CD4+ T-Cells are associated with multiple sclerosis," *Multiple Sclerosis* 20(8) (2013): 1033-1041.
[66] Biola M. Javierre, Henar Hernando, Esteban Ballestar, "Environmental Triggers and Epigenetic Deregulation in Autoimmune Disease," *Discovery Medicine* 12(67) (2011): 535-545.
[67] Javierre et al., "Environmental Triggers," 535-545.

that might underpin the origins of autoimmunity in all of these diseases via DNA-methylation and other processes are now being proposed and investigated.[68]

Epigenetic Effects of Poverty, Stress and Synergism

In addition to the research noted above, there is growing evidence that the conditions of poverty exacerbate epigenetic dysregulation. Inner city infants and children often live in environments with greater levels of air pollution due to cars, trucks, buses, and trains, and therefore higher PAH and PM exposures. Their proximity to industrial activities frequently produces higher exposures to an array of metals utilized in manufacturing, art glass, and foundry operations. Putting aside the greater exposure to environmental toxins typical of urban centers, there is a direct relationship between levels of childhood emotional stress and later development of an array of autoimmune diseases.[69] Like Flint, MI., many inner cities, especially those with residents who are lower on the socioeconomic spectrum, are stressful environments for children due to underfunded schools, elevated rates of crime, food insecurity, and many other poverty related issues. Stress causes an assortment of epigenetic changes including alterations in DNA methylation in the brain at genes involved in response to chronic emotional stress[70] with some evidence pointing to a stress related epigenetic component of depressive

---

[68] Aristo Vojdan, "A Potential Link between Environmental Triggers and Autoimmunity," *Autoimmune Diseases* vol. 2014, (2014) article ID 437231, 18 pages http://dx.doi.org/10.1155/2014/437231.

[69] Shanta R. Dube, DeLisa Fairweather, William S. Pearson, Vincent J. Felitti, Robert F. Anda, and Janet B. Croft, "Cumulative Childhood Stress and Autoimmune Diseases in Adults," *Psychosomatic Medicine* 71(2) (2009): 243–250; Stojanovich L., D. Marisavljevich, "Stress as a trigger of autoimmune disease," *Autoimmun Review* 7(3) (2008): 209-13. doi: 10.1016/j.autrev.2007.11.007.

[70] Adrian M. Stankiewicz, Artur H. Swiergiel, and Pawel Lisowski, "Epigenetics of stress adaptations in the brain," *Brain Research Bulletin* 98 (2013): 76– 92.

bipolar disorder.[71] Additional epigenetic changes are also associated with major psychoses[72] and there is a relationship between prenatal maternal stress due to natural disasters and DNA-methylation at genes controlling immune system function.[73]

These new concerns about heritable epigenetic changes related to increased exposure to urban air pollutants, and to the social stress associated with living in an impoverished environment, add to an already considerable body of evidence that the health of children exposed to air pollution is badly compromised. Prenatal exposure to higher PAH concentrations results later in childhood in reductions of the white matter surface of the brain in areas where deficits produce slower speed information-processing, more severe attention-deficit/hyperactivity disorder symptoms, and conduct disorder issues.[74] Congenital birth malformations in the circulatory system and genital organs are associated with higher prenatal exposures to PM and oxides of nitrogen (the latter primarily coming from auto exhaust).[75] Greater exposure to small PM during pregnancy

---

[71] Patrick O. McGowan and Tadafumi Kato, "Epigenetics in mood disorders," *Environmental Health and Preventive Medicine* 13(1) (2008): 16-24.

[72] Jonathan Mill, Thomas Tang, Zachary Kaminsky, Tarang Khare, Simin Yazdanpanah, Luigi Bouchard, Peixin Jia, Abbas Assadzadeh, James Flanagan, Axel Schumacher, Sun-Chong Wang, Arturas Petronis, "Epigenomic Profiling Reveals DNA-Methylation Changes Associated with Major Psychosis," *The American Journal of Human Genetics* 82(3) (2008): 696–711.

[73] Lei Cao-Lei, Renaud Massart, Matthew J. Suderman, Ziv Machnes, Guillaume Elgbeili, David P. Laplante, Moshe Szyf , Suzanne King, "DNA Methylation Signatures Triggered by Prenatal Maternal Stress Exposure to a Natural Disaster: Project Ice Storm," *PLoS ONE* 9(9) (2014) : e107653. doi:10.1371/journal.pone.0107653.

[74] Bradley S. Peterson, Virginia A. Rauh, Ravi Bansal, Xuejun Hao, Zachary Toth, Giancarlo Nati, Kirwan Walsh, Rachel L. Miller, David Semanek, Frederica Perera, "Effects of Prenatal Exposure to Air Pollutants (Polycyclic Aromatic Hydrocarbons) on the Development of Brain White Matter, Cognition, and Behavior in Later Childhood," *JAMA Psychiatry*. Published online March 25 (2015) doi:10.1001/jamapsychiatry.2015.57.

[75] Adel Farhia, Valentina Boykoa, Jonatan Almagorb, Itzhak Benensonb, Enrico Segrec, Yinon Rudichc, Eli Sternd, Liat Lerner-Gevaa, "The possible association between

is associated with increased odds of Autism Spectrum Disorder, with the greatest impact following high exposure in the third trimester of pregnancy.[76] Children exposed during the second trimester of pregnancy to higher levels of NO_2 and benzene (both prevalent in auto exhaust) had reduced lung function at 4.5 years of age, with stronger impacts on children from families with lower socioeconomic status.[77] A review that discusses the special vulnerability of early developmental stages to epigenetic dysregulation due to toxins and how this has impacts on adult health provides evidence for not only the materials already discussed in this article but also for the epigenetic impacts of prenatal exposure to tobacco smoke, Phthalates, and Bisphenol A.[78] There is also research supporting synergistic interactions between social stress or socioeconomic class and air pollution in producing asthma[79] and between early stress and mental health outcomes.[80]

---

exposure to air pollution and the risk for congenital malformations," *Environmental Research* 135 (2014): 173–1.

[76] R. Raz, A. L. Roberts, K. Lyall, J. E. Hart, A. C. Just, F. Laden, M. G. Weisskopf, "Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case–control analysis within the Nurses' Health Study II cohort," *Environmental Health Perspectives* 123 (2015): 264–270; http://dx.doi.org/10.1289/ehp.1408133.

[77] E. Morales, Raquel Garcia-Esteban, Oscar Asensio de la Cruz, Mikel Basterrechea, Aitana Lertxundi, Maria D Martinez López de Dicastillo, Carlos Zabaleta, Jordi Sunyer, "Intrauterine and early postnatal exposure to outdoor air pollution and lung function at preschool age," *Thorax* 70(1) (2014): 64-73 doi:10.1136/thoraxjnl-2014-205413

[78] Frederica Perera and Julie Herbstman, "Prenatal environmental exposures, epigenetics, and disease," *Reproductive Toxicology* 31(3) (2011): 363–373.

[79] J. E. Clougherty, J. I. Levy, L. D. Kubzansky, P. B. Ryan, S. F. Suglia, M. J. Canner, R. J. Wright, "Synergistic effects of traffic-related air pollution and exposure to violence on urban asthma etiology," *Environmental Health Perspectives* 115 (2007):1140–6; E. Chen, H. M. Schreier, R. C. Strunk, M. Brauer, "Chronic traffic-related air pollution and stress interact to predict biologic and clinical outcomes in asthma," *Environmental Health Perspectives* 116 (2008): 970–5.

[80] P. O. McGowan and M. Szyf. The epigenetics of social adversity in early life: implications for mental health outcomes. *Neurobiology of Disease* 39 (2010): 66–72.

Recent review articles would reward the curiosity of those whose interests in epigenetic health impacts and early exposure to pollution go beyond the scope of this paper.[81]

Epigenetics and Catholic Social Teaching

The preceding section offers compelling evidence that the environmental context of urban areas like Flint, Michigan goes well beyond the exposure to lead. The urban reality for many, particularly those at the lower end of the income spectrum, is that it is a sordid brew of multiple factors that can negatively impact genetic health, including social stressors such as poverty, airborne chemical compounds like PAHs and ubiquitous heavy metals such as mercury and lead. This urban scenario—at least on the surface—is nothing new. The urban poor have struggled with these social and environmental injustices for generations. What is new is the revealing research on how circumstances of social stress along with exposure to chemical compounds and heavy metals conspire in a deeper manner to negatively impact human health at the epigenetic level.

The debacle in Flint that may have exposed approximately 8,000 children to unsafe levels of lead in their drinking water might only be the tip of an egregious problem nationwide. According to a *Guardian* investigation—prompted by the Flint water crisis—33 cities in the U.S. use the same poor testing regimes for lead that were used in Flint. The *Guardian* report said that "Despite warnings of regulators and experts, water departments in at least 33 cities used testing methods over the past decade that could

[81] Perera and Herbstman, "Prenatal environmental exposures," 363–373; Carrie V. Breton and Amy N. Marutani, "Air Pollution and Epigenetics: Recent Findings," *Current Environmental Health Reports* 1 (2014): 35–45.

underestimate lead found in drinking water".[82] On June 15, 2016 the *Washington Post* reported on a new study on blood lead levels in children published in the June issue of the *Journal of Pediatrics*. Researchers Kaufman *et al.* found that while blood lead levels in children declined nationwide between 2009-2015 certain areas of the country were not so lucky. The *Post* article states that "In certain regions of the country, including parts of New York, Pennsylvania and Ohio, more than 1 in 7 children tested had elevated levels of lead in their blood. Minnesota had the highest overall rate of young children with disturbing blood lead levels, at 10.3 percent. That was followed by Pennsylvania (7.8 percent), Kentucky (7.1 percent), Ohio (7 percent) and Connecticut (6.7 percent).[83] The very same day the *Washington Post* article was published, the *Detroit News* reported that the American Medical Association at their annual meeting in Chicago called for routine testing of water at schools and day-care centers in Michigan and the elimination of lead pipes across the nation. The report indicated that "In 2015, children in 50 of Michigan's 83 counties had blood lead levels requiring medical treatment."[84] The *Detroit News* article went on to say that "The AMA noted that children exposed to lead require ongoing medical attention, and called for biologic testing of children with elevated blood lead

[82] Oliver Milman and Jessica Glenza, "At Least 33 US Cities Used Water Testing "Cheats" Over Lead Concerns," *The Gaurdian*, June 2, 2016. https://www.theguardian.com/environment/2016/jun/02/lead-water-testing-cheats-chicago-boston-philadelphia (accessed Nov. 23, 2016).
[83] Dennis Brady, "In Some Zip codes, 1 in 7 children suffer from dangerously high blood lead levels," *The Washington Post*, June 15 2016. https://www.washingtonpost.com/news/to-your-health/wp/2016/06/15/in-some-zip-codes-1-in-7-children-suffer-from-dangerously-high-blood-lead-levels/ (accessed Nov. 23, 2016).
[84] Karen Bouffard, "Physicians Group: Test for lead in schools, day care," *The Detroit News*, June 14 2016. http://www.detroitnews.com/story/news/michigan/2016/06/14/lead-testing-medical-association/85886344/ (accessed Nov. 23, 2016).

levels, health screening and nutritional support for all people exposed to lead through their public water systems."

The message from these snippets of recent information is that lead is back in the news in a big way and given the attention in this paper on the epigenetic consequences of lead exposure the news is alarming. In addition to being a major public health issue, lead exposure, particularly in children, is a matter of social and environmental justice and that raises the main question here: What do recent developments in epigenetic research mean for the Roman Catholic human rights tradition (aka Catholic social teaching)? Consider for a moment the dramatic uptick in epigenetic research. In 2000 there were about 16 published articles on the subject compared to 1435 in 2012 and the results, a small sample of which we have highlighted, are eye-opening and very disturbing. From the perspective of integral ecology two general observations can be made regarding the research. First human beings and their health are not simply a matter of inherited genetic traits but also include environmental factors both social and physical. In other words environmental factors including socio-economic context, diet, and air and water quality impact epigenetic processes that contribute to gene expression. Second these epigenetic markers are potentially inheritable. At the very least they will impact the children and grandchildren of a woman exposed to epigenetic toxins during pregnancy if she is carrying a female child. Many genes have their epigenetic marks erased shortly after conception, but this is not universally true, and the potential exists for some epigenetic alterations to persist heritably for multiple generations and have impacts beyond the

grandchild.[85] What does this mean for understanding and interpreting the basic characteristics of CST such as human dignity, the common good, human rights and justice?

It is well known in Roman Catholic circles that the cornerstone of CST is human dignity based on the theological principle of the *imago dei*. This interpretation of Gen. 1:26-27 that human beings are created in the image and likeness of God is considered a transcendental principle and it is the basis upon which we claim that human beings are endowed with inherent value and dignity. There is however another side to the human dignity question—it never exists in a vacuum and is consequently also influenced by historical, social as well as genetic and epigenetic factors. Mark Bratton writes that "The fact that human beings are genetically constituted of extraordinary complexity invites deeper reflection on the nature of the relationship between the 'whole person' and her genetically constituted parts."[86] Bratton raises an important caveat to our discussion—the temptation of reducing the whole person and his/her dignity to their genetic and epigenetic components. He correctly argues that this would be dehumanizing. Nevertheless while it is true that we cannot reduce human beings to their genetic and epigenetic components it is also true that we must recognize that human value and dignity is significantly shaped by our genetic composition and the epigenetic bio-molecular process that influences genetic expression. In other words, the human being, the byproduct of evolutionary creativity, is endowed with unique capabilities—the capacity

[85] Riya R. Kanherkar, Naina Bhatia-Dey and Antonei B. Csoka, "Epigenetics across the human lifespan," *Frontiers in Cell and Developmental Biology* 2 (2014): 1-19
[86] Mark Bratton, ed. *God Ethics and the Human Genome* (London: Church House Publishing, 2009), 20.

for language, rational discourse, critical intelligence, spirituality, culture, etc. These distinctive capacities are rooted in our genetic heritage. Moreover, insights and findings from epigenetic research clearly indicate that the dignity of the human person is not only shaped by theological and/or philosophical claims or by genes alone, but by epigenetic processes through our interaction with social and environmental factors—for good or for ill. The research accessed in this paper on the consequences of heavy metal and toxic exposure on epigenetic processes (e.g. DNA methylation, epigenetic dysregulation) indicates that it is a direct threat to genetic and epigenetic integrity and human dignity. The research also heightens the concern for children—the most vulnerable to the negative health consequences of toxic exposure and epigenetic malfunction. We have known for some time that children born today will already have been exposed to toxic substances *in utero* and will start life with a significant "body burden" of chemical compounds. The current research on epigenetic function however transforms those concerns to a new level of jeopardy by making toxic exposure a multigenerational epigenetic burden.

The *imago dei* can also be seen through the lens of the human genome and epigenome as an expression of what Peter Scott calls "genomic solidarity."[87] It is his view that the *imago dei* "can support genomic solidarity by insisting that all humans share in the *imago*" and that "all humans are bound together in genomic solidarity on account of an inheritance of imaging God held in common".[88] The idea of genomic solidarity and humans imaging God held in common naturally lead to a reflection on the common good and how the principle of the common good should be interpreted in light

[87] Peter Manley Scott, "The Human Genome and Theological Issues." In *God, Ethics and the Human Genome,* ed. Mark Bratton (London: Church House Publishing 2009),78
[88] Ibid.

of the human genome and epigenome. If the *imago dei* is the cornerstone of CST, the principle of the common good is the keystone whereby the protection (or lack thereof) of human dignity is measured in any given society.

Epigenetics and the Common Good

Over time in the history of CST, the principle of the common good has accrued several layers of interpretation and should be understood as an evolving norm. At its foundation the common good points to the inherent aspect of human sociability and the necessity of social relationships in maintaining human dignity that Lisa Cahill calls "the intrinsic sociality of persons."[89] She offers this insightful definition of the common good: "The common good defines a solidaristic association of persons that is more than the good of individuals in the aggregate" and she goes on to state that 'common good' says something about social communication and cooperation as essential to the fulfillment of our very personhood."[90] The emphasis here is on the intrinsic relationality of human personhood and is therefore an ecological necessity for human well-being. In *Laudato Si* (2015) Pope Frances pointed in this direction in his reflection on "integral ecology" when he declared that "Human ecology is inseparable from the notion of the common good, a central and unifying principle of social ethics." (*LS*, no. CLVI) The main point here is that the common good incorporates the significance of human social relationships and how these relationship are "integral" to human personhood.

Human sociability, the requisite need for relationship, often falls into patterns of behavior and these patterns of behavior can become habitual. In other words human

[89] Lisa Sowle Cahill, *Bioethics and the Common Good* (Milwaukee, WI: Marquette University Press 2004), 9.
[90] Ibid., 8.

relationships are prone to institutionalization particularly in the form of social, political, and economic institutions. Cahill makes note of this when she states that "This common good is a network of institutional and structural relationships, along with the guiding narratives, symbols of meaning, and derivative practices. This inclusive ethos and set of social relations is defined ideally as 'the common good.'[91] The principle of the common good recognizes the importance of institutions in protecting human dignity but it must also be recognized that some institutions—what can be called "structures of sin"—actually threaten human dignity and thereby work against the common good. This is precisely what happened to Flint, Michigan where political institutions—possibly tinged by racism—failed the people of Flint. This reality raises the necessity of human rights and the work of social and environmental justice to alter damaging institutions that diminish human dignity.

Human rights are the primary assurances for protecting and promoting human dignity. In the words of David Hollenbach "Human rights are the moral claims of all persons to be treated, by virtue of their humanity, as participants in the shared life of the human community."[92] He goes on to state that "These moral claims will be practically guaranteed when respect for them is built into the basic structure of society, i.e., into the main political, social, and economic institutions that set the overall terms of social cooperation."[93] When interpreted in this way human rights—essential for protecting human dignity—are the primary means whereby the common good is achieved. The common good is therefore maintained when the rights of all are respected and ensured.

---

[91] Ibid., 26.
[92] David Hollenbach, S.J. *The Common Good and Christian Ethics* (New York: Cambridge University Press, 2002), 159.
[93] Ibid., 159.

We will return to the significance of these moral claims particularly in conjunction with epigenetic dysregulation in our concluding reflections on the Flint water crisis.

In recent years the principle of the common good has evolved in two important ways. First it is now understood as a universal and global norm inclusive of the planetary commons—a significant development for a human-centered rights tradition. In other words ecology and the degradation of the global environment have widened the circle of moral concern recognizing that human well-being is dependent on earth's ecological processes. We can in fact apply the common good to creation itself as a comprehensive principle that recognizes existence as a complex interrelated web of life.

The second development is that the common good is now also interpreted in an intergenerational way that Pope Frances has called "intergenerational solidarity." Reflecting on the global economy in *Laudato Si* the Pope stated that "The notion of the common good also extends to future generations. The global economic crises have made painfully obvious the detrimental effects of disregarding our common destiny, which cannot exclude those who come after us. We can no longer speak of sustainable development apart from intergenerational solidarity" (*LS*, no. CLIX). We who are here today have an ethical obligation to generations not yet born. This is particularly significant in light of the inheritability of epigenetic consequences of toxic exposure. In a recent editorial in *Environmental Health News*, Frederica Perera, an epigenetic researcher at Columbia University stated that "Exposure to toxic air pollutants released during fossil fuel combustion contributes to low birth weight, cognitive and behavioral disorders, asthma and other respiratory illnesses… Children in low-income communities in the U.S., as well as globally, suffer most due to disproportionately high exposures to

polluting sources, which are more likely to be built in or near the neighborhoods in which they live… a growing body of evidence suggests that early-life exposures to air pollutants, nutritional deprivation, and stress may impact the health of future generations, possibly by altering the regulation of genes involved in disease pathways."[94] The above statement along with the on-going research on the human genome and epigenome requires an additional layer of interpretation of the common good. Two years before the conclusion of the Human Genome Project, Francis Collins, the leader of the project and current Director of the National Institutes of Health (NIH) composed a ditty about the human genome he sang at a meeting in Washington, D.C. The last verse went like this "We're joined together by this common thread."[95] The human genome and epigenome in all its complexity is the "common thread" that binds us together as a species and consequently we should also understand the common good, along with its various layers of meaning as a form of biological solidarity or what Scott called "genomic solidarity." Biologically the common good is grounded in our DNA and the genetic and epigenetic processes that make us human beings, and in light of the epigenetic research highlighted here we should also realize that the common good is threatened by economic, social and environmental realities. The consequences are far-reaching. Consider for a moment the impact of epigenetic dysregulation (caused by exposure to things like lead or PAHs) on chronic illness and the cost of health care that is social and intergenerational. Or consider

---

[94] Frederica Perera, "Opinion: The case for a child centered energy and climate policy," *Environmental Health News*, June 21 2016. http://www.environmentalhealthnews.org/ehs/news/2016/june/opinion-the-case-for-a-child-centered-energy-and-climate-policy (accessed Nov. 23, 2016).
[95] John Sulston and Georgina Ferry, *The Common Thread, A Story of Science, Politics, Ethics, and the Human Genome* (Washington, D.C.: The Joseph Henry Press, 2002), 260.

for a moment the health outcomes of lead exposure in Flint, Michigan a situation that calls for the re-articulation of the significance of human rights; a situation that calls for social and environmental justice.

Flint Re-visited: A Case for Social and Environmental Justice

The debacle in Flint, Michigan is an excellent yet tragic example of the failure of political and social institutions to promote the common good and protect human dignity. Within the comprehensive ethical framework of CST human rights have been violated. The specific moral claim from the perspective of CST is the violation of bodily rights—particularly the right to bodily integrity, health and safe water. Within this situation we must be particularly mindful of the children exposed to lead in their drinking water as they are from a biological view the most vulnerable to toxic exposure. Any remedy in the Flint case will require action for social and environmental justice—a requirement to repair the damage to persons and the common good. Our analysis, based on the principle of integral ecology suggests that there are three basic areas that must be remedied.

The first is to remedy the bureaucratic system failure that led to the water crisis in the first place by holding those responsible accountable. Thirteen people have already been criminally charged but the problem might be deeper than those thirteen. The Flint Water Advisory Task Force (FWATF) put the blame squarely on Michigan's Department of Environmental Quality and its culture stating in a December 29, 2015 letter to Governor Snyder that "We believe the primary responsibility for what happened in Flint rests with the Michigan Department of Environmental Quality (MDEQ). Although many individuals and entities at state and local levels contributed to creating and prolonging the problem, MDEQ is the government agency that has responsibility to ensure safe drinking

water in Michigan. It failed in that responsibility and must be held accountable for that failure."[96] According to the Task Force's investigation the MDEQ failed in three areas: regulatory failure, failure in substance and tone of MDEQ's response to the public, and failure in MDEQ's interpretation of the lead and copper rule. Particularly revealing of the MDEQ's culture is the following statement: "Throughout 2015, as the public raised concerns and as independent studies and testing were conducted and brought to the attention of MDEQ, the agency's response was often one of aggressive dismissal, belittlement, and attempts to discredit these efforts and the individuals involved."[97]

The second area of remedy is Flint's drinking water infrastructure—that is, remove the lead pipes. According to the *Detroit Free Press* that will mean "Replacing 13 miles of water mains every year for the next 50 years. Repairing or replacing five dams. Switching out at least 2,000 lead service lines every year for five years."[98] According to the report the price tag is estimated to be about $214 million. The *Free Press* stated that "The new cost estimate to replace lead-based water service lines alone is more than three times the $25-million funding request submitted under the proposed budget from Gov. Rick Snyder" and could take as long as eight years to complete.

The third area of remedy—to the degree it can be remedied— is the public health consequences of lead exposure especially in children. Of the three actions noted here this

---

[96] Flint Water Advisory Task Force letter to Gov. Rick Snyder, December 29, 2015. http://flintwaterstudy.org/wp-content/uploads/2015/12/FWATF-Snyder-Letter-12-29-15.pdf. (accessed Nov. 23, 2016).
[97] Ibid.
[98] Matthew Dolan, "Flint water woes reach beyond lead in water supply," *The Detroit Free Press*, June 6 2016. http://www.freep.com/story/news/local/michigan/flint-water-crisis/2016/06/05/flint-water-woes-reach-beyond-lead-drinking-supply/85288850/ (accessed Nov. 23, 2016).

is arguably the most important because of the direct threat to health. In addition to being a neurotoxin that can cause permanent learning and behavioral problems, lead is toxic to an assortment of organs including heart, kidneys as well as reproductive and nervous systems. According to the CDC "No safe blood lead level in children has been identified."[99] Noted earlier in this paper, the health consequences of lead exposure are aggravated by epigenetic impacts that can last at least 3 generations. At the very least the grandchildren of the Flint women who were pregnant with female children, who were exposed during pregnancy to lead in their drinking water, will also be impacted by DNA methylation. Research on the present children's children might help illuminate how many generations will be impacted. The primary issue however is that these children's right to bodily-genetic integrity has been violated and justice requires that they be given health monitoring and care during their lives. In CST when social/environmental justice is required, preference ought to be given to the most vulnerable. Never before have we realized that justice calls for a three generation commitment to health care monitoring and therapeutic efforts. In a 2010 article we discussed the "body burden" or sum of the toxic materials a person carries in their body but our new understanding of epigenetic impacts extends this concept to that of a multigenerational epigenomic burden as well.

[99] Centers for Disease Control and Prevention (CDC), "Lead," http://www.cdc.gov/nceh/lead/ (accessed Nov. 23, 2016).