EPIGENETICS AND THE ENVIRONMENT IN BIOETHICS

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ABSTRACT
A rich literature in public health has demonstrated that health is strongly influenced by a host of environmental factors that can vary according to social, economic, geographic, cultural or physical contexts. Bioethicists should, we argue, recognize this and – where appropriate – work to integrate environmental concerns into their field of study and their ethical deliberations. In this article, we present an argument grounded in scientific research at the molecular level that will be familiar to – and so hopefully more persuasive for – the biomedically-inclined in the bioethics community. Specifically, we argue that the relatively new field of molecular epigenetics provides novel information that should serve as additional justification for expanding the scope of bioethics to include environmental and public health concerns. We begin by presenting two distinct visions of bioethics: the individualistic and rights-oriented and the communitarian and responsibility-oriented. We follow with a description of biochemical characteristics distinguishing epigenetics from genetics, in order to emphasize the very close relationship that exists between the environment and gene expression. This then leads to a discussion of the importance of the environment in determining individual and population health, which, we argue, should shift bioethics towards a Potterian view that promotes a communitarian-based sense of responsibility for the environment, in order to fully account for justice considerations and improve public health.

INTRODUCTION
Despite more than 40 years of development, the definition of ‘bioethics’ remains contested and many still disagree on the scope of activity that is appropriate for this relatively young field of scholarship and practice. For some, the ‘bio’ refers exclusively to biomedicine (biomedical ethics, with a focus on clinical ethics); others – including ourselves – take a broader and more encompassing view of bioethics. This latter view includes the diversity of issues – and thus bioethics sub-specializations – related to health (e.g., ethics of care, public health ethics, global health). In this article, we focus on the debate surrounding the pertinence and importance of including environmental concerns in bioethics.

At the source of this debate is an over-emphasized dichotomy between the fields of environmental ethics and biomedical ethics, a phenomenon identified by Whitehouse as the ‘ecomedical disconnection syndrome’. The North-American medical approach, focused as it is to a large extent on biomedical and biotechnological interventions, has unfortunately led many bioethicists to dismiss the environmental determinants

of health. Many believe that they should focus their time and energy on applying ethics to an already significant number of important ethical dilemmas occurring in the clinic, in the field of biomedical research, and in the use of new biotechnologies in medicine. This is reflected, for example, in the clinically-oriented focus of many bioethics graduate programs and in the presentation of the Principles of Biomedical Ethics by Beauchamp and Childress as the reference text for students. This approach should be questioned since such a reductionist vision of bioethics is fundamentally problematic. A rich literature in public health has demonstrated that health is strongly influenced by and correlated with a host of environmental factors that can vary according to social, economic, geographic, cultural or physical contexts. Bioethicists should, we argue, recognize this and – where appropriate – work to integrate environmental concerns into their field of study and deliberations.

Since some bioethicists may still be reluctant to take this approach, we explore an argument that might help convince them of the need to expand their reflections beyond the limits of the biomedical model and beyond a focus on individualism that is so prevalent in North-American bioethics. We propose an argument grounded in scientific research at the molecular level that will be familiar to – and so hopefully more persuasive for – the biomedically-inclined in the bioethics community. Specifically, we argue that the explosive growth of the relatively new field of molecular epigenetics provides novel information that should serve as additional justification for expanding the scope of bioethics to explicitly include environmental concerns. In creating a ‘biochemical bridge’ between our bodies and the environment, epigenetics can also help build a ‘conceptual bridge’ between biomedical and environmental ethics, one that then supports arguments for an ecosystemic conception of bioethics, such as that presented by Van Rensselaer Potter in the early days of bioethics.

We begin by presenting two distinct visions of bioethics that appeared at the very outset of the field in the 1970s, and that eventually evolved into two different conceptualizations of bioethics: the individualistic and rights-oriented and the communitarian and responsibility-oriented. We follow with a description of the bioethical characteristics that distinguish molecular epigenetics from molecular genetics and highlight the very close relationship that exists between the environment and gene expression. Then, we describe the important role of the environment in determining individual and population health through the influence of epigenetic mechanisms, and argue that justice considerations (for instance in the context of public policies) should take into account environmental determinants of health. Building on the tension between the two visions of bioethics, we conclude by arguing for a bioethics that better supports a communitarian-based sense of responsibility on the part of citizens (and by extension, decision makers) towards the environment, in order to improve public health.

**TWO BEGINNINGS OF BIOETHICS**

When we look back on the birth of the term ‘bioethics’ in the early 1970s as designating a field of study, two visions stand out: that of Van Rensselaer Potter, a biochemist and professor of oncology at the University of Wisconsin, and that of Andre Hellegers, a physician and professor of obstetrics, physiology and biophysics at Georgetown University. Although ‘bioethics’ was used first by Potter to bring attention to the interplay of ecology, medicine and human values, the vision popularized by Hellegers and colleagues at Georgetown University involved a strict biomedical focus. Hellegers’ vision was narrower and intended to focus attention on the concrete ethical ‘problems’ faced by physicians and other health professionals, such as the rights and responsibilities of patients, health professionals, researchers, and research participants, and the ethical issues related to health policy. According to Reich, Potter’s vision was probably marginalized because of the medical context of the time. In the 1970s, issues such as patient autonomy and the right to die were central, while questions related to the protection of the environment and public health were still embryonic.

According to Potter’s vision, bioethics should have established a broader field of discussion that incorporated the relationship we have with nature and the importance of this relationship to health and the future of humanity. He also suggested that scholars develop and introduce ethical guidelines that would enable humanity to live in harmony “with the rest of the world” and the biosphere. Potter’s bioethics was humanistic and interested in preserving the environment and non-human...
biological systems. In the late 1980s, Potter attempted to integrate biomedical ethics with environmental concerns using the concepts of ‘acceptable survival’ – in the context of a sustainable way of living for humanity – and ‘global bioethics’ in the sense of encompassing environmental concerns within bioethics discourse. His ideas, however, did not take hold in North American bioethics scholarship. So while the term ‘global bioethics’ is now commonly used in the bioethics literature, it seems to have discarded Potter’s environmentalist vision and instead focuses on biomedical issues at an international level, such as whether bioethics principles are universal or culturally relative. The failure of the Potterian vision in shaping bioethics is highlighted by the fact that environmental concerns in bioethics differs according to the medical approach advocated by different cultures or communities. To illustrate this difference, a comparison of North-American and Latin-American visions of bioethics is helpful. In the United States (and to only a slightly lesser extent, in Canada) the medical approach is mainly curative and focuses particularly on the medicalization of health. This approach was greatly influenced by the progress achieved in early 20th century microbiology. The development of microbiology helped foster the idea that disease occurs through the invasive introduction of a pathogen from the environment into the body. This externalization of the causes of disease has led to the perception of the environment as posing a threat or a risk to individual health, rather than as a possible source of individual well-being and even survival. A consequence of this demonization of the environment is the anthropocentrism of North-American medicine and bioethics. Attention is focused on the individual patient who becomes the center of all interests, and not surprisingly, the principle of autonomy often prevails in ethical reflection. As Paul Root Wolpe notes: The conflict between liberal individualism (autonomy) and responsibility to the common good (justice, beneficence) has characterized bioethical thought since its inception, and so has the realization that struggle was being won by the ethic of individual liberty. Yet even on the broader level of policy, when justice and autonomy seem to conflict, American culture has been progressively favoring autonomy. The strong American tradition of privacy rights and personal liberties has elevated “the patient’s right to decide” as the rallying cry of both bioethical theory and medical jurisprudence. America is the most rights-centered society on Earth, and so it is not surprising that medical decision making so often gets recast in terms of personal rights.

Despite the hesitation of many North-American bioethicists to integrate environmental concerns into bioethics, it is evident that environmental factors have an important impact on individual health and on the healthcare system. These factors are being increasingly considered in contemporary bioethics, to the point that we are seeing the emergence of a burgeoning new sub-specialty called public health ethics, with an academic journal of the same name and increasing bioethics research being published in professional and academic journals of the public health community.

**TWO DISTINCT CONCEPTUALIZATIONS OF BIOETHICS**

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Although this individualistic vision of bioethics and its focus on autonomy is widespread, other cultural contexts have led to the development of more communitarian visions of bioethics. For example, scholarship from Ibero-American communities, and particularly from Brazil, supports the development of an ecosystemic model of medicine and bioethics, consisting of three essential considerations: health, environment, and mediation between the two (the conditions and lifestyle of a particular community). This representation of bioethics emphasizes the importance of solidarity and relegates individualism to second place; it promotes an ‘ethic of life’ that brings together, as in the original Potterian vision, biomedical ethics, ecology and human values.

Not surprisingly, it was Brazilian representatives at the UNESCO 2005 deliberations in Paris on the creation of a Universal Declaration on Bioethics and Human Rights that urged the introduction of a clause (Article 17) requiring the protection of the environment. That article supports the Potterian view of bioethics and is an important plea for the recognition of the direct interconnection between human health and well being, and the protection of the environment.

Hence, analogous to the tension between individualism and communitarianism is the tension between the rights-oriented and the responsibility-oriented approaches in bioethics. According to Whitehouse, rather than focusing primarily on the individual rights of the patient or the research participant, Potter developed a conception of bioethics that included as a fundamental principle a sense of responsibility on the part of human beings as active members of a global system that is the biosphere.

According to this vision, individuals should be accountable for the multitude of environmental determinants of health on which they exercise an influence.

During the last two decades, the emergence of environmental concerns such as the depletion of the ozone layer and global warming have brought increased attention to the environmental determinants of health. The environment is no longer perceived of as detached from human activity, and it is now clear that humans strongly impact the biosphere and by the same token, the health of individuals. Scholarship in environmental ethics has helped us understand that living in a closed system means living with limited natural resources, and so we should be concerned with the availability of these resources for future generations. Arguments such as equality of opportunity between generations and intergenerational justice have been put forward in order to promote the idea of sustainable development. In public health, similar concerns arise and so should increase attention to the relationship between human activity, environmental changes and human health, and – we argue – provide strong justification for supporting communitarian-oriented approaches in bioethics. A particularly useful example of this relationship is seen in the emerging field of molecular epigenetics.

**MOLECULAR EPIGENETICS: LINKING THE ENVIRONMENT TO GENE EXPRESSION**

Recent developments in the field of molecular epigenetics are changing the traditional conception of genetics and the factors that impact human development and health. The origin of the term ‘epigenetic’ is often attributed to geneticist and philosopher Conrad Hal Waddington, who in 1942 used it to designate the ‘branch of biology which studies the causal interactions between genes and their products, which bring the phenotype into being’. The investigation of the strictly linear nucleotide structure of DNA, epitomised by the mapping of the human genome in 2003, transformed into the study of gene expression control mechanisms, that is, the reading of genes and subsequent production of associated proteins. This then led many scientists to become interested in the field of molecular epigenetics, that is, the study of the coordinated involvement of the locus-specific three-dimensional structure of DNA (governed by enzymes-facilitated biochemical modifications) and the transcriptional machinery (responsible for DNA reading and subsequent protein production). In other words, molecular epigenetics is the study of biochemical modifications that modify chromatin structure and gene expression.

Epigenetic modifications have a major influence on the variability of gene expression between individuals and according to different situations. Unlike the genetic code, which is static and whose variation is largely explained by

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22 Ibid: 5.

23 UNESCO (2005) Universal Declaration on Bioethics and Human Rights. Adopted by acclamation on 19 October 2005 by the 33rd session of the General Conference of UNESCO (Paris) Article 17: ‘Protection of the environment, the biosphere and biodiversity: Due regard is to be given to the interconnection between human beings and other forms of life, to the importance of appropriate access and utilization of biological and genetic resources, to respect for traditional knowledge and to the role of human beings in the protection of the environment, the biosphere and biodiversity’. See also H. Wolinsky. Bioethics for the World. *EMBO reports* 2006; 9: 354.


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random mutations, the epigeome is directly influenced or governed by environmental conditions. Epigenetic modifications can be grouped into three categories, depending on the type of chemical modification they entail: 1) DNA methylation,26 2) chemical modification of histones,27 and 3) interference at the RNA level.28 The three-dimensional structure of chromatin and gene expression are tightly regulated by these modifications. Thus, the genetic code – the linear combination of the nucleotides A, G, C and T – is not the sole biological determinant of individual phenotype (physiology, psychology); variation in environmental exposure plays a crucial role in determining gene expression, protein synthesis and disease development in individuals and populations.30

Epigenetic modifications are associated with five characteristics that distinguish them from genetic mutations. First, they are dependent on the environment. Here we must think about the environment in the broadest sense of the term, from the intrauterine or postnatal micro-environment (microflora) to the physical (nutrition, temperature) and social environment (stress, quality of life).31 Environmental factors that may affect the mechanisms of epigenetic modifications include, amongst others, exposure to toxins, drugs, and physical activity. Unlike genetic mutations, which occur very rarely and are largely irreversible, epigenetic modifications are dynamic and reversible. Epigenetic modifications are also interdependent, a feature that creates unprecedented complexity for genetics research, to the extent that the quest for the identification of the human epigenome or ‘histone code’ is likely to be an even greater challenge than the mapping of the human genome. The last feature of molecular epigenetics, and perhaps the most surprising, is that some modifications may be heritable. Indeed, it has been shown that the patterns of DNA methylation of cells are transmitted through mitosis (cell division), but also through meiosis (production of spermatozoa and ovums). Thus, it appears that some epigenetic changes can have an intergenerational influence.32

The biochemical characteristic of heritability is not specific to epigenetics, and is in fact a characteristic that is principally associated with genetic molecular modifications that can be caused by exposure to DNA-perturbing agents in the environment, such as radiation or chemical carcinogens. Hence, genetic modifications are also to some extent dependent on the environment and can be transmitted to subsequent generations if germ (reproductive) cells are affected.

But there is an important difference in the temporality, causality and complexity of genetic and epigenetic heritability. First, the speed and frequency (dynamism) at which epigenetic biochemical modifications occur following environmental exposure are of a much greater magnitude than for DNA mutations. Second, the causal relation between the environment and the epigenome literally transcends the mere ‘accidental happenings’ of genetic mutations, and is directly related to the activation or inhibition of gene expression. Third, the fact that biochemical modifications are interdependent highlights the importance of considering the interrelations that exist between a specific biochemical modification, its modification of the molecular micro-environment and the very probability – that is highly influenced by the micro-environment status – of subsequent modifications on neighbouring sites.

To date, epigenetic biochemical modifications have been shown to be involved in normal development (cell differentiation, extinction of chromosome X), in adaptive response to the environment (stress resistance, personality traits), and in the development of pathological phenotypes. Several studies have demonstrated the impact of environmental toxicity (heavy metals, bisphenol A, vinclozolin) on epigenetic mechanisms, and the disruption of these mechanisms has been associated with diseases such as cancer, hypertension, type 2 diabetes and asthma. Psychological disorders such as bipolar disorder, schizophrenia and Alzheimer’s have also been correlated with altered epigenetic mechanisms.33

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The Barker effect is one widely accepted demonstration of the influence of the environment on gene expression and on the development of disease. It shows clearly that our individual history of nutrition and exposure to environmental toxins is biochemically imprinted in gene expression pathways, and that we somehow carry this ‘biomemory’ of our close biochemical relationship with the environment. A few studies in molecular epigenetics are now beginning to help identify the biochemical pathways behind this biomemory. For instance, a study of the methylation of the gene Igf2 in individuals whose mothers lived through the Dutch Hunger Winter in 1944–45 found that a deficiency in maternal caloric intake affected the methylation pattern of their children 60 years later. Another study has shown that exposure to pollution (diesel exhaust) and allergens (aspergillum fumigatus) can lead to abnormal methylation of genes, causing inflammatory lung hyper-reactivity in the first generation, and unusual patterns of methylation of other genes associated with asthma in the second generation.

As noted by McDermott in his analysis of the ‘thifty gene hypothesis’ and the Barker effect, a ‘limited concept of causation [genetic determinism] and a monopoly of concern with pathogenesis and treatment almost completely ignore the need to attend to environmental factors, including the socio-economic environment and prevention.’ With greater attention to the role of epigenetics, a more complete picture will appear of the full range of causal factors that influence the development of complex diseases, including but not limited to the genetic determinants of health.

**JUSTICE AND EXPOSURE TO EPGENETIC RISKS AS A DETERMINANT OF HEALTH**

The scientifically demonstrable influence of the environment on epigenetic mechanisms provides an additional argument – this time at the molecular level – for greater consideration of the environment as an important determinant of health. At the same time, it expands the analysis of justice in bioethics to include environmental considerations. Living conditions directly affect the regulatory mechanisms of gene expression and can at the same time cause epigenetic alterations that may be heritable. We should therefore question the equity in the distribution of risks and benefits associated with different environments and population groups.

To illustrate our point, the example of the uneven dispersion of pollution is particularly pertinent. It is well recognized that pollution takes some priority lanes with prevailing winds or ocean currents. Pollution is often carried far from the countries where it is produced and thus the population that suffers the most may not necessarily be responsible for creating the pollution. This population may be economically or technically unable to deal with the consequences of pollution due to an absence of infrastructure for water treatment, or nutrition that is particularly dependant on the local natural environment.

In addition, polluting factories or incinerators are invariably built in the poorest parts of cities, leading to an unfair distribution of risks to the integrity of the epigenome and of associated health disorders. The alterations that are being induced in the environment, and thus affect individuals, do not affect populations equally nor equitably, and this creates injustices that should be of interest to North American bioethicists.

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If fair allocation of resources to treat a disease is important, should not a fair allocation of preventive measures – in this case, a minimization of risks and threats to the epigenome that come from the environment – also be of interest to bioethicists? We argue that in many situations, the inequity with regard to the exposure to epigenetic risk factors of environmental origin is sufficiently important that it must be discussed by bioethicists, and eventually be considered in public health policies that are based on scientific knowledge. As Rothstein and colleagues argue, environmental factors that might disrupt the epigenome should be included in national environmental protection regulations, such as the USA’s Clean Water Act (CWA) and the Comprehensive Environmental Response Compensation and Liability Act (CERCLA). The question of fairness in relation to exposure to environmental determinants of the epigenome in the population also raises issues related to intergenerational justice. Indeed, the intergenerational heritability of epigenetic modifications should lead to ethical concern about the impact that present exposure to environmental disruptors will have on the integrity of the epigenome of descendants, and thus the health of future generations.43

Molecular epigenetics highlights the importance of considering the external parameters influencing a system (here the human body) in the resolution of a systemic problem such as a health disorder. The close biochemical interplay between genes and environment that is clarified by recent scientific discoveries in epigenetics is representative of the ecosystemic relationship of which we are a part, as human beings and as biological organisms. In our view, the genetic and the epigenetic approaches in biology can be seen to represent, metaphorically, the two distinct conceptions of bioethics described at the beginning of this paper: molecular genetics reflects an individualistic perspective and molecular epigenetics a communitarian view.

The genome shapes the biological characteristics that we are born with and are largely unchanging. To that extent, we argue that molecular genetics is conceptually (and in practice) related to individualist/rights-based approaches in bioethics. In focusing on genes/individuals and the right to biomedical innovations and ‘personalised medicine’ we do not pay sufficient attention to the dynamic interactions between socio-cultural and environmental contexts on one hand, and individual or population health on the other. Conversely, the epigenome is a biological characteristic that involves complex and dynamic interactions with the exterior of the body (the environment), illustrating at the molecular level, the important influence of the environment. In this context, molecular epigenetics is conceptually related to communitarian conceptualizations of bioethics that argue for more complex visions of individual and population health.

While it confirms the direct influence of environment and lifestyle on individual health, molecular epigenetics also highlights the scope and limits of individual responsibility, and thus the need for collective action and community responsibility. Individuals may be causally responsible for actions that impact the health of other individuals (stress, pollution) or for passing on certain illnesses or conditions to subsequent generations (due to nutrition or lifestyle). They may, nonetheless, have limited individual power and responsibility to remedy the situation or mitigate the consequences of their actions. It would thus be unfair to blame the poor for being malnourished or living in toxic environments, factors that, through epigenetics, can negatively affect their own as well as their children’s health. Yet individuals can, through collective action, lobby decision-makers, governments and industry to remedy environmental problems that are shown to have a negative effect on the epigenome, and thus on individual and population health; the ‘greening of cities’, the imposition of municipal clean air regulations, and the development of innovative social housing to counter ghettoization are but a few notable examples.44

In light of this close connection between exposure to epigenetic risk factors and issues of social justice, bioethicists need to broaden the scope of their reflections with regards to the ethics of health policies. Often focused on the allocation of resources for interventions that manage the symptomatic aspects of diseases, bioethical reflection about justice should be expanded to include public health considerations and the management of environmental determinants of health.

CONCLUSION

A major challenge emerging from the integration of environmental concerns into bioethics deliberations is the level of attention they require. In practice, it can be difficult or even impossible for bioethicists to take into account all the environmental aspects and implications that a particular decision entails, for all the stakeholders


or actors involved. Indeed, in some circumstances it might even become counterproductive to pay too much attention to environmental concerns, particularly if this would entail ignoring the curative aspect of a particular dilemma, which in many cases – depending on the urgency and gravity of the situation – must prevail. At the same time, when identifying and debating ethical dilemmas, bioethicists should also consider which scale of intervention is appropriate: the micro level (individual relationship), the mezzo level (organization, guidelines), or the macro level (public health policy, governance).

In this article, we have adopted Potter’s vision of bioethics, whereby bioethics is a vast field of discussion on a diversity of ethical issues arising in a global context and affecting both individual and public health. The vision of Hellegers, popularized by the Georgetown University School of bioethics, which is narrower and primarily focused on the biomedical field, is in our view too restrictive. The tension between these two visions is reflected in different philosophical foundations for bioethics (communitarianism and individualism) and in different conceptions of bioethics as being rights-oriented or responsibilities-oriented. We believe that bioethics should provide an opportunity for discussing both the way in which the human condition is shaped by the environment and the way that human activity is modifying our environment. The individualistic focus of North-American bioethicists neglects problems of environmental injustice, many of which have been closely associated with socioeconomic injustice, that have a direct impact on the health of individuals and populations. Bioethicists should be concerned with this type of injustice and work towards finding a more nuanced balance between the rights of individuals and their responsibilities as components of the biosphere and members of society. Considering the mounting evidence of epigenetic and environmental influences on individual and population health, we argue that environmental concerns must play a greater role in bioethics scholarship, alongside the substantial work that has already been done in dealing with issues that are particular to individuals.

Environmental concerns have too often been considered a distinct issue, as if they were ‘external’ to human well-being. Epigenetics show us clearly – through the lens of molecular biology – that we have a close biological and biochemical relationship with the environment. It also brings to the fore convincing arguments for the importance of making some sacrifices today for our own future condition, and even for that of future generations. It brings even more weight to concepts such as social/environmental determinants of health and sustainable development. In fact, molecular epigenetics – in comparison with molecular genetics – should transform our vision of health from being merely centered on the individual, to being inclusive of an ensemble of ecosystemic factors. Academic programs in bioethics would do well to encourage discussions of this expanded and more nuanced vision of health as involving both individuals and populations, and as having an intimate and dynamic relationship with the environment. This would make bioethics a richer and more inclusive field of study and deliberation, and one that is coherent with the truly complex and inter-related nature of human health.

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