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## Essay Review

### Broadening Heredity

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#### **Heredity Explored: Between Public Domain and Experimental Science, 1850–1930**

Staffan Müller-Wille and Christina Brandt (Eds.), MIT Press, Cambridge, MA (2016) 480pp. Price \$49.00 £40.95 hardcover, ISBN: 9780262034432

#### **Life Histories of Genetic Disease: Patterns and Prevention in Postwar Medical Genetics**

Andrew Hogan, Johns Hopkins University Press, Baltimore, MD (2016) 280 pp. Price \$40.00 hardback, ISBN: 9781421420745

Two revolutionary transitions have long provided the landmarks in our navigations of the history of the scientific study of hereditary phenomena. First, following the 1900 triple-rediscovery of Gregor Mendel's experimental breeding work with the garden pea, *Pisum sativum*, performed in the 1860s, heredity, how it was conceived and how it was investigated, became thoroughly Mendelised. Mendelism, with its discrete segregating factors transmitted according to predictable and verifiable rules, promptly displaced the speculative theories of the latter nineteenth-century; those associated with Charles Darwin, Francis Galton, August Weismann, and Hugo de Vries, for example. Mendelism also provided the foundation for the new science of genetics, a powerful discipline which studied the transmission of traits from one generation to the other via the passing on of Mendelian factors—re-christened “genes” (Johannsen, 1909). Genetics in the Mendelian mode went along happily and with many great successes through the first decades of the twentieth-century, a period during which its findings infiltrated many fields, from biology and medicine to psychology. They were also synthesised with Darwinian natural selection to yield the theoretical orthodoxy which to a large extent continues to underpin evolutionary studies today.

After World War II, though, revolution was once again in the air. With Watson and Crick's 1953 discovery of the double-helical structure of DNA, and biology's rapid uptake of tools, techniques, and even personnel from the physical sciences, the scientific study of heredity was rapidly and irreversibly molecularised. Andrew Hogan's *Life Histories of Genetic Disease* covers exactly the period of this transformation, and in one of the key contexts—medical genetics—in which the ramifications of this molecular revolution were supposedly most keenly felt. Staffan Müller-Wille and Christina Brandt's edited volume *Heredity Produced*, on the other hand, spans neatly the moment of the vaunted Mendelian break, setting up nicely the prospect of a “before-and-after-the-triple-rediscovery” type comparison.

All of this is to say that one might expect to be on familiar grounds with these volumes, each respectively updating and supplementing our pictures of these consequential ruptures in the history of a discipline. One would be mistaken. In fact, each work offers a ‘smearing-out’ of the sharp breaks which have been supposed to have occurred in the periods they address. Notions of continuity, heterogeneity, and the ongoing negotiation between old and new, challenge received narratives of sudden and decisive transformations in concepts and practices. In this essay I offer a necessarily incomplete survey of how each volume exercises these remedial aims, before exploring a couple of themes which might frame future investigation in lieu of the narratives which the present works challenge.

### **Getting the Monk off our Backs**

*Heredity Explored* is the latest of the Max Planck Institute’s long-term “A Cultural History of Heredity” project. Its predecessor *Heredity Produced: At the Crossroads of Biology, Politics and Culture, 1500-1870* (Müller-Wille & Rheinberger, 2007), detailed the complex story of the emergence of “heredity” as a biological concept. The roughly eight decades from 1850 to 1930 which the newest volume covers were, as its title suggests, ones during which thinking about the heredity was developed in a variety of directions, by a heterogeneous host of people in diverse contexts,<sup>1</sup> towards disparate ends. As already suggested, this angle may surprise readers expecting attention to this period to generate a story of consolidation of both the realm of heredity’s proper investigation—i.e. the emergence of the new science of genetics—and of the notion of biological inheritance as being hard, particulate, and above all Mendelian. Yet in their synthetic introduction, editors Staffan Müller-Wille and Christina Brandt make clear their intention, “in contrast to previous scholarship, [to] go beyond the focus on Mendel’s rediscovery” (p. 5). *Heredity Explored* emphasises the variety of people—physicians, publics, agriculturalists, gynaecologists—and contexts—medical, agro-industrial, policy, literary—involved in the formulation of ideas about heredity, as well as the heterogeneity and flexibility of the ideas themselves. For the cast of characters in many of the cases examined, fitting Mendelism into the post-1900 picture was far from unproblematic, and required considerable conceptual acrobatics, if it was to be attempted at all. Thus, at least with respect to Mendelism and its place within hereditary discourse, *Heredity Explored* paints a picture of relative continuity across the turn of the century, and of the significant negotiations required in reconciling seemingly discordant conceptual resources. As such, this ambitious volume challenges us not only to broaden our conception of what heredity qua biological concept has meant throughout its relatively short history, but also to widen the scope of the hows and whys of engaging with heredity as a historiographical object.

As intimated by its qualifying subtitle, the collection demonstrates that what was going on in the new laboratories of genetics was only one part of a rich story played out in

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<sup>1</sup> The editors utilise these various contexts in organising the volume into thematic sections: ‘Genealogy, Kinship, and Population’; ‘Heredity, Evolution, and Reproduction’; ‘Heredity in Agro-Industrial Contexts’; ‘Heredity in Medical Contexts’; ‘Mendelism’.

diverse cultural realms. Historians must hold this in mind when hoping to piece together the history of heredity. The varied contributions to this volume, dealing with asylums, vaccines, marriage laws, and the literary figure of the bachelor, in addition to more established topics like genetics research and evolutionary theory, well exemplify this broadening of the scope of where to look when we do the history of heredity. Though still centred on Europe and North America, the perspective achieved in this volume is still far wider than that of any previous work on heredity in this period, and it is much the better for it. In stepping outside of Mendel's pea garden or Morgan's fly room at Columbia, and into the Copenhagen Carlsberg Laboratory—Christophe Bonneuil, chapter 9 on “Pure Lines as Industrial Simulacra”— or the record offices of state Asylums—Theodore Porter, chapter 4 on “Asylums of Hereditary Research in the Efficient Modern State”, the conceptual and cultural richness of the story of heredity is brought home. Something which bleeds through many of the contributed essays is the notion that investigations of heredity were often far from efforts to merely explore it, but also to control it. Whether their ends were eugenic, medical, industrial, agricultural or otherwise, the historical cast of *Heredity Explored* were generally intent upon not just understanding, but also influencing and managing the transmission of biological and behavioural traits. As Bonneuil's essay demonstrates, for industrialist-breeders dealing in plant lines for food production, the purity of stocks and the reliable recurrence of desirable traits were serious business and key to their marketability; J. Andrew Mendelsohn's chapter “Message in a Bottle: Vaccines and the Nature of Heredity after 1880” shows that the same was the case for the mass-production of standardised vaccinations.

It was in these so called “agro-industrial” contexts that Wilhelm Johannsen formulated his notion of the “pure line” and his 1909 genotype/phenotype distinction, effectively driving a wedge between heredity on the one hand and development on the other. Towards the aims of mass-producing serialised and stable lines of biological individuals, the abstraction of heredity from individual ontogeny and historical contingency was a productive move. Such was not necessarily the case in other contexts, notably the medical one. Jean-Paul Gaudillière and Ilana Löwy, in their chapter on “The Hereditary Transmission of Human Pathologies between 1910 and 1940,” show that Mendelism, which rapidly became deeply linked to Johannsen's distinction, received a rather cool reception in some British, French and American medical circles. Whilst the abstraction of inheritance away from individual ontogeny was amenable to the aims, methods, and large populations of the industrialists and breeders, such was not necessarily the case for physicians dealing with the pathologised or aberrant individual. As the volume's editors nicely put it, “as far as the epidemiology of disease is concerned, questions of infection, immunization, and heredity remained confounded in such a way that the vertical and the horizontal dimensions of the transmission of diseases could not be disentangled” (p. 12). The inheritance of diseases or propensities to develop them seemed a much more complex affair than the passing down of discrete factors in accordance with Mendel's newly rediscovered laws, and one in which environment, ancestry, and a host of contingent factors were seen to play irreducible roles. Gaudillière and Löwy conclude that, although physicians were aware of the successes of laboratory Mendelism, many questioned its relevance to their own pursuits. Bernd Gausemeier, in his chapter (14) on populational studies of pathological heredity, explains that although many

practitioners were explicitly committed to the notion of Mendelian unit factors, “their discourse remained widely shaped by older concepts of ancestral “influence” and familial bloodlines” (p. 353). As the work of Jonathan Harwood (2015) and others have done for breeding practices, this picture challenges the notion of a sharp break or rapid uptake of Mendelism in medicine in the first decades of the twentieth-century. The feeling we get from the contributions to *Heredity Explored* more generally is that, to the extent that Mendelism was incorporated into existing conceptual and experimental practices, its place therein was fragile and subject to significant negotiation.

### **More than Molecules**

By the time we reach the postwar setting of Andrew Hogan’s *Life Histories of Genetic Disease*, medical thinking on heritable disease had been thoroughly Mendelised. The standard “break” narrative which provide’s one of Hogan’s foils is not the Mendelian revolution, but the “molecular” one. Several scholars, Hogan tells us, have proposed a schism to have occurred in postwar medical genetics, after which biomedical practitioners ‘visualized life at the molecular level ... replacing the clinical gaze of medicine with a new style of thought and way of seeing ... the “molecular gaze”’ (p. 208). Hogan’s revised and compelling picture is one in which

the era between the 1970s and the present did not reflect a transition from one style of thought to another—from the clinical gaze to the molecular gaze—but rather the ongoing development of a genomic gaze, which incorporated both (p. 210).

Thus, what Hogan calls the “chromosomal infrastructure” (p. x) built up through cytogenetical research in concert with clinical investigation was not discarded wholesale with the rise of molecular sequencing and other techniques. The vision of the genome embodied in chromosomal ideograms of the 1950s with their familiar banding patterns remained a touchstone for medical geneticist, who endeavoured not to displace but to integrate the wave of DNA-sequence information with this older picture. The continued emphasis on the chromosome in what was supposedly the age of the gene resonates with Luis Campos and Alexander von Schwerin’s contribution to *Heredity Explored*. Their essay on “Transatlantic Mutants” explores how Albert Francis Blakeslee and Erwin Baur, whose broadly Mendelian work focused, respectively, upon mutations at levels “above”—i.e., chromosomes—and “below”—Kleinmutationen— that of the classical gene.

Hogan paints his picture through an impressively detailed and engaging reconstruction of how it is that physicians and geneticists in the postwar period came to define genetic diseases, correlate them with particular genetic abnormalities, and detect and visualise these abnormalities in patients in the context of prenatal diagnostics. With this in mind, the title he has chosen for his book plays fruitfully and self-consciously upon a double-meaning. Medical folk speak of genetic diseases as having “life histories” in the sense of an identifiable developmental pattern in the presentation of traits, tendencies and symptoms throughout each individual patient’s lifetime, with room for some variation, of course. But

they were also well aware that the diseases they dealt with have conceptual life histories of their own. That is, understandings of disorders, within the profession and without, evolve through time in response to changing ideas about their causes, diagnosis, and proper treatment. Hogan's narrative is driven by, and in turn buttresses, the notion that disease concepts are responsive to, and actively constructed by, human intervention.

Hogan brings this point home starkly in his fifth chapter, which explores an instance in which two disorders—DiGeorge syndrome and velo-cardial-facial (VCF) syndrome—previously thought to be distinct, were lumped together. Medical scientists' rationale for this move was the successful application of a novel mapping technique imported from molecular biology, namely, *in situ* hybridisation, in the identification of a chromosomal mutation shared by patients diagnosed with either syndrome. One of Hogan's major protagonists, the medical geneticist and author of the influential *Mendelian Inheritance in Man*, Victor McKusick, complained that clinical observations of patients could be misleading; manifestations of similar sets of symptoms were often and erroneously taken to represent instances of the same disorder. What mattered in delineating these conditions, for McKusick, was not what was seen of the patients' bodies and behaviours in the clinic, but what was seen in their chromosomes (*Life Histories*, p. 16).

These practices of definition and delineation, then, were concrete enactments of McKusick's proposed one mutation—one disorder ideal. The influence and elaboration of this powerful principle provides a narrative touchstone for Hogan, one that is bolstered by its essential circularity. As he observes “in order to count as a mutation in medical genetics, a genetic variant needed to cause some discernible pattern of bodily malformation. At the same time, in order to count as a discrete genetic disorder, a condition had to result from a single recurring mutation” (p. 16). Hogan's chosen arrangement, in which odd-numbered chapters zoom in on the life histories of particular diseases and their medical delineation—e.g., Fragile X; Prader-Willi; DiGeorge and VCF syndromes—and the even-numbered chapters document the development of new tools and techniques for visualising and mapping the chromosomes—banding patterns, high-resolution chromosomal analysis, genome-wide microarrays, and more—well showcases the profound extent to which McKusick's ideal has shaped the entities and approaches of medical genetics from the postwar period to the present day. Nowadays, reminders of the perils of a too naïve conception of one-to-one mappings of particular diseases to specific, heritable genetic abnormalities are almost as commonplace as manifestations of the views being warned against. Nevertheless, what American political scientist Leonard Cole has termed the “gene-a-week” phenomenon remains a salient aspect of the practice and perception of medical genetics (1996, p. 708). Cole's coinage refers, of course, to our bombardment by headlines claiming that scientists have identified the “gene for X”. Practices of identifying genetic bases for certain traits (notably diseases) occupy an ever more central place in science, medicine—including Hogan's chosen domain of prenatal diagnostics—law, and indeed wider culture.

## **Whose Heredity?**

Müller-Wille and Brandt's chosen subtitle, "Between Public Domain and Experimental Science, 1850-1930" is thought-provoking as well as apt. Immediately the reader is faced with a juxtaposition of two seemingly distinct cultural spheres, that of the "public", and that of the expert scientific elite. The suggestion, furthermore, is that hereditary discourse took place between these spheres, rather than strictly in one or the other. To the extent that we subscribe to the notion of two such separate and definable spheres today, *Heredity Produced* arguably deals with the historical moment at which they came into meaningful existence. The decades up to and immediately following the turn of the twentieth century is when, according to a significant body of scholarship, science underwent "professionalisation," and the "scientist" qua trained, paid, expert emerged as a widely recognisable identity in Western societies. But it was also, and not coincidentally, when scientific publics—that is societal groups who consumed, discussed, interpreted, wrote about, celebrated, condemned, and were materially affected by, scientific knowledge and its uses—came into being. The mutual interactions and intermingling of "public" and "expert" discourses have shaped science's trajectory ever since.

Perhaps no setting for these interactions presents itself as regularly, and often controversially, as do discourses on human heredity and its management via planned scientific intervention, in particular. *Heredity Explored* and *Life Histories of Genetic Disease* each provide various snapshots of such encounters, some surprising, all suggestive. Diane Paul and Hamish Spencer's contribution to *Heredity Explored*, concerning "Anglo-American Critiques of Cousin Marriage in the Nineteenth and Early Twentieth Centuries," is arguably of the former variety. Opinion among eugenist-activists upon such practices was, Paul and Spencer show, split, as fears that inbreeding through first-cousin-marriages harbours greater risk of inborn defects—Charles Darwin's worries about his own knotted family tree are well known—met approving invocations of the "racial purity" which limiting outcrossing supposedly ensured. The wider public was less ambivalent; the steady rise in the number of states legislating against cousin-marriage in this period seems attributable not to the lobbying of eugenisists, but to "folk" understandings of heredity which "enormously exaggerated" the dangers of cousin-marriage (p. 61).

Whilst the self-proclaimed experts in Paul and Spencer's story did not feel that the potential costs or benefits to public health associated with a particular matter of heredity (cousin-marriage) were sufficient to compel the scientific establishment's intrusion, the opposite has very often been the case. In Bernd Gausemeier's (ch. 14) account of "The Study of Human Heredity before and after the Mendelian Break," we hear that physicians advocating systematic studies into the inheritance of diseases "often derided degenerationism as a popular superstition which had to be controverted by sober scientific investigation" (p. 340). As Gaudillière and Löwy (ch. 13) show, physicians in the early-twentieth-century actively grappled with the popular hereditarian-cum-fatalistic understanding of cancer, which they perceived to contribute to folk neglecting to look out for early signs or seek medical help at an early stage when the chances of successful treatment were highest. To combat this, physicians and cancer charities put out pamphlets and public statements proclaiming the non-

heritable nature of the disease. Often, such statements were at odds with the more nuanced views voiced by the same experts behind closed doors (p. 318).

Certain broad-brushstroke but telling differences are discernible in the characterisations of both publics and experts implicit in the episodes detailed in *Heredity Explored*, and those documented by Hogan. In his chapter on “Asylums of Hereditary Research in the Efficient Modern State”, Theodore Porter uses practices of data-gathering and record-keeping regarding mental patients to explore the emergence of two late-nineteenth-century phenomena; the statistical treatment of populations, and the notion of the character of a nation-state as closely tied to the make-up of its citizens (*Heredity Explored*, ch. 4). Much like the industrialist-breeders’ pure lines of plants discussed by Bonneuil in chapter 9, the heritable character of human populations, increasingly viewed, during this period, as resources for the nation, came under attempts at top-down control and manipulation. This, of course, was part of the conceptual backdrop to the widespread rise of state-legislated eugenic sterilisation, and in the Nazi case, extermination, of supposedly “inferior” types.

The Second World War, and emerging recognition of the horrors of Nazi eugenics, notably falls in the gap between the temporal coverage of these two volumes. Nevertheless, its ramifications bubble away in the background of the medical and scientific communities at the focus of Hogan’s narrative. While it is commonplace to attribute the postwar decline in vocal support for eugenic legislation to Nazism, it is now becoming equally conventional to assert that eugenics never really went away (Kitcher, 1996; Comfort, 2012). We continue to practice eugenics; we have simply done away with the dirty word. Hogan is acutely sensitive to this growing consensus. His introduction is titled “Pursuing a Better Birth”, and in his preface explains that studying how “physicians and geneticists developed the confidence necessary to diagnose a disorder based on a mutation that was made visible prenatally, with few or no clinical findings to back it up” struck him as “a substantial consideration, given that a diagnosis often led parents to choose preventive abortion” (p. ix). In his words, *Life Histories of Genetic Disease* “examines the role of postwar medical genetics in facilitating and enhancing eugenic choice” (p. 4).

Commentators often observe that in the act of seeking such prenatal information we are practicing eugenics, whether or not we decide to act upon the information. Charges of unnecessary provocation aside, we can observe that if this act indeed be “eugenics,” it is of a very different kind than that which swept across the globe early last century. 1967 saw the right to abortion granted in Britain, meaning pregnancies could be terminated for various reasons, including if there was judged to be a significant risk that the child would suffer from serious mental or physical abnormalities. The United States followed suit in 1973 via a Supreme Court ruling on the *Roe v. Wade* case (Kevles, 1985). Genetic counseling clinics quickly proliferated on both sides of the Atlantic, offering parents prenatal testing for various heritable disorders, utilising many of the tools and techniques whose development Hogan meticulously documents.



Fresh memories of Nazism and the Cold War climate of rejecting governmental meddling meant that prescriptive top-down policies were off the table; the decision whether or not to abort was left squarely with the parents, although as Hogan shows throughout, experts offered circumspect advice on risk-levels. Because of the free-market availability of these procedures, particularly in the US case, many scholars have come to talk about them as exemplifying “liberal” or “laissez-faire” eugenics. Implicit in this is the fact that by the 1970s heredity, and its management, had left the purview of the state and come to be viewed as pertaining to individuals and families. “Bad inheritance” was gradually reconceived as a threat to families and individuals, as opposed to wider society, the nation, or the race. Perhaps these developments evidence what Diane Paul has perceived as a shift throughout the twentieth-century from “reproductive responsibility” to “reproductive autonomy”, in which procreation is widely viewed as “a human right, with which the state has no business meddling” (2002, p. 87).

### **From the “Historical” to the “Horizontal” (and back again?)**

It is clear there have been significant changes in our attitudes concerning whose right it is to make decisions upon heredity. What about corresponding shifts in our very conceptions of the nature of heredity? In their introduction, Müller-Wille and Brandt make a passing suggestion which certainly merits considered reflection. One legacy of the speculative theories of heredity in the latter nineteenth-century, they explain, was an emphasis on the place and space of inheritance; that is, the identification of heredity with a particular part of the cell, the nucleus. Once conceived as a “force,” heredity was made material, morphological. Relatedly, these theories progressively de-emphasised the particular ancestral relationships of individuals, and instead conjured the image of a hereditary substrate shared throughout the population. We are subject to inheritance not just from our parents or our family-line, but from a common stock, be it Francis Galton’s stirp, August Weismann’s germ-plasm, or Wilhelm Johannsen’s genotype. With this perspective in place, thinkers shifted the emphasis from the “ancestral” or “historical” relationships between living individuals to the “horizontal”.

Through such transformations, the editors suggest, heredity became associated with “the future rather than the past, with projection rather than with legitimization, associations that occurred in the context of the all-pervading late-nineteenth-century theme of progress” (p. 17). Mendelian factors were immutable, unaffected by the life experiences of those transiently carrying them, who pass them on unchanged, but in new combinations. Tradition, ancestry, and the constraints of history, then, could be left at the door, whilst Mendelism’s mosaic picture of the make-up of organisms promised, via analogy with synthetic chemistry, rapid biological progress through recombinatorial innovation. Nineteenth-century pessimism, perfectly exemplified by grip that “degenerationism” held on the public imagination, was replaced with a profound optimism surrounding what could be achieved down the line once a particular conception of inheritance was in place (see for instance, Endersby, 2013; Esposito 2017). Indeed, optimism of this kind is a trope which arises in Hogan’s analysis, as when he

explains that postwar medical genetics was “based on the premise that variations in the genetic makeup of individuals could reveal something about their present or future health. Based on this, medical geneticists promised that improvements on genetic knowledge and testing would enhance public well-being” (p. 20).

Whereas it seems that all manner of developments in genetical science and technology, from the Human Genome Project to CRISPR-Cas9 are similarly future-facing, and surrounded by discourses of hype and optimism, history is rapidly re-entering the frame, with profound implications. A century after its thorough de-historicising, our hereditary material is once again being thought about temporally. The genome of an individual, it is suggested, changes importantly through time and can even be thought to experience youth and old age (Lappé & Landecker, 2015). Our life experiences impinge upon our genomes, materially and functionally altering them; a process whose implications may not be limited to our own lifetimes. “Ancestral influence”, jettisoned from our conception of heredity around the turn of last century, seems to be re-entering the picture as an increasing number of studies investigate the intergenerational effects, via epigenetically modified hereditary material, of the experiences of earlier generations, including traumas, nutrition, lifestyle, and disease (Meloni, 2016, ch. 7). If the move from the removal of “historical” considerations had such profound effects upon the understanding of heredity and efforts to manage it as we have seen, then we might expect the impact of their reintroduction, if successful, to be similarly profound.

### **Concluding Remarks**

Change is afoot. As we leave the “century of the gene”—to borrow Evelyn Fox Keller’s phrase that is both descriptive regarding the centrality of the gene in the science of last century, and prescriptive regarding the need for us to leave the gene behind as we enter the present one (2000)—further behind us, challenges to the biological orthodoxy continually strengthen and proliferate. Many of these challenges are centred upon how inheritance works and the importance and implications of epigenetic phenomena. Within the biological sciences, then, we find ourselves in an intense period of reflection and introspection with respect to, amongst other things, the nature of biological inheritance. Something similar can be said, in parallel, of the historiography of the science of heredity. Whilst contemporary biologists and philosophers emphasise complexity and heterogeneity in the face of a perhaps-too-simplistic orthodox picture of how heredity works, historians are similarly complicating and heterogenising the earlier recounted standard narratives of how we got here. Among the many fruits of the works here reviewed are their contributions to this broadening, remedial project, by helping us to throw the Monk off our collective backs, and to move past “molecularisation”. Yet despite, or perhaps because of, their axe-grinding, they are highly constructive and stimulating works, which will cause the historians, philosophers, sociologists and scientists who read them (and they all should!) to think in new and interesting ways about biological inheritance.

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