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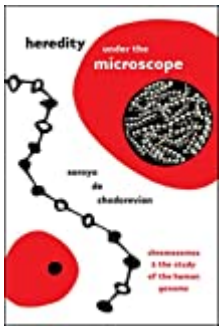

Soraya de Chadarevian. *Heredity under the Microscope: Chromosomes and the Study of the Human Genome.* Chicago: University of Chicago Press, 2020. 309 pp. $112.50, cloth, ISBN 978-0-226-68508-3.

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Only in the last decade have historians of postwar genetics begun to escape the gravitational field of molecular biology and the ensuing celebratory narratives resulting from its outspoken leaders. Among other things, this has meant an absence of historical work on the science of human genetics—too closely aligned with the flawed science of eugenics and race science—and an exclusive focus on the epistemic, institutional, and material cultures of biochemistry, biophysics, molecular genetics, and crystallography. With few exceptions, like Susan Lindee's excellent *Suffering Made Real: American Science and the Survivors of Hiroshima* (1994) and *Moments of Truth in Genetic Medicine* (2005), or Nathaniel Comfort's *The Science of Human Perfection: How Genes Became the Heart of American Medicine* (2012), the literature on this most significative scientific field of the second half of the twentieth century still lags behind the many studies of the molecularization of biology.

Heredity under the Microscope seeks to repair this absence. It moves the locus of the history of genetics from the analytic epistemology of molecular biology to the visual culture of microscopy; from microorganisms to humans; from molecules to chromosomes; from stand-out institutions to a multitude of scenarios that go from research facilities, hospitals, and multilateral agencies, to the courts and even the Olympic Games. Such diversity is supported by a corresponding extensive reliance on institutional archives and interviews, with collections scattered in Great Britain, France, Italy, Canada, the United Sates, and Switzerland. Also, the author draws extensively on an ever-growing historiography and popular accounts of the events described. As Soraya de Chadarevian argues in the first pages, the iconic presence of human chromosomes in science and popular culture "took off at exactly the same time when molecular approaches to heredity were celebrating their biggest advances" (p. 1). Yet chromosomes and the scientists who devoted their investigations to them have remained largely invisible in the predominant historical arc of the science of genetics.

The introduction presents the main threads linking the contents of the book: the intimate relation between the study of cytogenetics and human heredity, the visual culture of the study of chromosomes, and chromosomes as subjects and tracers of historical processes in the second half of the twentieth century. Each of the five chapters is self-contained, locating the growing interest in chromosomes in the contexts of concerns on radiation and mutation (chapter 1), the clinic (chapter 2), the popular interest and research on sexual chromosomes (chapter 3), global populational studies of chromosomes and automation (chapter 4), and the growing relation between chromosome research and the human genome (chapter 5). The book closes with a brief reflection on the epistemic space opened up by chromosome research as it became the technology that replaced blood studies and pedigrees in the study of human heredity and variation, and as an all too often forgotten tradition that continues to feed genomic studies and clinical analyses up to the present.

The first chapter, "Radiation and Mutation," introduces the reader to the broader context where preoccupations about the impact of radiation and pollutants after the war created the first institutions and academic careers of the new radiobiology establishment. Like other books on the subject—the above-mentioned ***Suffering Made Real*** or more recently Luis Campos's ***Radium and the Secret of Life*** (2015)—the chapter explores the value of mutations and hereditary anomalies as sources for knowledge. The UK Radiobiological Research Unit at Harwell provides the setting to explore and advise on the implications of radiation for human health and to take the impetus from nuclear physics to the development of postwar biology. De Chadarevian's previous research on the large experimental program concerning low-irradiation effects on large mice populations is largely left aside to focus here on the efforts to visualize mutations at the Cytogenetics Section under botanist Charles Ford, who became a world-leading expert in the field and the first to independently corroborate Joe Hin Tjio and Albert Levan's establishment of the correct number of human chromosomes in 1956, from forty-eight to forty-six.[1] As the author and other historians, like María Jesús Santesmases, have argued before, many of the technical advancements that transformed the study of cytogenetics came from the seemingly unrelated field of botany, and Ford's laboratory soon became a passage point for students and researchers who came to learn the experimental techniques and visual skills needed for chromosome research.

Edinburgh soon became a site for vanguardist human genetics research, the locus of some of Britain's boldest research programs in the decades after the Second World War. The bulk of chapter 1 focuses on the growing interaction between the lab and the clinic—and further on, the collection of data and registries, especially in the career of Michael Court Brown, a radiologist with a medical background. His monumental studies on the long effects of radiation on leukemia, carried on in collaboration with dozens of epidemiologists, radiotherapists, and clinicians, covered more than fourteen thousand patients and appeared for the first time in 1956, becoming one of the most relevant and comprehensive studies on the carcinogenic effects of radiation. The chapter attests to the shifting professional careers of biologists, as atomic concerns had a transformative impact on their field, and clinicians like Court Brown—who headed the Medical Research Council (MRC) Unit for Research on the Clinical Effects of Radiation in Edinburgh—extended the unit's role and collaborations beyond Britain. Patricia Jacobs, also at Edinburgh, and others in selected institutions in the United States and other countries, extended the cytogenetics studies to explore the link between leukemia and chromosome damage, contributing to the early genetic theory of cancer. Equally important, the author convincingly draws attention to the importance of visualization and standardization as part of the research culture of cytogenetics. It was in this agitated environment where a

rapid succession of technical innovations in the extraction, preparation, observation, standardization, and representation laid the ground for chromosome work in the next decade.

Chapter 2, "Chromosomes and the Clinic," covers the rapid transformation of cytogenetics from a relatively esoteric research interest to a burgeoning scientific field and medical specialty, as shown by the exponential growth of publications reporting chromosome findings between 1950 and 1975 (figure 2.2, p. 51). The upsurge in interest began once the "normal" human chromosome number of forty-six set the stage for the discovery of abnormal counts related to diseases. The discovery by Jêrome Lejeune and his group at the Hôpital Trousseau in Paris of three boys with Down syndrome showing forty-seven chromosomes was soon followed by the establishment of other chromosome diseases: the Turner (forty-five chromosomes) and the Klienefelter (forty-eight) syndromes, in particular, stemmed from collaborations between clinical studies in London and Harwell, while the "superfemale" (a women with a triple X chromosome) was reported in Edinburgh. These observations opened the door to a totally new category of diseases and possible interventions but also to complex questions surrounding the relations between chromosomes and disease and, more interestingly, between apparent and genetic sex. A simple correlation between chromosome number and shape was not enough to explicate the complex results arising from the Barr body test, which had crucial implications in the understanding of sexual syndromes.

An important question across this chapter is the relative importance of the clinical setting, as opposed to the atomic research establishment. If the latter provided the initial resources and impetus, it was the interaction between cytogenetics and hospital-based medicine that created most opportunities in the study of chromosomes. With the creation of the Pediatric Research Unit at Guy's Hospital in London, Paul Polani's career illustrates the growing role of cytogenetics in research on congenital diseases, prenatal diagnosis, and genetic counseling that we usually associate with human chromosome research. The National Health Service established in the United Kingdom after the war, as well as hospital-based research in countries like France and Sweden, provided the context where new services were offered to large populations: tissue sampling, photomicrographs, amniocentesis, and the consultation room were some of the new tools in the pediatrician's kit. A different but correlated type of study was carried on by the continuation of Court Brown's research at the Edinburgh MRC unit, which, not surprisingly, was closely integrated with Western General Hospital. In this case, De Chadarevian provides one of the most intriguing case studies in the history of postwar human genetics: the development of a national registry to collect information on karyotype abnormalities and cancer, and of sex-chromosome complement, sexual phenotype, and cardiovascular disease. The extension of the registry attests to the enormous efforts and resources devoted in the UK to the epidemiological consequences of cytogenetics, only equalled by Victor McKusick's Medical Genetics Division at Johns Hopkins University in the United States. Moreover, it is in relation with the clinic where human genetics was extended from the realm of heredity to the realm of horizontal somatic alterations, as in the study of some forms of cancer.

Chapter 2 also covers the convenance of the international chromosome standardization conferences, the first taking place in Denver in 1960. De Chadarevian's well-researched case study supports one of the book's main arguments concerning the requirements and peculiarities of the visual culture of chromosome research. In this case, the need for proper standard representations of the images of chromosomes is fully developed. Images played a powerful role, not only on research but also on common representations of the new hereditary identity of individual humans, exerting a mesmerizing effect that went beyond the clinic

and the laboratory. The standardization of the image of the human karyotype, and the analysis of abnormal counts, provided a representation that superseded the clinical diagnosis of a patient and offered an insight into the supposed inner mechanisms of heredity, variation, and even identity.

These developments had a profound impact on broader audiences, beyond the research setting and hospital, and in the analyses of human chromosomes nothing stood out more than the general interest in sexual chromosomes and what they revealed about the individual human. Chapter 3, "Y and X," follows the presence of these tiny particles from research objects to scientific tools, providing the most accessible entry to the study of linkage characters and anomalies. The chapter focuses on two research programs linked to research on sexual chromosomes that had wider implications in general culture: the epidemiological research on the relation between sexual chromosome anomalies and criminal disposition and the use of chromosome research in the sexing of female athletes. The first case concentrates on a wealth of new historical research, and De Chadarevian is at her best when interpreting both the bidirectional relation between scientific research and public interest particularly in well-publicized criminal trials and the careful—though contested—epidemiological design of these studies. While giving voice to the contemporary critics of these studies—most notably, those coming from the anti-reductionist Science for the People organization at the end of the 1960s—she also calls attention to the divergent positions of individual scientists (Lejeune, Ashley Montagu) in public debates and to the evolving research design in scientists' long-term research. Jacobs's original surveys of the karyotypes of 197 patients from the Scottish State Hospital at Carstairs —a hospital for mentally ill serious offenders—reported an unusually high number of XYY men (p. 89). These results were soon contested by W. H. Price and P. B. Whatmore in the United States, who found that XYY males were indeed less prone to violent crimes than a control group. Without dismissing Jacobs's results, Court Brown's review of the link between extra Y chromosomes and social behavior offered a qualified retraction and called for more research on the subject, including long-term newborn programs. These calls led to the establishment of the Registry of Abnormal Karyotypes in the Edinburgh MRC Unit, which by the mid-1960s was surveying 1,200 newborns in ten maternity units per month. The systematic approach, led by pediatrician Shirley Ratcliffe—ended in 1979—now included the follow-up of families and children with chromosomal anomalies, with comprehensive checkups every six months that included a pediatrician, a psychologist, and a nurse, recording their physical, sexual, and cognitive development.

Similar longitudinal studies were carried out in other countries, most notably, the National Institute of Mental Health-supported program of Stanley Walzer, a Harvard child psychiatrist, and Park Gerald, a geneticist at the Boston Hospital for Women. As the Harvard study caught the attention of members of Science for the People, questions were raised on the use of "doubtful genetic information" to provide evidence for "incarceration" and "unsuccessful therapy" (p. 101). In De Chadarevian's account, the debate was enmeshed within other local issues, such as the rise of molecular biology in Harvard—and the ensuing debate on genetic recombination—and the ethics of medical research. The upheaval led to hearings at the Committee on Medical Research at Harvard Medical School and the newly established Committee on Human Studies, as well as the US Court of Appeals at the District of Columbia. All three bodies recommended continuation of the chromosome studies, yet the highly publicized relation between XYY karyotypes and crime remained, despite alternative—and inconclusive—studies that aimed to show the positive effects of the extra Y, for instance, in the competitiveness of basketball players. Genetic reductionism, after all, was the core of the critics' attention. Simultaneously, there was growing concern in the UK on the ethics of the information shared

with patients, after the Edinburgh scientists recognized that chromosome anomalies were not initially reported to families in order to avoid bias in their nurture of children. One gets the impression that the thousands of personal records and registries that those longitudinal studies produced were left aside less for the knowledge they produced with the extensive recording of data than for the changing attitudes regarding the explanation of human behavior in the late 1960s and 1970s. Gender verification for female athletes using chromosome analysis, on the other hand, quickly ran into technical and epistemic difficulties, reaching its climax at the Olympic Games hosted in Mexico City in 1968. Soon after, however, some of the critics of the whole enterprise took charge of these evaluations, in order to provide a more nuanced and less mechanistic view of the complexities of sex identity and athletic performance.

The postwar multilateral agencies and the international research projects of the cold war era provide the context for chapter 4, "Scaling Up," where we learn of the efforts to take the visual tools associated with cytogenetics to the epidemiological level. This chapter focuses on two interrelated subjects that have been left aside by historians of biology of this period: the fact that individual representations of chromosomes and human karyotypes do not run alongside populational studies, a subject introduced earlier in the book in the epidemiological projects of Court Brown and others; and the difficult search for automation tools and the introduction of computers into an activity whose main goal was relatively simple, to establish the correct number and appearance of chromosomes. Collecting data for large-scale human chromosome studies was possible once blood samples replaced biopsies of bone marrow, and registries—such as the Registry of Abnormal Karyotypes in Edinburgh—were put into place, only to eventually vanish as the new regulations and changing attitudes toward the use of individual information changed in the 1990s. As in other places where computers came into relation with biological research (see, for example, De Chadarevian's *Designs for Life: Molecular Biology after World War II* [2002]), De Chadarevian does a brilliant job detailing the technical and epistemic difficulties of automating the supposedly simple skills of microscope observation into a reliable format that could make massive population studies possible. Because of this, the chapter offers a healthy dose of disappointments with computers and software, and a validation of the required relationship between the computer and human expertise and observational skills. On the other hand, the chapter shifts to populational studies beyond the national scale and introduces multilateral agencies, such as the World Health Organization, and international projects, such as the one carried on by James Neel on the Xavante Indians of Brazil, Cavalli-Sforza's evolutionary studies of human populations, and the International Biological Program of the 1960s, where anthropological approaches and large studies on chromosome and genetic variation were announced as providing an updated evolutionary view of "the human race," one that—nevertheless—fed into conflicting views about the diversity of the human species and the idea of race (p. 142).

All this provides the broader context where the two traditions of human genetics—the "visual" of cytogenetics and the "logic" of molecular biology—eventually come together, in chapter 5, "Of Chromosomes and DNA." This final chapter takes on the technical advances in the 1980s and 1990s in molecular tracing and visualization, and the incorporation of new materials and tools, such as fluorescence, hybridization, and PCR (polymerase chain reaction), which opened the door for renewed interest and collaboration between the study of chromosome mapping and structure, and the study of the human genome. Though I am not sure the use of Peter Galison's distinction between imaging and calculation helps the author's case, the contrast and the complementarity between these two traditions in the history of human heredity is illuminating of the absences that have made

the molecular revolution the protagonist of late twentieth-century human genetics. As the chapter proceeds, and the Human Genome Project and human diversity studies go on, the mapping and visual cultures of chromosome research give way to a much more subtle and complex history of the study of heredity and variation than the one popularized by scientists and many historians. If this chapter is the culmination of a narrative, it is not one of the triumph of the visual over the analytical culture, but of the numerous points of relation and distance, of interrupted, contingent, and scattered developments in the growth of knowledge of the hereditary constitution of humans. The end view is not one of synthesis or integration of purposes and tools but a mosaic of everything that constitutes the enormous field of the study of human variation and heredity: the epidemiology at the heart of the clinical studies, the automation and visualizations tools, the collection practices, and the observational skills. In all this diversity of tools and approaches, the image of the human karyotype stands out as one of the most fascinating and suggestive representations of science, and a final comment must be made on the wonderful images of chromosomes—at once uniform and peculiar—that illustrate the book and help realize the complexity of the task.

De Chadarevian's book fully meets its main goal: that of reintroducing chromosomes and cytogenetics into a still simplistic narrative of the history of the understanding of human heredity that traverses the twentieth century. It provides new historical sources, nuanced interpretations, and new protagonists around the world to help crumble the historic edifice that many of us (including of course De Chadarevian herself!) have contributed to: that of the molecularization of heredity in the second half of the twentieth century. It is a most welcome development in the history of biology.

Note

[1]. Soraya de Chadarevian, "Mice and the Reactor," *Journal of the History of Biology* 39 (2006): 707-35.

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