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The human autonomous karyotype and the origins of prenatal testing: Children, pregnant women and early Down's syndrome cytogenetics, Madrid 1962–1975

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ABSTRACT

Through their ability to reveal and record abnormal chromosomes, whether inherited or accidentally altered, chromosomal studies, known as karyotyping, became the basis upon which medical genetics was constructed. The techniques involved became the visual evidence that confirmed a medical examination and were configured as a material culture for redefining health and disease, or the normal and the abnormal, in cytological terms. I will show that the study of foetal cells obtained by amniocentesis led to the stabilisation of karyotyping in its own right, while also keeping pregnant women under the vigilant medical eye. In the absence of any other examination, prenatal diagnosis by foetal karyotyping became autonomous from the foetal body. Although medical cytogenetics was practiced on an individual basis, data collected about patients over time contributed to the construction of population figures regarding birth defects. I study this complex trajectory by focussing on a Unit for Cytogenetics created in 1962 at the Clínica de la Concepción in Madrid. I incorporate the work and training of the clinicians who created the unit, and worked there as well as at other units in the large new hospitals of the national health care system built in Madrid during the mid-1960s and early 1970s.

1. Introduction

In 1961 the young MD and recent PhD, Andrés Sánchez Cascos, was granted a fellowship by the Fundación Juan March (Madrid) to spend ten months at Guy's Hospital in London, where he would develop his specialisation in congenital heart diseases, the subject of the thesis he had recently submitted to the University of Madrid Medical School (Sánchez Cascos, 1960). Receiving supervision in London from the cardiologist Dennis Deuchar, the biologist G. E. H. Foxon, and, more significantly for Sánchez Cascos' later medical career, the geneticist and head of the Paediatric Research Unit, Paul Polani, Sánchez Cascos was introduced to cytogenetics—the study of the structure and function of the cell, particularly the chromosomes. After his training in the production of karyotypes, and on his return to Madrid in 1962, Sánchez Cascos and the young MD, Emilia Barreiro, established a laboratory for cytogenetic diagnosis at the Clínica de la Concepción at the request of its director, Carlos Jiménez Díaz.[1] The laboratory subsequently became a pioneering setting for cytogenetics, training many other young doctors and establishing medical genetics as a clinical speciality.

Blood samples from hospital patients diagnosed in obstetric and paediatric departments were the sources from which chromosomes would be rendered visible in the cytogenetics laboratory, using a recently described technique also common to cytogenetics units in other clinics.[2] Karyotyping—the recording of chromosomes—became the basis upon which medical genetics was constructed, both in Madrid and in clinical settings in Europe and

[1] On Jiménez Díaz, see Jiménez Casado (1993).

[2] See below for similar work done in other clinical departments abroad, and see de Chadarevian, in this issue, and Löwy, in this issue.

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North America. Karyotypes were the visual evidence of a disorder identified by medical examination. Among the earliest conditions diagnosed in this manner were those relating to fertility problems in adults and Down's syndrome (DS) in children. This was an artisanal practice of human heredity in the laboratory: a manual, handcraft practice of obtaining images of chromosomes and ordering them by size. By participating in a medical examination, the set of chromosomes obtained redefined health and disease, or the normal and the abnormal, in cytological terms.

I will argue that karyotyping became stabilised as a laboratory practice through the study of foetal cells by amniocentesis. When amniotic fluid was extracted from the wombs of pregnant women, the foetal cells contained could be analysed and the chromosomes karyotyped. As the foetus could not undergo direct medical examination, foetal karyotyping became autonomous. By qualifying karyotype as autonomous, I suggest that this early practice of prenatal diagnosis—the observation of foetal cell chromosomes under the microscope—became seen as a reliable representation of a foetus' health or disease. As I will discuss, the diseases that tended to be identified in this way were those associated with mental retardation, the physical lesion site of which had never previously been witnessed. By representing bodies in karyotypes, prenatal diagnosis became a practice of visualising the secrets of women, as amniocentesis participated in an exploration of the inner uterus.[3] This representation of the foetus stabilised the autonomy of medical genetics.

In Spain, between 1980 and 2007, the number of newborns with DS decreased significantly in mothers over 34, by an average of 28 cases per 100,000 newborns every year (Bermejo, Cuevas, Mendioroz, Grupo periférico ECEMC, & Martínez Frías, 2008; in newspapers, Francescutti, 2001; Ruiz de Elvira, 2004). The Spanish registry of newborns (*Estudio Colaborativo Español de Malformaciones Congénitas*, ECEMC) attributed this decrease to two changes: the introduction of prenatal diagnosis programmes specifically targeted at detecting the disorder, through karyotyping the foetal cells of pregnant women over 34; and the passing of the abortion law in 1983 (Barreiro, 2000; Bermejo et al., 2008, pp. 77–78). These statistics were based on medical practice, originating in the collection of cytogenetic data provided by a set of clinics in Spain. The aim of this essay is to present a history of early medical genetic practices in Madrid, the origins of which, in the cases I have studied, cannot be separated from medical examination. The decreasing number of DS newborns was associated with an artisan laboratory experiment in which images of chromosomes were produced from blood and amniotic samples, photomicrographs were made, and a chromosome portrait of the patient was manually constructed.

The association of such experiments with data recorded in Japan on the biological effects of radiation following the bombs on Hiroshima and Nagasaki (Beatty, 1991; Lindee, 1994; Smocovitis, 2011) constitutes the background landscape of the history of human genetics during the second half of the twentieth century. Statistically significant data was retrieved through medical care from the late-1950s onwards in cytogenetic units in Europe and North America, with chromosomes employed as diagnostic tools. As prenatal karyotyping of foetuses became possible, and combined with changes in abortion law, statistics returned to the fore, revealing new changes: most prominently, the decreasing occurrence of DS among newborns. This essay contributes to the historical reconstruction of human cytogenetics as a clinical practice that produced—and is still producing—statistically significant collections of data about human heredity. Through analysis of early karyotyping in Spain, this historical reconstruction traces the trajectory toward the autonomy of human genetics as a medical space in the early practices of prenatal diagnosis. Firstly I will discuss the circulation of early cytogenetic practices, while framing the origins of cytogenetics at the Clínica de la Concepción in Madrid. This includes consideration of how the institutional configuration of the Spanish health care system disciplined medical genetics and created a space for conceptualising karyotypes as representations of human heredity. I will then analyse the emergence of the autonomous karyotype in the early days of prenatal diagnosis, so as to retrieve the origins of contemporary associations between anatomies and populations in the case of health statistics based on karyotyping.

2. Karyotyping: a laboratory technology for clinical examination

The technology of karyotyping—of constructing clear slides displaying distinct and ordered human chromosomes—produced a form of medical characterisation. Samples for this practice were obtained from blood extracted by venepuncture. A particular logic was constructed through the use of this technology in the hospital: a technology that connected medical examination with a test consisting of identifying chromosomes, classifying them and making them reliable objects to be correlated with medical examination.

Medical authorities in contemporary societies played a key role in the construction of human heredity as it was integrated into clinical practice.[4] By incorporating the karyotype, clinicians were introduced to cytology at a time when it was mainly the domain of agronomists and botanists (in plant breeding and crop improvement, through the selective breeding of animals and plants) and theoretical population geneticists.[5] To animal and plant breeders and human trait statisticians, clinicians interested in human chromosomes appeared ignorant about cell biology and genetics. In turn, early medical cytogeneticists regarded population genetics as overly mathematical and theoretical, while karyotyping was the laboratory practice of human genetics, since it related to medicine and the diagnosis of human disorder conducted for the patient's sake.[6]

The clinical laboratory established in Madrid in 1962 incorporated the contemporary language of human cytogenetics—that of chromosome number and shape—into medical discourse. Karyotyping circulated as a diagnostic tool among physicians and clinicians, and between clinical laboratories; the techniques for obtaining good slides were regarded by early practitioners as simple tasks, provided you knew the details, developed the skill and trained the eye. I consider this practice to be clinical because the source of samples was the medical practice of diagnosis. The spaces maintained for decisions regarding the new techniques were the consulting room and the clinical laboratory.

Cytogeneticists produced lineages of alterations for medical records, in the form of familial genealogies or genealogy trees. Such trees were drawn in order to reveal hereditary explanations for the cases observed in the microscopic slides of human chromosomes (Harman, 2004; Harper, Reynolds, & Tansey, 2010). The microscope never stood alone in the diagnostic process; medical examination by the physician's naked eye retained authority, with the karyotype becoming part of the clinical record. Over time, the importance of

[3] On the woman's body as an old secret in anatomy see Park (2006). On the pregnant woman's body and the uterus, see Duden (1993).

[4] For the role of nineteenth-century medical communities in developing the concept of heredity, see López Beltrán (2004, 2007).

[5] Müller-Wille & Rheinberger (2012), Barahona (2009), and Santesmases (2013).

[6] I am grateful to Carlos San Román for a conversation on these early days of medical genetics as opposed to population genetics.

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