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'Your true and proper gender': the Barr body as a *good enough* science of sex

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Abstract

In the late 1940s, a microanatomist from London Ontario, Murray Barr, discovered a mark of sex chromosome status in bodily tissues, what came to be known as the 'Barr body'. This discovery offered an important diagnostic technology to the burgeoning clinical science community engaged with the medical interpretation and management of sexual anomalies. It seemed to offer a way to identify the true, underlying sex in those whose bodies or lives were sexually anomalous (intersexuals, homosexuals and transsexuals). The hypothesis that allowed the Barr body to stand in for 'chromosomal' or 'genetic' sex was provisional, but it supported the expectation that genetic information established one's primary identity, and the conviction that the animal world could be neatly divided into two, and only two, sexes. Ultimately, this provisional hypothesis, and its status as an unambiguous arbiter of true sex, was overturned. But during much of the 1950s, Barr's thesis about the identity of the Barr body was consistent with a coherent set of theories and evidence explaining sexual development and sexual pathology. Though provisional, the scientific status of the sex chromatin within this system of knowledge was *good enough* to support a flourishing research enterprise in the clinical sciences.

Keywords: Good enough science; Intersex; Hermaphrodite; Barr body; Sex determination; Sex chromatin; Sex chromosomes

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1. Introducing the 'Barr Body'

How doth the telltale chromosome
Make sex distinctions clearer
And send a doubting Thomas home
A doubting Thomasina?
Rejoice, hermaphroditic folks
In Doc Barr's deed of splendor.
A moment's glance from him evokes
Your true and proper gender.
(Anon., *The skin game*, ca. 1953)[1]

In the fall of 1948, Murray Barr, a professor at the University of Western Ontario, and his graduate student, Ewart Bertram, were researching the effects of stress on the nervous system. They electrically stimulated the nervous system of cats to observe any changes in cellular anatomy and soon began paying close attention to a deeply staining body in the nucleus of the cell. They observed that these bodies, while obvious in the cells of some animals, were absent in the cells of others. Upon further investigation, they recognized that the distinction was tied to the sex of the cats: while the neural cells of female cats demonstrated this body, those of male cats did not (Barr, 1988; Potter & Soltan 1997). Barr and Bertram (1949) confirmed this observation in other cats and in humans at autopsy. They also proposed a credible theory to explain it: that the 'Barr body' (as it came to be called) indicated the presence of the female's two X chromosomes (the XX pattern). They then published their findings in the prestigious journal *Nature* in 1949.

Barr's discovery was important for allowing scientists and clinicians to 'see' something that was otherwise effectively invisible. When Barr made his discovery, scientific knowledge of the human chromosome constitution was extremely limited. It was not until 1956 that techniques for processing human cells were sufficiently advanced to allow the correct identification of the total number of human chromosomes (forty-six, not forty-eight, as had been believed for over thirty years). As a result, reliable, direct analysis of human chromosomes only became viable in the late 1950s. Further, it was not until approximately 1960 that processing techniques were developed to allow analysis of chromosomes from a readily accessible tissue—human blood rather than bone marrow, spleen or lymph cells—rendering chromosome analysis more clinically palatable.[2]

For almost a decade, the Barr body (also termed the 'nucleolar satellite' or 'sex chromatin') served as a clinically accessible tool providing *indirect* evidence about the sex chromosome status of an individual: trained observers could see the presence or absence of a dark spot within a cell nucleus, and by proxy, the presence or absence of a female sex chromosome constitution. This tool was used in the medical interpretation and management of the sexually anomalous, primarily those whose bodies provided confusing evidence about their sex, the hermaphrodites (or intersexuals, as they were coming to be known), and, to a

[1] Doggerel sent to Murray Barr by Bill Dafoe, 19 February 1953, after Barr's presentation on the sex chromatin at the Academy of Medicine in Toronto (National Archives of Canada, Murray Barr Papers, Accession MG30 B111, File 3–21, ca. 1953). Hereinafter, I will refer to the Barr papers by NA, File number and related details.

[2] M. Susan Lindee (2005) has provided a brief history of cytological developments relating to reading human chromosomes in chapter four of her book.

lesser extent, those whose lives conflicted with embodied standards of sexual and gender conduct and identity, such as homosexuals and transsexuals (often termed 'inverts' at the time).

In this period, the Barr body was used to demonstrate that transsexuals were the sex they appeared physically to be, and not the sex that their behaviour—to 1950s observers—implied. This demonstration supported the growing recognition that transsexuals were not intersexes (Meyerowitz, 2002), and was used to directly disprove the thesis that transsexuals might be genetic intersexes—a thesis advanced by Christian Hamburger of Copenhagen, the physician who achieved notoriety for performing a sex change operation to convert George Jorgensen, an American GI, into Christine Jorgensen, a 'blonde beauty' (Hausman, 1995; Meyerowitz, 2002, pp. 51–97). The Barr body was also used to sex children studied by John Money and his co-workers, Joan and John Hampson, of Johns Hopkins, and to substantiate their thesis that neither gender identity nor sexual orientation were inevitably linked to the biological sex of the infant. This thesis underpinned the—now infamous—protocol for the medical management of intersexed persons advanced by Money and the Hampsons (Money, Hampson, & Hampson, 1955b). The protocol had two main parts: first, that sex assignment through surgery and hormones should comply with the psycho-social (or gender) identity; and second, that when sex assignment decisions were being made in infancy, which was optimal, priority should be given to the extent to which the individual's genitalia could be made to approximate 'normal' genitalia—in effect this meant obsessive attention to the size of the phallus (Kessler, 1990, 1998). Finally, the Barr body was used to support clinical practice in managing the sexual identity of several classes of intersexuals, notably, to confirm that many children born with virilized genitals as a result of what was then termed the 'adrenogenital syndrome' were female,[3] and even to declare new classes of intersexuality, notably, to suggest the fundamentally intersexual nature of two syndromes that demonstrated sexual peculiarities: Turner and Klinefelter syndromes.[4]

The story of the discovery and use of the Barr body is inherently interesting. It was an important discovery in microscopic anatomy and it played a decisive role in the evolution of knowledge about sexual anomalies. But what makes this story especially interesting is that the interpretation of the Barr body as a marker of the female sex chromosome constitution was erroneous. When Barr and Bertram made their discovery, they proposed that the Barr body embodied two X chromosomes (the female XX chromosome constitution),

[3] Today, this condition is consistently termed 'congenital adrenal hyperplasia', CAH, which captures a family of recessively inherited genetic disorders in which cortisol synthesis is inadequate. While the condition affects both males and females equally, classic cases of CAH cause virilization in females, which is apparent at birth (www.genetests.org). In the period under review, the 'adrenogenital syndrome' was construed rather differently. For Barr and his colleagues this was a hormonal condition involving the production of extra androgens and often the suppression of the production of other hormones; it could be caused by androgens produced by the fetal adrenal cortex, by the mother or by a tumour. Occurring prenatally, it was believed to primarily affect fetuses with ovaries (Williams, 1950). These virilized female children were the primary subjects of Barr body investigation.

[4] Turner and Klinefelter syndromes have, since 1959, been recognized as caused by sex chromosome anomalies (a single X chromosome in the former, and an extra X chromosome in an XY case in the latter). They were clinically recognizable entities before this time but their etiology was unknown. Klinefelter syndrome is a complex in a male involving small testes and infertility; Turner syndrome is a condition in a female involving streak gonads, infertility and a range of other congenital anomalies (such as, for example, short stature, webbed neck and heart defects).

and then conducted several years of work to substantiate this hypothesis. It was this provisional hypothesis that permitted the reading of a dark spot as evidence of an XX pattern, but it was wrong. The association between the Barr body and the X chromosome was not demonstrated convincingly until 1959, when the Barr body was demonstrated to embody one rather than two X chromosomes (Ohno & Hauschka, 1960). Also at this time, scientists discovered the existence of sex chromosome anomalies in humans (Jacobs & Strong 1959). Some of the persons diagnosed by Barr's methods in the mid-1950s as having a female or male sex chromosome status were re-read as having an XXY (post-1959 read as male, previously female) or XO (i.e., a single X chromosome, post-1959 read as female, previously male) sex chromosome status.

I argue that, despite the provisional way in which Barr offered his hypothesis, and despite the fact that—in hindsight—it was wrong, the Barr body was a *good enough* tool for the identification of sex chromosome status through much of the 1950s. Dumit (2000) investigates the notion of 'good enough' knowledge in medical science, drawing on Wittgenstein to highlight the problem of knowing when there is enough explanation of a phenomenon to consider it settled. He answers that, in the case of the socio-medical disorders he is examining, matters are not 'settled' permanently or satisfactorily in biology, but only temporarily in local settings and contexts. I build on this notion to consider the local and temporary features that made the 1950s interpretation of the Barr body 'good enough'. Specifically, I highlight three interrelated features of the cultural and scientific environment that supported Barr's provisional hypothesis. First, I suggest that the Barr body offered practical support to the clinical and cultural demand for a sexually dichotomous world (Findlay, 1995; Dreger, 1998). As a related but separate point, I argue that the status of the Barr body as a mark of 'genetic' or 'chromosomal' sex (both terms were used regularly) gave it elevated authority in identifying a dominant or true sexual identity (Rose, Lewontin, & Kamin, 1984; Nelkin & Lindee, 1995). Finally, I argue that Barr's theory was embedded within a coherent system of scientific belief that sustained observational evidence about the Barr body, and scientific theories about sexual development, in a mutually supportive relationship. The provisional status of Barr's theory was never lost sight of, and some alternate readings of Barr body evidence were offered in the 1950s. Indeed, some of these interpretations appear prescient, but appearances can be deceiving.[5] These alternate ways of reading sex chromatin evidence were not intended as competing interpretations of the Barr body, and were embedded in the same system of belief that supported Barr's provisional hypothesis.

In making these arguments, I build on the work of Alice Dreger (1998) who has argued that nineteenth and early twentieth century medical science sought to reduce the social threat posed by the hermaphrodite by defining him/her out of existence. Christening the period of its emergence 'the Age of Gonads', Dreger (1998, pp. 145–146) highlights the importance of a taxonomic system that defined the true sex of hermaphrodites by their gonads. Though clinically impractical (the truth could often only be revealed at autopsy), the gonad-based scheme defined most hermaphrodites as pseudo-hermaphrodites,

[5] There are many accounts of 'prescient' insights in the history of genetics, including the stories of Gregor Mendel and Archibald Garrod. Many historians of science argue that these apparent discoveries were, in fact, embedded within the intellectual world view of their time and spoke to contemporary, rather than future, debates. (Olby 1979; Sapp, 1990a, 1990b).

suggesting that their gonads spoke the truth about their sex, no matter how confusing were the sexual signs revealed by their bodies or their lives.

The gonad-based nosologic system, eponymously called the Klebs system, remained in force in the 1950s, but its authority was increasingly in question.[6] Medical scientists had new tools with which to manage sexual anomaly in this period, notably, advances in endocrinology (for example, the new hormonal therapy of cortisone) and plastic surgery (rendered more technically advanced after World War II) (Hausman, 1995). The Klebs classification system implied that abdominal surgery to examine the gonads would generally be required in assigning individuals with ambiguous genitalia (or anomalous sexual identities) to one sex or another. Even then, information about gonads was not of decisive importance: the secondary sex characteristics, the physiology of the individual, the limitations of surgical and hormonal intervention, or that person's lived experience, could contradict the truth dictated by the gonads in making decisions about the appropriate sex to make of an intersex person.

The Barr body was originally proposed as a solution to this conundrum. Barr and colleagues hoped that it might identify the *dominant* sex (Barr's term), one that made sense of both unseen gonads and ambiguous genitalia more easily and accurately than surgery (Moore, Graham, & Barr, 1953). It failed to do this. The Barr body quickly proved to be no more reliable as a single guide for the management of sexually anomalous bodies than the gonads had been, and clinical judgement and personal preference remained ultimate arbiters. Indeed, Bernice Hausman (1995, p. 77) has argued that physicians at this time were faced with a multitude of medical signifiers of sex—through hormones, physiology and chromosomes—so much so that, 'The body was found to be unable to present unfailingly a unilateral or absolute sex'. Unlike Hausman, however, I would argue that physicians, and society as a whole, *retained* their faith in 'a unilateral or absolute sex.' The sex chromosome status, as revealed indirectly by the Barr body in the 1950s, provided support for that faith—pointing as it did to a genetic (and thus ontologically superior) marker of sexual identity. The Barr body, as the gonads before them, exposed the 'pseudo' nature of intersexuality, even where the limitations of medical science, or the seeming-perversions of personal preference, meant that bodies and lives could not be made to approximate the true sex.

This paper draws on the extensive archival papers of Dr. Murray Barr, a microscopic anatomist at the University of Western Ontario, in London, Ontario, together with a review of international scientific literature on the Barr body throughout the 1950s.[7] Murray Barr was at the centre of research on the sex chromatin during this period.[8] He participated in key controversies and developments in the clinical science of the sexually

[6] Dreger suggests that the Klebs classification schema was never entirely clinically definitive, but it was not until 1915 that its clinical efficacy was openly questioned (Dreger, 1998, pp. 157–158).

[7] Murray Barr donated his beautifully maintained and detailed papers to the National Archives of Canada, in Ottawa, Canada: Accession MG30 B111.

[8] Barr's work, and the use of the Barr body as a test of chromosomal sex, was widely hailed. Towards the end of 1956, Barr's scientific colleagues learned that he would be in Britain the following year. In honour of this, and to bring together the wide range of scientific workers interested in 'nuclear sexing,' and in meeting Murray Barr, a symposium was organized for the fall of 1957. At that gathering a veritable 'who's who' of scientists, including Lionel Penrose, Alfred Jost, and Ruth Sanger, was in attendance. While there was scientific debate and disagreement, the importance of Barr's discovery in providing access to information about 'genetic sex' was uncontested. See Smith & Davidson (1958).

anomalous, and in debates about the status of the sex chromatin. He collaborated with Christian Hamburger of Copenhagen, John Money of Johns Hopkins, and leading sex endocrinologists Melvin Grumbach and Lawson Wilkins, also from Johns Hopkins. Further, his hypothesis about the origin of the sex chromatin remained dominant through most of the decade.

In the rest of this paper, I briefly review the system of scientific beliefs within which Barr's provisional hypothesis was sustained. I then turn to the clinical research undertaken with the Barr body in the 1950s, specifically, clinical research on intersexuals and 'inverts'. I recount Barr's contribution to the study of transsexuals and homosexuals, and then review his more sustained research with the intersex. Finally, I consider the meaning of a selection of seemingly prescient interpretations of Barr body evidence that were offered in advance of the intellectual changes wrought at the end of the 1950s.

2. The origin of the Barr body: the provisional hypothesis

When Barr and Bertram identified the 'nucleolar satellite,' they suggested that it 'may be derived from the heterochromatin [compact and deeply staining portion] of the sex chromosomes' (Barr & Bertram, 1949, p. 677). But in 1949 this was far from certain. It might, for example, simply be a secondary sex characteristic, a cellular artefact of female hormones. Testing this thesis demanded years of work studying the effect of sex hormones, through castration experiments and studies of embryonic development.[9] By the early 1950s, Barr had concluded that his initial hypothesis was correct: the Barr body embodied the compacted portions of both X chromosomes.[10]

Barr's thesis about the origin of the Barr body was embedded within a coherent system of scientific beliefs. Cytological evidence suggested that the Barr body had two component parts, supporting the notion that it incorporated two X chromosomes (Barr, 1958; Klinger 1958; Ohno & Hauschka, 1960). In addition, Barr's thesis was embedded in then-prevalent theories of sexual development. At the time, genetic research in non-human organisms (notably *Drosophila*), and experimental embryology, combined to suggest a balance theory of sexual development.[11] Male and female genetic sex determiners were understood to be present in both sexes, with a quantitative balance of genes determining the sexual direction in which the embryo would develop. Specifically, the two doses of female determiners in the XX chromosome pattern were believed to be sufficient to overcome male determining

[9] M. L. Barr, 'The role of heterochromatin and the nucleolus in nucleoprotein synthesis,' Progress report, National Cancer Institute of Canada, NCIC, 1949, (NA, File 5–10). See also, M. L. Barr, L. F. Bertram, & M. Graham, 'A study of the nucleoli-associated chromatin,' Progress report, National Research Council, NRC, 20 December, 1950, (NA, File 5–17); M. Barr, & M. Graham, 'A study of nuclear morphology in mature and embryonic somatic cells,' Progress report, National Health Grants Program, NHGP, Mental health grant, 18 November 1952, (NA, File 5–29). M. Barr & M. Graham, 'A study of nuclear morphology in mature and embryonic somatic cells,' Progress report, NRC, 17 December 1952, (NA, File 5–30).

[10] By this logic, the male's XY sex chromosomes might also be compacted and form a dense particle of chromatin in the cell's nucleus, but the particle would usually be too small to see: 'There is good evidence that male cells do in fact contain sex chromatin', Barr wrote, 'though it is usually so small as to be at the limit of resolution with standard optical equipment'. M. L. Barr, 'Sex chromosomes and the neurone', lecture to the Montreal Neurological Society, 28 November 1951, p. 8. (NA, File 18–24). See also Noguchi & Webb (1959).

[11] This balance theory harkens back to much of the unfinished theorizing about sex determination at the turn of the twentieth century detailed by Jane Maienschein (1984). See also Danon & Sachs (1957), Segal & Nelson (1957) and Brush (2002).

genes on autosomes, with one dose in XY being insufficient for the dominance of female factors. The Y chromosome was not seen as an influential force in sex determination—a fact that changed dramatically as the 1950s became the 1960s (Barr, 1959b). Yet while genes and chromosomes established the sexual orientation of the embryonic gonad, hormones played a pivotal role, and could override genetic orientation. Alfred Jost's (1953) fetal castration experiments suggested that the female orientation was the default option, occurring in both females and in castrated males; the male developmental orientation, by contrast, depended on the expression of male hormones in utero.

Over the course of the 1950s, the science of the Barr body supported researchers in an emerging three-stage model of sexual differentiation. The first stage in this model was occupied by the sex chromosomes and sex related genes, the sex hormones governed the second stage, and the environment played a role during the third stage. Early in the 1950s, Barr referenced a two-stage model. First were 'the particular combination of sex chromosomes and the genes which they bear [which] determine whether the initial indifferent gonad develops into an ovary or a testis'. But while genes were seen to make a sexually-differentiated gonad, 'Subsequent sex differentiation . . . is largely under hormonal control'.[12] By the mid-1950s, under the influence of John Money, Barr confirmed the third stage of this model which, 'extends from infancy to maturity and is the period when all facets of psychosexual attitudes are gradually fitted into place. Environmental influences appear to be especially important here'.[13]

Barr's provisional hypothesis about the origin of the Barr body was robust because it referenced this broader system of belief. Competing hypotheses about the status of the Barr body were obliged to make sense of this belief system. For members of the burgeoning 'nuclear sex' research community, the most credible alternate hypothesis through much of the decade was that the Barr body mass represented the 'autosomal locus carrying the hypostatic (suppressed) male determiners' (Segal & Nelson, 1957). The Barr body, as Murray Barr summarized this alternative hypothesis, 'derived from regions of a pair of autosomes that contain male determiners, these regions being genetically inert when they are heterochromatic [that is, condensed] (females) and genetically active when they are euchromatic (males)' (Barr, 1958, p. 184).

It was not until 1959 that this system of beliefs began to shift decisively. In that year, Susumu Ohno, who had conducted extensive basic research to illuminate the Barr body's association with the X chromosome, announced that the Barr body represented a *single* X chromosome (Ohno & Hauschka, 1960). While an enthusiastic supporter of Ohno's work,[14] Barr was not immediately convinced (Barr 1959c). Other developments in 1959 were crucial for disrupting the total system of belief, by contesting the theories that made sense of sex development. In that year, two clinical syndromes were re-interpreted as cyto-

[12] M. L. Barr, 'Sex chromosomes and the neurone,' lecture to the Montreal Neurological Society, 28 November 1951, pp. 2–3. (NA, File 18–24). Indeed, the 'transcendence of hormonal sexuality over genetic sexuality', was confirmed by most cases of congenital sex anomaly that came to Barr's attention (Prince, 1952, p. 39).

[13] M. L. Barr, 'Psychosexual attitudes in sex reversals,' lecture to the Ontario Psychological Association, February 7 1958, p. 3. (NA, File 18–30).

[14] Barr reported that he learned first-hand about the new interpretation at the American Genetics Society meeting. Susumo Ohno knocked on Barr's door in the dormitory in which he was sleeping to announce: 'I know the origin of the sex chromatin' (Barr, 1988, p. 81). Barr then curtailed his own keynote address for the symposium on the sex chromatin to be held the next morning to make time for Ohno to present his findings (Potter & Soltan, 1997).

genetic anomalies involving the sex chromosomes. Klinefelter syndrome was revealed to be caused by an extra X chromosome (the XXY chromosome complex), with Turner syndrome caused by the absence of an X chromosome (the XO chromosome complex) (Jacobs & Strong, 1959). As Barr noted at the time, these developments radically altered the then-prevalent view of sexual development: 'the Y chromosome, far from having a passive role in sex determination, contains potent male determining genes' (Barr, 1959b, p. 685).

Barr did not immediately concede defeat for his provisional hypothesis. As he noted in the same 1959 article, drafted on the cusp of these developments, 'The view that the sex chromatin is an XX chromosome marker is consistent with an XXY-complex for patients with Klinefelter syndrome and a female chromatin pattern, and with an XO-arrangement for patients with Turner syndrome and a male chromatin pattern' (ibid.). In 1960, still unconvinced by Ohno's thesis, Barr corresponded with Tijo, who had correctly identified the human chromosome number as forty-six in 1956, seeking the latter's opinion of Ohno's work—which was equivocal.[15] It was not until 1961 that Mary Lyon and others published a credible explanation for the single X origin of the Barr body, to consolidate a new system of scientific belief.[16]

Through the 1950s, Barr's provisional hypothesis about the origin of the Barr body was relatively secure, fitting both empirically and theoretically into a coherent system of scientific belief. This *good enough* knowledge allowed the Barr body to serve as a marker of sex in the clinical domain—to identify an underlying truth about sexual identity in the bodies and lives of intersexuals and inverts.

3. The Barr body in the clinic: diagnosing sex

By 1952, confident in his provisional hypothesis, Barr began to use the Barr body as a diagnostic tool in clinical research.[17] He had high hopes: 'Our hope is that the chromosomal sex will prove to be a reliable indicator of the *dominant* sex of the patient as a whole' (Moore et al., 1953, p. 641; emphasis added).[18] This statement of hope was frequently repeated, and expressed many desires.[19] It highlighted Barr's hope for the clinical significance of his discovery, it disclosed faith in the ontological priority of genetic knowledge in defining sexual identity, and it expressed the long-standing expectation that medical science would prevail over clinical judgement in the practice of medicine (Oudshoorn, 1994; Wailoo, 1997).

This hope was not realized. The underlying sexual identity revealed by the Barr body was not necessarily the same as the sexual identity that the individual preferred, or that

[15] Barr to J. H. Tijo, 15 January 1960; Tijo to Barr, 21 January 1960 (NA, File 4–1).

[16] This was a hypothesis of X inactivation, explaining how it was that the female mammal could safely carry twice the quantity of X chromosome genetic material in her cells as the male (Lyon, 1961).

[17] Key to this was the development of a skin biopsy technique to permit information about the sex chromatin to be acquired in clinically useful ways (unlike the analysis of neural tissue).

[18] Barr was often even more definitive in his pronouncements on this, identifying the sex chromatin as 'a cytological test of the true chromosomal sex in man' (Barr, 1952, p. 477).

[19] M. Barr, & M. Graham, 'A study of nuclear morphology in mature and embryonic somatic cells,' Annual Progress Report to the Advisory Committee on Medical Research, Division of Medical Research, NRC, 17 December 1952 (NA, File 5–30). See also Barr's speech before the Toronto Academy of Medicine (NA, File 3–21, ca. 1953).

medical science could create. But this failure did not diminish interest in the Barr body. On the contrary, articles continued to be published in specialist and non-specialist journals. Moreover, Barr and others undertook technical innovations to expand the clinical utility of the Barr body beyond that provided by a skin biopsy, developing both a blood smear and a mouth swab test (Davidson & Smith 1954; Marberger, Bocabella, & Nelson, 1955; Moore & Barr, 1955; Dixon & Torr 1956). And Barr remained eager to promote all three procedures for 'detecting the nature of the sex chromosome complex (XX or XY) in anomalies of sex development' (Barr 1957b, p. 251).[20] The growing importance of the Barr body in 1950s medical science reflected its role as a *good enough* indicator of a true, underlying sex, even if this truth could not be medically or socially realized. It performed this work for two distinct populations of the sexually anomalous: intersexuals and inverts.

3.1. Inverts

In 1953, Christian Hamburger and his co-workers reported the case of Christine Jorgensen, a case of 'genuine transvestism' (as transsexuals were often called at the time). Believing the condition to be constitutionally conditioned, they proposed the thesis that 'some of the most pronounced transvestites might be intersexes (sex intergrades) of the highest degree. . . The male organs in these persons, who according to their chromosomes are women, must be regarded as malformations'. They encouraged future investigations 'into the genetics and chromosome distribution in transvestites [to] decide the possible validity of this working theory' (Hamburger, Sturup, & Dahl-Iversen, 1953, pp. 391–392).

In March of 1953, Hamburger contacted Barr to inquire about the latter's 'remarkable studies on the sex chromatin'.[21] Barr's assessment of chromosomal sex in 'inverts' predated Hamburger's invitation of collaboration, as popular attention had encouraged clinicians and the affected to contact him.[22] Barr reported that his group had 'seen only two cases so far, both male homosexuals with typical male epidermal nuclei'.[23] He then tested Hamburger's thesis with case material and biopsies provided by Hamburger,[24]and with biopsies provided by individuals who made their own way to him.

In the summer of 1953, at least two male transsexuals from New York contacted Barr as a result of Hamburger's encouragement. One wrote that, 'there *must* be a physical basis for a desire that I have had all my life—the desire to be female in every respect. Therefore you may perhaps appreciate the tremendous surge of hope that I felt last month when Dr Hamburger told me of your sex chromosome studies. This, I thought, is the chance for which I've been waiting all my life—the chance to prove to the world that I'm truly female and entitled to the surgical intervention and hormonal treatment that would enable me to take my place (as nearly as possible) as female, which I'm sure God intended me to be'. Barr referred him to Franz Kallman of the NY State Psychiatric Institute, a notable

[20] In overview articles on the sex chromatin, Barr generally identified these as various techniques for testing 'chromosomal sex'. See Barr (1957a), Grumbach & Barr (1958), and Rathbun, Plunkett, & Barr (1958).

[21] Hamburger to Barr, 9 March 1953 (NA, File 3–21).

[22] See especially Barr's lengthy correspondence with 'Anomaly' of Ottawa, author of *The invert and his social adjustment*, first published in 1927; to which was added a *Sequel by the same author* in 1948, published by Bailliere, Tindall and Cox of London (NA, File 5–1).

[23] Barr to Hamburger, 15 April 1953 (NA, File 3–22).

[24] See correspondence between Hamburger and Barr: Hamburger to Barr, 27 June 1953; Hamburger to Barr, 11 July 1953, located between Case 9 and 10 (NA, File 9–1); Barr to Hamburger, 8 July 1953 (NA, File 3–22).

behavioural geneticist (Grob, 1998), to collect the skin biopsy sample and deliver the news that this was an XY male. In this case the news did not dissuade the man from his desires. When Barr next heard from him in the fall of 1955, she reported that 'I have been living as a woman for the last three months' having moved to California. 'After a year of treatment in London and NY with estrogen substances', she noted, 'I was operated on in Amsterdam and Copenhagen'. 'I feel, quite honestly,' she added, 'that feminizing hormonal and surgical treatment is of great value in enabling sufferers to lead happier lives'.[25] Another male transsexual from New York also referred by Hamburger in the summer of 1953, and also referred to Franz Kallman for the test and results, presented a more solemn story. He reported to Barr that Kallman had informed him he was 'biologically, genetically and morphologically male ... In my telephone conversation with him, Dr Kallman wisely offered me no solution to my problem, since in my country there is no solution except the final one that comes to all of us, some sooner than others'.[26]

From the first, Barr lacked confidence that his test would demonstrate a chromosomal anomaly in these cases.[27] He believed that the Barr body was most likely to be instructive in 'errors of structural development' not 'inversion'.[28] Consequently, he tried to test the Barr body on the 'constitutionally' affected, those with 'deep-seated' homo- or trans-sexualities.[29] Barr had limited faith in the thesis of physiological inversion, and felt that a chromosomal inversion was too gross an anomaly for the clinical symptoms; he thought it more likely that the error was at the genetic, hormonal, or environmental level.

Barr's only published article on inverts took Hamburger's thesis as a starting point, and argued to the contrary that the 'male transvestite bears the male XY sex-chromosome complex', though he and his colleague added that 'the abnormality may have a genetical basis' (Barr & Hobbs, 1954, p. 1110). In the fall of 1955, when Barr reported to his funders on the progress of his research on sexual inversion, the data were conclusive. Study of twelve male 'transvestites', nine male homosexuals, one female 'transvestite' and two female homosexuals had established that 'their emotions and the direction of their sexual drives are at variance with the type of sex chromosomes (XX or XY) they bear'.[30]

[25] Correspondence and test results (NA, File 9–1).

[26] Correspondence and test results (NA, File 4–18).

[27] Barr wrote about one patient, a male transsexual, referred by Hamburger for a sex chromatin test that, 'The chances are overwhelmingly in favour of a male XY result. However, the Copenhagen group has advanced the extreme, and to me unlikely, postulate that transvestites bear the XX complex and represent the most extreme inversion physically. In view of this I would like to study a biopsy if possible . . .' Barr, letter to Kallman, 29 June 1953 (NA, File 4–18). Nonetheless to Hamburger, after demolishing his thesis, Barr wrote that, 'Since cases of transvestitism are rare, I feel that we should do a skin biopsy test for chromosomal sex in all cases that present themselves to you'. Barr, letter to Hamburger, 9 July 1953 (NA, File 4–18).

[28] Barr wrote to one woman who loved women and wanted to be a man that 'some patients confuse inversion with hermaphroditism'. His belief that her case was not one of those involving 'errors of structural development' encouraged him to refuse her request for a test of her sex. Barr, correspondence with anonymous, Philadelphia, Penn, 27 February, 2 March, 7 March, 16 March 1953 (NA, File 4–18).

[29] Barr noted of six cases of male inversion tested that, 'Two, and possibly three, of the patients would be considered to belong to the deep-seated, organic[?], type of homosexuality with markedly feminine bodily habitus and mannerisms. The others probably belonged to the environmental type of homosexuality'. Murray Barr, 'Nucleoprotein metabolism of the brain, with special reference to the psychoses, A cytological and cytochemical study', NHGP, Mental Health Grant, Progress Report, 10 November 1953, p. 23 (NA, File 5–33).

[30] M. L. Barr, 'Cytology and cytopathology of the neuron, with special reference to mental disease', NHGP, Mental Health Grant, 18 November 1955 (NA, File 6–4).

Contrary to the expectations of their sex, their genders and sexualities were decidedly queer. By this time, bolstered by the results of studies performed cooperatively with John Money and Joan and John Hampson, Barr concluded that this 'further emphasizes the importance of environmental influence in shaping psychosexual attitudes'.[31] In doing so, Barr subscribed to the growing conviction that transsexuals were a distinct category of sexual anomaly, unlike intersexes (Meyerowitz, 2002).

Barr never did publish his findings on homosexuals, despite Hamburger's encouragement,[32] though he continued to apply his test to homo- and trans-sexual patients into the late 1950s in response to requests from clinicians. While this was a minor research area for Barr, and a minor research area in the burgeoning field of 'Barr body' studies, research on the Barr body in inversion did continue (Slater, 1958a, 1958b), and demonstrated the faith that researchers preserved in a fruitful, if provisional, hypothesis.

3.2. Intersexuals

Barr's major clinical research interest involved hermaphrodites or intersexuals. Here, Barr's conclusions were less decisive than had been the case for inverts, but they were also more instrumental in interpreting and managing the phenomenon. When Barr first announced the application of the skin biopsy test in cases of hermaphroditism, in 1953, the nineteenth-century Klebs classification system was still in use (Dreger, 1998). Barr expressed his faith in the evidence revealed by the Barr body in relation to general dissatisfaction with the Klebs classification system. He argued, 'The primary importance which is attached to the gonads is a disquieting feature of this classification. The secondary sex characteristics in pseudohermaphrodites often run counter to the type of gonad. Absurdities result if the Klebs nomenclature is carried over literally into the management of certain cases' (Moore et al., 1953, p. 642). In a private letter, Barr put his hope more bluntly: 'One encounters cases with perfectly female body development and psychosexual outlook and testes in the pelvis. I suspect that these may be genetic females and that it would be kinder to remove the testes and let them live out their lives as females'.[33]

The first clinical publication from Barr's group involved a study of two hermaphrodites. This article clearly expressed the hope that the Barr test would prove clinically definitive in these 'tragic' cases (ibid., p. 641). Case one was an infant assigned at birth to the female gender but with ambiguous genitalia—an enlarged clitoris, larger than normal labia majora, absent labia minora and the absence of a vagina. Abdominal surgery confirmed the presence of the uterus, tubes and ovaries. In this case the Barr body assessed the infant as female—bearing the female, XX, sex chromosome complement. The cause of the anomaly was hormonal: the adrenogenital syndrome. Case two involved a man of twenty-four

[31] Indeed, 'it seems likely,' Barr wrote, 'that sexual inversion may result from adverse influences that were brought to bear on the patients during childhood'. M. L. Barr, 'Cytology and cytopathology of the neuron, with special reference to mental disease', NHGP, Mental Health Grant, 18 November 1955, pp. 2, 8 (NA, File 6–4). See also: M. L. Barr, 'Psychosexual attitudes in sex reversals', lecture to the Ontario Psychological Association, 7 February 1958, pp. 14–15 (NA, File 18–30).

[32] Hamburger wrote: 'I likewise find that there could be reason to publish your investigations on the sex chromatin in cases of transvestism and male homosexuality . . .' Hamburger to Barr, 12 November 1953 (NA, Case 14, File 7–4).

[33] Barr to Bill Dafoe, 2 May 1952 (NA, File 3–20). Barr was discussing his Case #1, see below, who was referred by Dafoe from Toronto.

years, who had had ambiguous genitalia at birth but was raised as a boy. At puberty he had had a bilateral mastectomy but abdominal surgery revealed no apparent female internal organs. He had next been admitted to hospital at the age of twenty-four,

> with complaints of tender swellings in the groins and monthly pelvic distress lasting about 8 days, associated with hematuria [blood in urine]. The patient was of indeterminate build with no important masculine or feminine characteristics. There was no growth of hair on the face and the distribution of the pubic hair was feminine. The phallus was small. The urethra opened at the base of the phallus... (Moore et al., 1953, pp. 646–647)

Surgery this time revealed what appeared to be two testicles and the patient was given testosterone. Confirming this, the Barr body indicated that this was a male, with XY sex chromosomes. The cause of the anomaly was unclear, but because a sibling was similarly afflicted, it was theorized that a genetic (that is, hereditary) factor was involved (ibid., p. 647).

Cases in which guidance provided by the Barr body aligned with clinical judgment were not rare. Indeed, in most of the cases of female pseudohermaphroditism, in which the female fetus had been exposed to virilizing hormonal influences, the Barr body test was clinically persuasive.[34] By 1950, Lawson Wilkins at John Hopkins had demonstrated the efficacy of cortisone treatments in controlling some of the associated electrolyte disturbances and masculinizing effects in classic cases of what was then termed the adrenogenital syndrome. However, many of the cases that Barr came in contact with in the 1950s had been assigned to the male sex before cortisone therapy; some had had female internal organs removed; many had been raised as boys. But Barr's test added to an evolving conviction, enabled by the hormonal technology of cortisone, that these cases did involve persons who were truly female.

Dr Seckel of Chicago wrote to Barr in 1955 that 'we are very much impressed with the results and potentialities of your method of sex determination from skin biopsies. Your diagnosis in the second case of ours, that of [name removed], 3 years old, was correct too'. This child had been diagnosed at birth as a boy, though with hypospadius (the urethral opening was not at the tip of the penis) and undescended testicles; however the child began to go through premature puberty at the age of three—a sure sign of adrenal malfunction. Abdominal surgery 'confirmed the diagnosis of female sex'. Consequently, Seckel wrote, 'The child's sex is going to be reversed socially and legally'.[35]

Another case suggests even more strongly the growing conviction that these persons were truly female. In this instance, which Barr had diagnosed as having 'clearly female nuclei', the case history revealed a set of clinical and personal negotiations that had contradicted this underlying truth, and which were therefore understood as flawed. 'I am sorry to tell you', wrote Dr Greenhill, also of Chicago, in 1954, 'that the patient from whom I removed the skin which I sent you was a sort of botched case'. Greenhill had delivered the child, and recognizing an enlarged clitoris, had diagnosed the child as female; other clinicians had disagreed however, and their view had prevailed. When the child was five years old, Greenhill was called in again, this time after an exploratory operation had revealed the

[34] See note 3.
[35] Helmut Seckel to Barr, 13 January 1955, Case 49 (NA, File 8–2).

presence of 'a normal uterus, tubes and ovaries'. 'There was nothing I could do at this time', Greenhill wrote to Barr, 'because the psychiatrist, the two pediatricians, the surgeon and the family insisted that the child be made into a male because the breasts were developing like that of a female. I was elected to remove the uterus, tubes and ovaries much against my will. I am sorry that I had to participate in this messed case, because in reality the child was a complete female. All that was necessary later in life was to amputate the penis and build a vagina, both of which would have been easy'.[36] Barr responded: 'I understand exactly how you feel about this case. Your hand would have been strengthened, probably decisively, had it been possible to do a skin biopsy shortly after the child was delivered'.[37]

In these cases then, the Barr body was taken to be diagnostic of a true, underlying sex in both a theoretical and a practical sense (Bunge & Bradbury, 1957; McGrew, Rosenthal, & Bronstein, Kiefer, 1957). In fact, I would argue that Barr's test contributed to the growing belief that the hermaphroditism in these cases was indeed pseudo.[38] As Barr argued, 'The results which are being obtained with cortisone in adrenogenital cases give promise that these patients can be oriented successfully toward life in the female role, in accordance with the anatomy of their internal genitalia and the female structure of their nuclei' (Barr, 1954, p. 186). Yet the success of Barr's test in the adrenogenital cases was tempered by its clinical failure in other cases, especially male pseudohermaphrodites.[39]

The second of the two cases that Barr had initially used to illustrate the definitive importance of the Barr body in his first publication on hermaphrodites highlighted this failure. Case number two had been referred to Barr from doctors at the Toronto General Hospital in the summer of 1952. But this young man had visited many hospitals with his complaints, and two years later, Barr was contacted by a doctor at Hamilton General Hospital concerning the same patient. Dr Green reported to Barr that they had recently admitted a patient 'in whom there is some doubt as to his true sex'. They were interested in 'determining his true genetic type' and offered a skin biopsy for Barr to test. They revealed also that, 'three weeks ago his perineum was revised to the female type'. Barr's notes indicate that the skin biopsy revealed 'typical male morphology'.[40] Citing this case in 1958, Barr and his co-authors saw it as confirming John Money's framework, and 'demonstrating the folly of changing sex after early childhood, for this patient is now very emotionally disturbed'.[41]

Also in 1954, a case from the Sudan was referred to Barr involving what appeared to be a true hermaphrodite.[42] This Sudanese man had been raised as a boy; he had male

[36] J. P. Greenhill to Barr, 7 September 1954 Case 34 (NA, File 8–2).

[37] Barr to Greenhill, 9 September 1954 (NA, File 3–25).

[38] Indeed, Barr wrote that '[Lawson] Wilkins reserves the term 'intersex' for cases of hermaphroditism in which no evidence of adrenal pathology can be demonstrated' (Barr, 1954, p. 185).

[39] 'A proportion of male pseudohermaphrodites have strongly female characteristics, anatomically and psychologically', Barr noted, 'and they are more suited to life as females. At the outset of these nuclear studies it was hoped that the epidermal nuclei of such patients might have a female morphology. In such an event, the skin biopsy test would give a better indication of the dominant sex . . . than the nature of the gonads'. However, he added, 'This hope has not been realized' (ibid., p. 186).

[40] Dr. W. G. Green to Barr, 24 August 1954; Barr's notes, Case 1 (NA, File 7–4).

[41] The published version of the case does not directly reference Barr's Case 2, but the details are so close that it must be the same (Rathbun et al., 1958, p. 381).

[42] For some reason Barr has categorized this case as a female pseudohermaphrodite; perhaps because he could not confirm the presence of ovarian and testicular tissue by biopsy; nonetheless the correspondence is clear in asserting the existence of both. See Case 32 (NA, File 8–2).

genitalia and no vagina, but at puberty he grew breasts, had monthly bleeding, and developed a female pattern of hair distribution. The doctors noted that, 'On physical examination his bodily habitus is female, the face suggests a woman and he has large breasts. His muscular development is small for a labouring man [he worked in the fields] and his bones and pelvis are female'. Despite these gross characteristics, the doctors noted that, 'He has been brought up as a boy, regards himself as one and wants his breasts off'. Moreover, 'He claims to get erections and wet dreams and to have an illegitimate daughter'—a claim the doctors saw as bragging. Nonetheless, the doctors were convinced of the value of making him a man, 'In this country,' they argued, 'it is terribly important not to be female, and particularly not a sterile one, so we must at all costs make him as male as possible'.[43] When Barr reported that this man demonstrated a female chromosomal pattern the colonial physician expressed surprise, but the clinical decision had been made and the social value of that decision was clear to the doctors involved,[44] and to Barr.[45]

3.3. The status and significance of the Barr body

As the author of, and leading scientific authority on, the clinical science of the Barr body, Barr issued occasional cautions about its status and significance. Barr's first caution, issued in 1954, argued that—contrary to his initial hopes—the Barr body diagnosis should not override clinical judgement about the appropriate sex for the patient.

> For the intersex patients, the decision as to the wisest course of action remains a matter of clinical judgement based on all available data. It is desired to stress this point, in order that no one will be tempted to extend the results of the skin biopsy test into practice literally, where other considerations make such a course of action inadvisable. (Barr, 1954, p. 186)

In 1956, Barr issued a further caution about the provisional nature of the thesis interpreting the Barr body, and about the use of language in respect to the test. Barr reminded his colleagues that the true identity of the Barr body was unknown, and he added that, 'it is premature to equate female-type nuclei with genetic femaleness or male-type nuclei with genetic maleness ... for our present methods give no direct information concerning the genes that are concerned with sex determination and sex differentiation'. He further suggested that instead of the terms 'female nuclei or male nuclei' and 'genetic female and genetic male' the 'less committal expressions', 'chromatin positive or chromatin negative' should be used (Barr 1956a, p. 47).

Barr's recommendation that the language of sex be replaced with chromatin positive or negative was specific to a clinical and patient audience.[46] He continued to use the former

[43] Hugh Morgan to Dr. J. S. L. Brown, Montreal [who referred the case to Barr], n.d., Case 32 (NA, File 8–2).
[44] Hugh Morgan to Barr, 7 April 1955, Case 32 (NA, File 8–2).
[45] Barr commented to Morgan that, 'so far as we can see now, there is no correlation between the type of nuclei and the most appropriate social sex'. Barr, letter to Dr. Hugh Morgan, Kitchener School of Medicine, Sudan, 15 April 1955 (NA, 4–20).
[46] In his letter to the editor, Barr asked for the use of caution when 'applying cytological test of sex clinically'. He added that he 'would prefer to see used in the clinic such less committal expressions as ''chromatin positive or chromatin negative''' (Barr, 1956a, p. 47).

language in the research context.[47] This linguistic camouflage was proposed to avoid placing a psychological burden on patients of a truth about their sex that their physical condition might not approximate; it reflected the clinical consensus that where such truths contradicted social sex, they should be withheld.[48] This terminological strategy did not suggest a reduced faith in the truth revealed by Barr body evidence. Indeed, Barr's caution came as the Barr body was performing its most consequential feats of interpretation. By the time Barr published his cautionary note, the Barr body test had been used to re-interpret two patient communities as intersexuals: Turner syndrome and Klinefelter syndrome.

3.4. Making intersexuals

In 1955, Melvin Grumbach and colleagues from Johns Hopkins, with assistance from Murray Barr, published a comprehensive review of a syndrome they called 'gonadal dysgenesis'.[49] This syndrome involved patients with 'normal but infantile female external genitalia,' with 'no evidence of female secondary sex characteristics'. It was generally associated with 'rudimentary ovaries' and 'decreased stature'. The names 'ovarian agenesis', 'Turner syndrome', and 'Bonnevie–Ulrich syndrome' had been applied to it (Grumbach, van Wyk, & Wilkins, 1955, pp. 1162–1163). The authors' purpose was to clarify the understanding of the syndrome, proposing a new name and a theory of the disorder's etiology that made sense of all available evidence, including a crucial piece of new evidence: the majority of patients with this disorder had the male Barr body pattern.

'Individuals with this syndrome', the authors wrote, 'had always been considered to be females'. But experimental evidence that 'emphasized the importance of the embryonic testes in counteracting the inherent tendency of the fetus to feminize', had for some years suggested an alternate explanation—'that some patients with this disorder should be chromosomal males' (ibid., pp. 1161–1162). Grumbach et al confirmed in this important article that the older hypothesis was in fact true. Henceforth, these previously female persons were to be understood as intersexuals.[50]

This 1955 article understood the evidence provided by the Barr body to be clear—these patients did not just have male chromatin patterns, they *were* chromosomal males. Understood this way, such evidence had manifold implications. It meant that, 'titles implying only an ovarian defect or deficiency should be abandoned'. The authors proposed instead the sex-neutral title 'gonadal dysgenesis' (Grumbach et al., 1955, p. 1162). Moreover, these patients provided decisive evidence 'that female differentiation of the genital ducts and

[47] In a 1957 article, for example, under the heading of 'Cytological tests of chromosomal sex' Barr stated that, 'The terms ''female nuclei'' and ''male nuclei'' are used in this report. However it is advisable to use the less stigmatising terms ''chromatin positive'' and ''chromatin negative'' for female and male nuclei respectively when discussing cases of sex reversal in clinical surroundings and when recording the findings of cytological tests on hospital charts' (Barr, 1957b, pp. 251–252).

[48] For a discussion of the prevalence of patient deception in the clinical management of intersex cases, see Kessler (1990). Alice Dreger notes that in the late nineteenth century, the conventions concerning dissemination of such information, especially in France, were quite different; not only the patient, but indeed the larger community, might be informed (Dreger 1998).

[49] Barr analyzed the skin biopsies and he reviewed the manuscript, which he thought 'splendid': Barr, letter to Grumbach, 6 June 1955 (NA, File 1–13).

[50] This was a review article; the fact that many of these cases demonstrated male sex chromatin patterns had been known since 1954. See Polani et al. (1954).

external genitalia always occurs in the absence of fetal testes' and, 'exemplify the essential and primary role of the testis in human embryonic sex development' (ibid., p. 1182). They were the human analogue of Alfred Jost's fetal castration experiments in rabbits from the 1940s (Jost, 1953). The authors went further still, and argued that in fact, these patients should be regarded 'as the most severe and extreme form of male pseudohermaphroditism' (ibid., p. 1189).

Having so decisively re-interpreted the meaning of this syndrome in research terms, Grumbach and his colleagues offered cautionary comments about clinical matters. 'The sexual orientation [of the patients]', they argued, 'has been entirely feminine, irrespective of the chromosomal sex pattern'. They cautioned that, 'the patients and their families should not be informed concerning their chromosomal sex when a male chromatin pattern is found, in view of present-day misconceptions of the importance of chromosomes in determining psychosexual outlook' (ibid.).

Barr, who had reviewed all the Barr body evidence, wrote that 'About 80 per cent of patients with gonadal dysgenesis have male nuclei, which suggests that they developed in the female direction when deprived of the masculinizing hormone or inductor of embryonal testes' (Barr 1957b, p. 251).[51] This evidence made sense of all aspects of the three-stage model of sex development, with the Barr body indicating true chromosomal sex, a presumed hormonal error explaining the failure to masculinize, and the detachment of sex from gender and sexuality (with the latter two internally and heterosexually consistent) explained by the environmental control of psychosexual identity.

This episode was not the only one that involved a rather radical reinterpretation of some extraordinary bodies. In fact, in 1955, Murray Barr was even more deeply involved in the effort to redefine another syndrome. Instead of apparent females demonstrating a male Barr body pattern, however, apparent males were shown to have a *female* Barr body pattern. These cases too were re-made as intersexuals, but with more confusion and uncertainty given their divergence from the 1950s model of sexual development.[52]

Barr and his colleague, Earl Plunkett, offered one of the first reports of seeming sex reversal in Klinefelter syndrome (Plunkett & Barr, 1956a). The patients evidenced a range of symptoms: the defining element was significant atrophy of the testes and hence infertility; there might also be a 'female' distribution of fat and hair, and sometimes obesity and gynecomastia (growth of breasts). The identification of chromatin-positive nuclei in these patients suggested 'that certain types of congenital testicular hypoplasia are the result of a genetic error in subjects with two X-chromosomes (XX or XXY?)' (ibid., p. 830).

In first describing the new findings, the researchers made clear their surprise at the phenomenon of chromosomal females having testicles: 'Although some true hermaphrodites with both testicular and ovarian tissue have chromatin positive nuclei, until the inception of the present work, patients with chromatin positive nuclei and testicular tissue only had

[51] See also Barr (1956b); M. L. Barr, 'Role of the fetal testis in the maturation of the reproductive tract' [1955], presented at annual meeting of Canadian Physiological Society (NA, File 12–21). Barr wrote, 'most patients with Turner's syndrome are derived from male embryos that feminized because testes with their masculinizing evocator failed to develop' (Barr, 1959a).

[52] Barr's publications on this include Plunkett & Barr (1956a,b); Barr (1957b) Earl Plunkett, & M. L. Barr, abstract, 'The occurrence of the sex chromatin in congenital testicular hypoplasia', Meeting of the Endocrine Society, June 1956 (NA, File 13–4).

not been observed' (Plunkett & Barr, 1956b, p. 853). Early on, Grumbach, Barr and others suggested an interpretation of these cases as 'true hermaphrodites' (Grumbach, Engle, Blanc, & Barr, 1956; Grumbach, Blanc & Engle, 1957).[53] But they were ultimately satisfied to simply define these cases as examples of the more common varieties of the intersexed: as a 'congenital error of sex development' (Plunkett & Barr, 1956b, p. 856).

In this case, the Barr body evidence did not integrate readily with the three-stage model of sex-making. If these patients did have a female chromosome pattern—which the researchers thought most likely—then how could the dominant role of hormones in this model make sense of a masculinized female? It was true that female pseudohermaphrodites might have masculinized external genitalia, but their gonads helped their sex chromosomes to speak the truth about their sex. Here were patients who had both masculinized secondary sex characteristics and masculine gonads. If, as the model of sex making suggested, females were those who failed to masculinize because of the absence, or the inadequacy, of testicles, how could there be testicles in a female? There was no ready experimental analogy—no castration experiment—that could make sense of this.

The lack of a hormonal explanation forced Barr and others back to the under-used chromosomal and genetic explanations in their model of sex development. In the absence of a credible hormonal explanation, the case of the Barr body positive Klinefelter was interpreted as demonstrating pathology farther back in the sequence of sex making—in the genes. 'It seems more likely', Plunkett and Barr wrote, 'that the abnormality is the result of a fault in the sex-determining genes in a zygote which bears two X chromosomes' (ibid.).

The following year, Barr was more decisive: 'It has recently been shown that a proportion of sterile males with hyalinisation and fibrosis of the seminiferous tubules have female nuclei', he wrote. 'They appear, therefore, to represent an almost complete female → male sex reversal from an early stage in embryonal development'. Barr added that, 'Since the condition appears to be a female → male sex reversal, Nelson . . . is technically correct in suggesting that it be designated as ''female pseudohermaphroditism with gonadal dysgenesis'''. 'But in the practical situation', Barr added, 'the patients are clearly males, and a terminology that suggests otherwise is best avoided' (Barr, 1957b, pp. 251, 255).

The social world of 1950s sex researchers was small and cosy. The research that suggested the reality of radical sex reversal in Turner and Klinefelter supported the work of John Money and his colleagues the Hampsons. Money and Joan and John Hampson are credited with authorship of an approach to sexual development that suggested the greater importance of social over biological influences in the development of a person's sexual identity and orientation (Kessler, 1990). They confirmed the clinical wisdom of making sex assignment decisions on the basis of the physical appearance of genitalia, and the personal and social preference of the intersex person, if not assigned at birth.[54]

[53] See also: M. Grumbach, E. Engle, W. Blanc, & M. L. Barr, abstract, 'The sex chromatin pattern in testicular disorders: relationship to pathogenesis and to true hermaphroditism' [Endocrine Society, June 1956] (NA, File 13–4).

[54] Money and the Hampsons were providing theoretical justification for an extant set of clinical standards. From the first, for example, Barr was disposed to consider such matters as sex of rearing, occupational style (feminine or masculine) and psychosexual outlook in making clinical decisions about sex assignment. See: Barr letter to Dr. P. Crassweller, Toronto General Hospital, 28 July 1952 (NA, File 3–20).

The psychiatric and psychological research conducted by Money and the Hampsons was highly reliant on the status of the Barr body as a definitive marker of genetic or chromosomal sex, and was practically reliant on the technical expertise of Murray Barr and his team in reading the cellular evidence of sex.[55] They used the Barr body to establish the facility with which people might establish a gender role and sexual orientation consistent with assigned sex, and opposite to all varieties of physiologic sex, including the ontologically superior chromosomal or genetic sex (Money, Hampson, & Hampson, 1955a). Research on Turner syndrome women was especially important to the Money team. These cases exemplified the inappropriateness of using any single physiologic criterion, be it gonads or chromosomes, to assign sex of rearing (Hampson, Hampson, & Money, 1955). Money and the Hampsons reported on eleven of these patients whose 'chromosomal sex' was male. These women had previously been thought to have 'ovarian agenesis', they reported, but were now more accurately identified as cases of 'gonadal agenesis' in light of their intersex status (ibid., p. 207). Despite this sex reversal, the Money team confirmed that these chromosomal males

> were found unequivocally to fulfil the cultural and psychological expectations of femininity. The salient finding to emerge from the study was that a person's conviction of himself as a man or herself as a woman—the gender role and erotic orientation—is a variable quite independent of genes and chromosomes. (ibid., p. 225)

While technically in error, this interpretation of Barr body evidence was a key support for Money's thesis, and for the system of sex assignment that he and his colleagues authored (Money et al., 1955b).

4. Alternate readings of Barr body evidence: debates within a system of scientific belief

Through most of the 1950s, researchers retained an overarching faith in Barr's provisional hypothesis about the origin of the Barr body. For clinicians and clinical researchers this meant that it served as definitive evidence of either a male, XY, or female, XX, sex chromosome constitution, and referenced a true, underlying sex. In 1959 this began to change. In this year, Ohno offered his evidence for the single X chromosome origin of the Barr body; more importantly for clinicians, researchers announced in this year that Turner and Klinefelter were better understood as chromosome anomalies than as sex reversals. Barr's provisional hypothesis was not immediately disproved. Indeed, it was not until 1961 that a convincing explanation for the Barr body's existence as a single X chromosome was published. Nonetheless, with the 1959 announcements, the system of belief within which Barr's provisional hypothesis had been housed was disrupted. A balance theory of sex development was no longer tenable: the inert Y chromosome had become the potent Y.

Prior to the developments of 1959, Barr and other researchers occasionally offered alternate interpretations of the Barr body evidence. For example, Barr and Plunkett were especially surprised by the Klinefelter cases, and noted that 'there might conceivably be an XXY or other unusual sex-chromosome complex that includes two X chromosomes,

[55] M. Barr, 'Cytology and cytopathology of the neuron', Progress Report, NHGP, Mental Health Grant, 30 November 1955, (Ontario Archives, Box 16, File RG 10–22–0–176). The Johns Hopkins team cited Barr's involvement in their papers (Hampson et al., 1955; Money et al. 1955a).

rather than the normal XX complex of female cells' (Plunkett & Barr, 1956b, p. 855).[56] In 1959, researchers revealed that Klinefelter syndrome was, in fact, the product of a sex chromosome anomaly, specifically XXY (Jacobs & Strong 1959). Perhaps some of these alternate interpretations were prescient? I review here some of the sustained research that offered alternate readings of Barr body evidence. I argue that to interpret these alternative readings as anticipatory insights is to misread the historical record. While alternate interpretations of Barr body evidence were offered, they were made tentatively. Further, alternate explanations were offered in *conformity* with the broader theoretical framework that explained sex development and sex pathology in the 1950s. This theoretical straightjacket did not begin to shatter until 1959. Rather than being prescient insights that were somehow right, these were tentative suggestions that were offered in support of the broader theoretic system within which the *good enough* science of the Barr body prevailed.

Barr and his clinician researcher colleagues from the endocrinological community (who were most engaged with intersex patients) did voice alternate interpretations of the Barr body evidence, but it was workers outside endocrinology who conducted more sustained research on the subject, and who offered the most apparently prescient alternate interpretations. One such group, led by Paul Polani in England, was oriented toward human genetics research, having strong links to Lionel Penrose, one of the grandfathers of the discipline (Kevles 1997). In line with this genetics orientation, Polani and colleagues conducted a series of studies designed to assess the genetic/chromosomal sex of persons of anomalous sex using genetic criteria, such as sex-linked conditions (for instance, the higher incidence of colour blindness in males).

Polani and colleagues began their studies in this area auspiciously, with the first publication to indicate that, according to Barr body evidence, at least some Turner syndrome women 'have a chromosomal pattern that is characteristically seen in males' (Polani et al., 1954, p. 121). They were inspired to undertake this research because of the high incidence of coarctation (narrowing) of the aorta in these women, a condition more often seen in males, leading them to wonder 'whether Turner's syndrome females are in fact females' (ibid., p. 120). In conformity with the theoretical framework explaining sex development at this time, they added that, 'The findings . . . are those one would expect if the testicles failed to develop fully or were destroyed in early intra-uterine life . . . as in the castrated animal embryos of Jost . . .' (ibid. p. 121). Polani and colleagues followed up this publication two years later with a report on colour blindness in Turner cases (Polani, Lessof, &

[56] The possibility of variations in the chromosome constitution was broached in various publications, but the XX chromosome constitution was deemed more likely. Barr wrote that, 'Although the exact genetic mechanism is not known, there is good evidence that it operates within the framework of an XX- or an XY- sex chromosome complex, i.e., there is no need to postulate an unusual sex chromosome complex such as XO or XXY'. M. L. Barr, 'Chromosomal sex and sex reversal', American College of Obstetricians and Gynecologists, 2–4 October 1958 (NA, File 11–19). Barr and co-authors also wrote that 'The error may lie in the presence of an unusual sex chromosome complex, such as XXY. . .' but they added, 'If these patients bear the XX sex chromosome complex, which is more likely. . .' (Plunkett & Barr, 1956b, p. 856). Grumbach and co-authors offered that 'Although in patients with seminiferous tubule dysgenesis and a female chromatin pattern, the sex chromatin may represent a more complex sex chromosome constiution (for example, XXY), it is not necessary to postulate such a chromosomal aberration' (Grumbach et al., 1957, p. 725). For alternate suggestions from Barr's international colleagues: the XXY constitution was suggested by W. D. Davidson, clinical pathologist, King's College Hospital, London England, letter to Barr, 20 February 1956, Case 43 (NA, File 9–3); the XXY or XXXYY patterns were suggested by H. David Mosier, The Johns Hopkins Hospital, letter to Barr, 27 January 1956, Case 47 (NA, File 9–3).

Bishop, 1956). Their results lent 'support to the hypothesis of the genetic maleness of patients with "ovarian agenesis"' (ibid., p. 119). While their results were primarily offered in support of Barr's interpretation of the Barr body, they conceded that alternate explanations were possible, notably, that they might 'be dealing with persons who have an XO pattern of sex chromosomes' (ibid.). Yet this seemingly prescient observation was offered with the caveat that 'Whether such a condition is possible in man is unknown,' and with the reiteration of the then-prevalent theory of sex development in which these cases provided the human analogue of embryonic castration experiments in animals (ibid.).

Polani and colleagues also pursued colour blindness studies in the Klinefelter case. Soon after Plunkett and Barr's announcement, they published a request for samples from the research community, to assess 'genetic sex' in light of other sex-linked anomalies, such as colour blindness (Bishop, Polani, & Lessof, 1956). Two years later they reported 'confirmation of the presence of two X-chromosomes in males with Klinefelter's syndrome and female nuclear sex and their presumptive "sex-reversal"' (Polani et al., 1958, p. 1092).[57] They noted that while the absence of the Barr body was generally taken to imply an XY sex chromosome constitution, the 'validity of this identity ... does not amount to absolute proof' (ibid., p. 1093). They thus restricted their findings to the confirmation of the presence of two X chromosomes without commenting on either the origin of the pathology, or the presence or absence of the Y chromosome. In other publications, however, Polani's collaborators were clearer about the conformity of the Klinefelter case with then dominant theories of sex development. In line with the genetic-balance theory, they suggested that the Barr body evidence in Klinefelter cases could be explained by an autosomal translocation, specifically, 'a chromosomal aberration involving the autosomal masculinizing (M) loci with triplication in the chromatin positive, genetic female (XX) cases and deletion in the chromatin negative, genetic male (XY) cases' (Stewart, lzatt, Ferguson-Smith, Lennox, & Mack, 1958, p. 126). They also suggested that the 'chromatin-positive (female)' cases of Klinefelter had testes that 'have some resemblance to the organs produced by exposing the ovary to abnormal environments, as in the freemartin ... and it may well be that the gonad in these cases can be regarded as a modified ovary and not a testes in origin' (Ferguson-Smith, Lennox, Mack & Stewart, 1957, p. 169).

Experimental biologists Mathilde Danon and Leo Sachs from Israel also did sustained research on the intersex, and offered alternate interpretations of Barr body evidence. Approaching the issue from a different research tradition, their alternate explanations were unlike those offered by Polani and his colleagues, and were sometimes explicitly at odds.[58] However, like Polani and colleagues, they embedded their alternate explanations within then dominant theoretical frameworks about sex development. The burden of Danon and Sach's work was to offer a genetic/chromosomal architecture for classifying sex anomalies. While agreeing with other authors that most cases of intersex had an immediate

[57] In a preliminary report they had confirmed that 'chromatin positive cases have in fact an XX sex chromosome constitution' (Bishop et al., 1958, p. 132).

[58] See the comment by Ferguson-Smith et al. that their examination of the nature of the Klinefelter testes (as being analogous to a modified ovary) might 'provide a basis for an explanation of the occurrence of Klinefelter's syndrome in genetic females alternative to that recently propounded by Danon and Sachs (1957)' (Ferguson-Smith et al., 1957, p. 169).

endocrinological explanation, in line with evidence from fetal castration experiments, they sought to provide evidence of chromosomal imbalance (with excess or too few sex chromosomes) and genetic anomaly (mutation) for other cases, and to reiterate the primary role of genes in sex development. In conformity with this approach, Klinefelter syndrome posed no interpretive challenges. This was a case of 'complete sex reversal', where the potentiality of the fetal gonad was altered by some 'genetic factor' (Danon, 1958, pp. 56, 58). Further, the Barr body evidence was understood to clearly demonstrate a female sex chromosome constitution (XX) (ibid.). In the case of Turner syndrome, Danon and Sachs agreed with the consensus that these cases exemplified Jost's fetal castration experiments. However, they also offered a chromosomal explanation that appears prescient. They suggested that some of these cases might be chromosomal mosaics, with mixed populations of XO and XY cells. This explanation was offered to make sense of cytologic data in which Barr body populations appeared mixed, depending on biopsy location (Danon & Sachs, 1957; Sachs & Danon, 1958). On the face of it, this explanation appears to conform with current evidence and theory, but Danon and Sachs offered this theory as a human analogue of the *Drosophila* case, highlighting its source in a foreign theoretic framework (Danon & Sachs, 1957, p. 24). Further, their work consistently cited a balance view of sexual development, in which the Y chromosome was inert, and they were most insistent about their theory that women with testicular feminization carried an XXY sex chromosome constitution—-a thesis that now reads as absurd (Danon 1958).

5. Conclusion

When Murray Barr and his graduate student, Ewart Bertram, made their announcement in 1948, they appeared to offer a mark of genetic or chromosomal sex to a clinical research community with no other way to assess sex chromosome status in the sexually anomalous. Barr interpreted the Barr body as the physical embodiment of the female's double X chromosome constitution. He and other workers were aware that this thesis was unproven, but it was consistent with a coherent system of scientific belief incorporating evidence about the bipartite state of the Barr body, and a balance theory of sexual development in which the Y chromosome was inert. In addition to this robust scientific belief system, Barr's provisional hypothesis was supported by its clinical and cultural utility as a genetic guarantor of a dichotomous sexual universe. Alternative interpretations of the origin of the Barr body, and alternate readings of Barr body evidence, were offered, but they paid homage to the scientific belief system that supported Barr's provisional hypothesis. During the bulk of the 1950s, then, this hypothesis was *good enough* to permit the Barr body to serve as a definitive mark of a true, underlying sex.

The power of the Barr body in making sense of intersexuals and inverts was great, but the clinical impacts were variable. In some cases, such as the female pseudohermaphrodites due to adrenal malfunction, the Barr body worked with the new technology of cortisone to confirm these as the bodies and identities of women. In other cases, such transsexuals, or those male pseudohermaphrodites with bodies that were insensitive to androgens (then termed testicular feminization), the Barr body served as a scientific fact, and a potential aid in diagnosis, but often also a hidden truth in these 'tragic' lives. Finally, there were the cases of Klinefelter and Turner syndrome. These extraordinary bodies had

not previously been hermaphroditic.[59] No one had doubted their sex before 1955 because evidence of doubtful sex was visible only with the application of the new Barr body technology. Because of the power of this genetic truth, however, Turner and Klinefelter syndromes were reinterpreted as intersexual phenomena, with profound implications for theories and protocols for the medical management of the intersex.

Some things changed as the 1950s became the 1960s, but much remained the same. The Barr body was reinterpreted as a single X chromosome, and the Y chromosome was newly seen as a potent determinant of sexual identity. But the cultural and clinical faith in the sexually dichotomous nature of the human species, and the valuation of genetic information in defining that sexual identity, continued. When Barr's 1950s reading of the Barr body was revealed to be in error, the faith in scientific markers of true sexual identity merely switched its object. After 1959, the Y chromosome (and more recently, the sex determining region of the Y chromosome, SRY) became the arbiter of a true, underlying sexual identity. As for the clinical findings that the Barr body had supported in the 1950s: many were not overturned. Whether Klinefelter and Turner syndrome are instances of intersex is not an empirically answerable question, but depends on what is taken to define both surface and true underlying female and male identities. Further, though the Barr body does not actually *embody* two X chromosomes it is, in many instances, an adequate proxy. This fact mitigated against any radical rewriting of the clinical research record in the 1960s, and supported a continued bracketing of the scientific errors that had been committed.

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[59] Persons with these syndromes shared with many hermaphrodites the symptoms of infertility, and problems with achieving sexual maturity at puberty, which meant that many were seen in the endocrinological clinics that some hermaphrodites also frequented. Endocrinologists thus had ready access to these cases for research on hermaphroditism, but this shared clinical reality did not imply their definition as intersexes prior to the research outlined above.

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