

Surveying 'slides': clinical perception and clinical judgment in the construction of a genetic diagnosis

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ABSTRACT *The work of clinical geneticists includes the inspection of visible abnormalities and their allocation to clinical categories. Drawing on observations of departmental clinical meetings in a medical genetics service, we describe how diagnostic work is accomplished through the practical observation and reasoning of clinical professionals. We suggest that, while the use of molecular tests is increasing the diagnostic repertoire in various ways, clinical perception and clinical judgment govern the adjudication and use of such tests in diagnostic work.*

Introduction

Techniques of molecular analysis have enabled considerable advances to be made within the broad field of scientific research in genetics, in the molecular characterization of the human genome, and in the isolation and functional exploration of particular sequences of DNA. In parallel with this, there is a growing literature on the social impact of molecular genetics, in particular on the extent to which genetic understandings (lay or professional) of illness and of behaviour are becoming privileged over other types of discourse, and with what consequences. Current research is documenting the ways in which users of clinical genetics services negotiate the implications of genetic risk information (e.g. Shaw, 2000), and is exploring the implications of genetic categorizing beyond clinical contexts, for issues of identity, and of individual rights and choices (Richards, 1993; Conrad and Gabe, 1999).

Given both the pace of molecular genetic research and the corresponding interest in the social and ethical issues surrounding the use of molecular technology, particularly with respect to gene transfer between organisms and gene therapy (e.g. see Yoxen, 1983), we might expect new genetic technologies to play an equally large role within contemporary clinical diagnostic processes, particularly within the medical speciality of 'clinical genetics'. To date, however, there has been a dearth of research on how clinical judgments are made in

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contemporary diagnostic practice, and on how new genetic technologies are used in clinical contexts. Is the increasing use of molecular tests in diagnostic work leading to the "death of the clinic" (Haraway, cited in Rabinow, 1992, p. 245), or are "older cultural classifications" being "joined by a vast array of new ones to 'cross-cut, partially supersede and eventually re-define the older categories'?" (Rabinow, 1992, p. 245).

Any general examination of the place of new genetic technologies within clinical processes must recognize that clinical processes take various forms, because clinical medicine is itself heterogeneous and has different contexts and locations (Atkinson, 1995). Here, we offer a preliminary exploration of the place of genetic technology in one area of diagnostic decision making, the clinical genetics department. Clinical work in this medical speciality involves risk assessment in relation to developing such conditions as breast cancer and heart disease, as well as the diagnosis of conditions involving dysmorphic or unusual physical features. Here, we make particular reference to the sub-speciality that is known as dysmorphology, the medical study of unusual human forms (Aase, 1990).

Clinical genetics in its contemporary form became an established medical speciality in Europe and America after the Second World War. The first genetic advisory clinic in Britain was established in 1946, at the Great Ormond Street Hospital for Sick Children in London; in the USA the first advisory clinic was probably the Heredity clinic established at the University of Michigan in 1940 and the second was the Dight Institute, established at the University of Minnesota in 1941 (Kevles, 1985, p. 253). Clinical staff offered a diagnostic service for persons possibly affected by genetic disorders, and advised couples with a genetic disorder in their family history about the risk of having affected children. Eventually, Sheldon Reed, the second director of the Dight institute, coined the term "genetic counseling" in 1946, "as an appropriate description of the process which I thought of as a kind of genetic social work ..." (1974, p. 335). By 1960, there were about thirty clinics offering 'genetic counselling' in the UK and the USA (Kevles, 1985, p. 254). The diagnosis of genetic conditions and the assessment of reproductive risk are the main components of contemporary work in the discipline. Our concern here is with diagnosis rather than with risk assessment.

The diagnosis of genetic syndromes initially rested largely on the description of observable characteristics (the phenotype), supplemented by techniques for microscopic characterization of chromosomes (karyotyping). Over the past thirty years, the speciality expanded considerably in relation to technical advances in detecting single gene and sub-microscopic genetic alterations (Bosk, 1992; Rapp, 1988, 2000). Today, clinical geneticists make increasing use of various relatively new techniques of molecular analysis, including Southern blotting, polymerase chain reaction (known as PCR; see Rabinow, 1996) and fluorescent *in situ* hybridization (known as FISH). This is because many dysmorphic syndromes involve submicroscopic changes in DNA sequence.

We suggest here that an assessment of the extent to which clinicians in this

sub-speciality now rely on new genetic technology in their diagnostic work, rather than on physical observation and checks against standard observational and developmental measures, must take into consideration the social structures and processes of clinical decision making. We do this by presenting an account of clinical decision-making that shows how these processes continue older traditions of medical classification and display at the same time as they incorporate new technologies of representation and investigation. We suggest that the use of new genetic technologies in this medical sub-speciality is adjudicated through the hierarchies and traditions of clinical practice, and we reflect on the reasons why, despite their increasing use in assisting diagnosis, molecular technologies have not had the impact on medical diagnostic processes that they have had in basic genetics research.

Methodology

The paper is based on Shaw's observations of departmental meetings within one clinical genetics service. These observations were made at intervals during 1998–2001 as part of pilot research towards a project on understandings of genetic risk (Shaw, 2000). Initially unfamiliar with the clinical context and with the clinical and technical terms employed at these meetings, Shaw began to make fieldnote jottings (Emerson *et al.*, 1995), which included substantial portions of the verbatim dialogues that accompanied slide presentations, as well as details of the accompanying dynamics of diagnostic performance and interaction between clinicians. Using pseudonyms in all the extracts from her notes on the dialogues, she presented initial analyses at a Genetics and Society discussion group meeting in Cardiff (November 2000) and at a Brunel University Research Conference in February 2001. Drawing on Shaw's observations, the present collaboration examines diagnostic processes in the genetics clinic as a backdrop for further exploration of the use of genetic technologies in clinical work.

The paper begins with a description of how clinicians assess cases involving dysmorphic features, making particular reference to regular departmental clinical meetings. We show how photographic images of patients are presented and discussed at these meetings, and suggest this is a contemporary manifestation of a long-established tradition of public presentation and representation of the bodies of patients. We then describe processes of clinical reasoning, and suggest that these processes recapitulate aspects of long-established Western preoccupations with observing, classifying and interpreting departures from 'normal' human forms, at the same time as contemporary clinical genetics can be distinguished from early twentieth-century eugenics. We then turn to the question of the role of molecular methods in diagnostic processes, and offer case material to show that the use of these technologies is best understood through an analysis of clinical decision making, that is, through the exercise of clinical perception and clinical judgment. Finally, we reflect on the extent to which this is particular to clinical dysmorphology, and indicate some lines for further research.

Clinical assessment

In their diagnostic work, clinicians are looking for patterns in symptoms and signs that may reveal an association with an underlying genotype (genetic characterization). This usually involves careful observation of 'dysmorphic' features, which are those that fall outside the range of normal variation (see Aase, 1990). Structural abnormalities of development are often associated with problems in motor and intellectual development, and indicative of an underlying genetic disorder. Physical features such as a 'hairy back', a 'heavy brow', 'widely spaced eyes', eyes 'set at an angle', a 'white forelock', 'eyes of different colours', or patches of darker pigment on the body called '*café-au-lait*' spots, are in themselves not necessarily pathological, but when found together with signs such as heart problems, hearing loss, impaired kidney function or intellectual disability, they suggest particular genetic syndromes.

Observation of physical features plays a key part in diagnosis. An experienced clinician may consider a particular diagnosis is likely simply by observing specific physical features. The presence of many more than five or six *café-au-lait* spots on an otherwise healthy and non-dysmorphic baby may be sufficient for a consultant to suspect neurofibromatosis, for instance, even without other typical presenting features such as short stature, learning difficulties or visible neurofibromas, although a firm diagnosis can only be made where there are at least two clinical indicators from a set of clinical criteria. Alternatively, noting that distinguishing physical features are absent, such as, in the case of Marfan syndrome, disproportionately long limbs in relation to the torso and lax joints, may allow an experienced clinician to rule out a particular diagnosis without waiting for laboratory test results.

Clinicians usually make these observations during the first clinical consultation, following the routine procedure of history taking, observation and examination, investigation and diagnosis. The doctor (consultant or registrar) makes case notes of the clinical history and any relevant family history, and usually draws a pedigree (family tree) (Nukaga & Cambrosio, 1997). He or she may perform a physical examination to rule out the most obvious diagnoses (differential diagnosis), and at this point take a photograph of relevant or dysmorphic bodily features. The resulting photographic images, especially if they are obtained at regular intervals, may enable clinicians to chart the natural history of a particular disorder, and can be central to the diagnostic process. Since a genetic diagnosis can take considerable time, the photographic record can assist 'watchful waiting' (Aase, 1990, p. 21), and enable other clinicians to 'see' the case, and offer suggestions for further investigation and diagnosis. This happens regularly at the departmental clinical meetings.

Departmental meetings and 'slides'

Weekly departmental meetings are held in the library, a large room surrounded by shelves containing textbooks and journals, with the clinical staff and other

participants sitting round a large table. These meetings are for research and teaching as well as to assist in the delivery of care for patients, and they bring together all members of the clinical teams (consultants, specialist registrars and genetic specialist nurses), together with clinical scientists and representative staff from the genetic laboratories. Laboratory staff occasionally attend, because both chromosome karyotyping (cytogenetic tests) and, increasingly, molecular tests assist the diagnosis of dysmorphic syndromes. Because the genetics department is also a training facility for the medical school, departmental clinical meetings double up as educational occasions, with medical students and other trainee clinical staff present. Similarly structured meetings take place in clinical genetics departments in other parts of Britain, and there are less frequent specialist national meetings.

Preceded by 'journal club', which is a routine review of publications in medical and scientific journals, and by short presentations from genetics laboratory staff or the prenatal service and brief discussions of matters of internal audit, the central presentation of the departmental meeting usually involves one of the consultants showing 'slides'. These are photographic images of patients obtained with the patients' consent during their clinic consultations. The photographic image, as we shall see, is central to these departmental presentations, so much so that the clinical presentation itself is often referred to as 'slides'. 'Slides' enables routine cases as well as those regarded by clinical staff as problematic or interesting to be presented and discussed by the clinical team. The event therefore has the function of the medical ward round, but in contrast with the grand round, ward round or teaching round of the hospital (Atkinson, 1981, 1995; Sinclair, 1997), the patients are absent. They are instead 'assembled' (Latimer, 1997, 2000a, b) as clinical cases through the presentation of clinical observations, test results and photographic images.

When the consultant who is presenting the slides indicates that she/he is ready to start, the lights go out and, with the click of the control button, the participants gaze towards the slide screen on which the first image appears. The images are photographic representations of patients, nearly always of their faces, and sometimes of whole bodies or particular parts of their bodies. 'Slides', as the slide presentation is referred to, is about defining the significance of these parts. As the participants, sitting in a semi-circle, gaze at the images on the screen, the presenting consultant describes some of the patient's other clinical characteristics such as medical and genetic test results. The verbal presentation, combined with the visual image or images of the patient, elicits comments and responses from fellow consultants, senior clinicians and other staff. These interactions are not merely a story of detection, they constitute a performance that can have a competitive edge, in which all participants, including the nurses and scientists may engage, but in which the senior consultants are the main actors. The following extracts exemplify these typical features of 'slides':

Extract 1: This is from a departmental meeting which included two senior consultant geneticists, Dr Black and Dr White, and a specialist

registrar, Dr Green, who is working with Dr White's team. Dr Black is making the clinical presentations. Several images show a girl's face, from different angles:

Dr Black: This girl was referred at birth because the paediatrician thought she was dysmorphic, but when she started walking the parents did not want to pursue it.

Dr Green: She looks chromosomal.

Dr White: She has the look of Floating Harbor.

Dr Green: It is not a 22q nose.

Dr Black: It is a big nose, with the tip turned down. And note the long philtrum.

Dr Black gives a brief account of the case, not offering a standard medical or genetic history, but informing those present that this child has not yet had a diagnosis. Dr Black notes that the parents did not want to 'pursue' a diagnosis once their child was walking, and, presumably, developing 'normally', and does not offer details of the circumstances of the child's re-entry into genetic clinical processes.

Dr Black does not indicate how other participants should view the face; rather, other members offer their comments unsolicited. Dr Green aligns with Dr Black and the paediatrician by affirming that the face looks 'chromosomal'. Discussion explores the possible significance of the features, as suggestive of one genetic disorder or another: the '22q nose', or the appearance of 'Floating Harbor'. Dr Black draws attention to the appearance of the nose, stressing its significance as indicating something abnormal.

Extract 2: From the same departmental meeting as extract 1: a slide shows the front of a girl's face, and another shows her back:

Dr Black: This is a three-year old girl. She has mild aortic stenosis [a heart defect] and look at her back [the slide shows it is hairy] [Clicking back to the slide of her face.] Note the odd cranio-facial appearance. It is not Crouzon. There is quite a bit of frontal bossing.

Dr White: [looking carefully at the image]: Maybe she has got sagittal stenosis. It would be worth doing an AP (skull X ray). If there is cranial stenosis, there might be management implications. She is not really Noonans. Check out what aortic stenosis is linked with.

In this extract, Dr Black opens by showing two slides of the patient, simultaneously putting into play some key clinical features, of age, sex and medical diagnosis. She does not present a full history of the patient or the results of any clinical examination, but moves directly to the slides and draws attention to the features they represent, which, through this process, take on the significance of abnormality. She excludes one genetic condition, Crouzon, but implies that

there is a genetic basis to the configuration of features she has drawn attention to, by noting, 'there is some frontal bossing'. She does not at this point 'risk' a diagnosis, but leaves the field open to elicit suggestions. Dr Black and Dr White are both consultants, but here Dr Black, in effect, defers to Dr White's expertise in diagnosing dysmorphic syndromes, offering her the opportunity to refine the observation of abnormality by close examination of the image of the girl's face—'maybe she's got saggital stenosis'—and suggesting further tests (the skull X-ray). The diagnostic process is being managed not just through the sharing of opinion and knowledge, but through explicit instruction, offered, as this exchange implies, through hierarchies of expertise.

Both these extracts illustrate how diagnostic dysmorphology provides a contemporary example of the clinical gaze in action (Foucault, 1973), because much depends on the clinicians' perception, recognition and adjudication of physical anomalies. This has long been a feature of the Western medical tradition. The public presentation of bodies and of patients, and their pictorial representation was a dominant feature of medical practice during the Renaissance, as illustrated in the anatomy theatres of Leiden and Padova, and in Vesalius's drawing of dissected figures (Sawday, 1995). Ward rounds and anatomy classes were established features of medical training, in France for example, and in eighteenth-century hospitals in Leiden, Vienna and Edinburgh (Atkinson, 1981; Sawday, 1995). Traditions of presentation and display continue to be deeply entrenched features of the creation and transmission of medical knowledge. Ward rounds and other techniques for teaching students how to elicit the signs and symptoms of disease and how to interpret them remain central to contemporary medical training (Atkinson, 1981; Sinclair, 1997). In this respect, then, 'slides' represents a continuation of a much older tradition of representation and display.

As the above extracts indicate, genetic diagnosis is rarely immediate, and sometimes a firm diagnosis is impossible. Major birth anomalies are rare (about 2% of all births), and individual syndromes occur with even greater rarity. Diagnostic work employs the principles of diagnostic categorization, and draws upon the specialist expertise and experience of consultants, individually and in public display through 'slides'. Their expertise includes the ability to distinguish genetic and non-genetic dysmorphic features, for some dysmorphic conditions have non-genetic origins (e.g. fetal alcohol syndrome), similar phenotypes can have very different causes, and some signs and symptoms are shared across a range of disorders. In identifying particular syndromes, clinicians exercise and display their particular expertise and experience. Skilled consultants may have a 'gut feeling' that a particular collection of features has a genetic basis, or is linked with a particular syndrome.

To describe someone as 'looking chromosomal' generally refers to dysmorphic features suggestive of a chromosomal abnormality (a trisomy, deletion or translocation), of which Down syndrome, involving trisomy (three copies) of chromosome 21, is the most well known. In commenting, 'This child looks facially dysmorphic. He's a query Kabuki. He is probably chromosomal', or

'This one looks a bit dysmorphic. Looks Williamsish. But it's a guess really', the consultant is linking particular dysmorphic features with chromosomal abnormalities, and with particular named genetic syndromes. The phrases, 'having the look of Floating Harbor'; looking 'not really Noonans', or 'not Crouzon'; 'looking Williamsish' or 'being a query Kabuki', refer to aspects of the phenotypic characteristics of syndromes with these labels. 'Kabuki', for example, refers to distinctive facial features that one consultant described as 'having eyes like a Japanese actor, as if they have eyeliner drawn round them'. 'Looking Williamsish' in clinical discussion means having the 'elfin-like facial features' associated with the condition, along with the clinical sign of a heart murmur.

Clinical dysmorphology in a historical context

Within the Western medical tradition, the observation, classification and interpretation of human developmental differences and departures from 'normal' forms have been associated with now discredited evolutionary and racial classifications. For instance, in 1866, Dr John Langdon Haydon Down compared the distinctive and easily recognized features of Down syndrome (a round face, a small, rather flattened nose, a thick and furrowed tongue, short and wide hands and feet, and mild to severe learning difficulties—which have been known since 1959 to result from trisomy 21) with the features of 'Orientals', and he named the condition Mongolism (or Mongolian idiocy). His comparison was rooted in the racist evolutionary theory of the nineteenth century. He reasoned that if embryonic development recapitulates the evolution of the species, and if idiots are people with arrested development, then their features will resemble those of the 'lower races', and he discerned signs of various racial types in the dysmorphic features of 'congenital idiots' (Gould, 1980, pp. 134–5). In time, the theory was discredited, but "his name for one specific anomaly, Mongolian idiocy ... stuck long after most physicians forgot why Down had coined the term" (Gould, 1980, p. 138). It was not until the 1970s that professional scientists argued that the condition be renamed after Dr Down, and not his discredited theory.

Twenty years after Dr Down perceived human ancestry in the morphology and intellectual characteristics of some of his patients, the Italian physician Cesare Lombroso used measurements and photographs to scrutinize the bodies of prisoners, and concluded that they displayed atavistic physical characteristics, the signs of the inferior races. His theories that criminality has physical as well as behavioural features, and that these features are akin to those of (other) animals and of contemporary savages (see Gould, 1980, pp. 124–5), fuelled biological rather than sociological theories of human behaviour, and profoundly influenced the development of criminology (through the concepts of the criminal personality and the indeterminate sentence; see Gould, 1980, pp. 140–3). In Down's and Lombroso's theories, intellectually, physically or socially 'abnormal' whites represented less evolved human forms.

In England at the same time, Charles Darwin's cousin Francis Galton used

photographs and anthropometric measures to classify human types and infer character and personality from physical appearance. Galton viewed most behavioural traits as strongly heritable, pioneered modern statistical methods in quantifying the heritability of behavioural and physical characteristics, and lent scientific justification to the prevailing racist evolutionary theories of the day through his demonstration of the heritability of intelligence (Gould, 1981; Wilson and Herrnstein, 1985; Kemp and Wallace, 2000; Kevles, 1985). He advocated selective breeding from superior men and women to produce "a highly gifted race of men" (Galton, 1869, p. 1) and founded the British eugenic movement, coining the term 'eugenics' in 1883 to describe strategies of selective breeding. 'Positive eugenics' ... aimed to foster more prolific breeding among the socially meritorious, and 'negative eugenics' ... intended to encourage the socially disadvantaged to breed less- or, better yet, not at all" (Kevles, 1985, p. 85).

As knowledge of the complexity of human heredity and genetic variation increased, racial theories and eugenic ideals were undermined on scientific grounds; instead, there emerged a "reform eugenics" devoted to "the use of genetics for medical purposes" (Kevles, 1985, p. 253). With the revelations about the Holocaust, and following public aversion to the term 'eugenics' in the UK and the USA (Kevles, 1985, p. 250), the eugenics institutes and journals were eventually renamed, the *Annals of Eugenics* becoming the *Annals of Human Genetics* in 1954, for instance, and *Eugenics Quarterly* becoming *Social Biology* in 1968.

Contemporary medical genetics is historically descended from the early eugenics movement (Reed, 1974; Porter, 1977, p. 25; Paul, 1998). And in its emphasis on visual representation and measurement in understanding physical differences, contemporary dysmorphology clearly shares some of its performative and taxonomic features with earlier evolutionary theory. However, 'genetic counselling' is usually distinguished from explicit eugenics, through its concern with the medical health of individuals rather than with population improvement (Reed, 1974, pp. 332–3), and through the philosophy of non-directiveness. A central tenet of current practice is that counsellors provide diagnostic and risk information, but should not force or even recommend the prevention or termination of a pregnancy associated with physical and/or intellectual disability, for such decisions are the responsibility of prospective parents. However, whether any or even no reproductive choice constitutes a form of disguised eugenics remains a matter of debate (see for instance Kitcher, 2000; Paul, 2000).

Contemporary ethical and social science concerns about aspects of the use of new genetic technologies are thus shaped at least in part by an awareness of the history of the misapplication of genetic science earlier this century. The empirical exploration of different contexts of practice, looking, for instance, at how access to genetic services and information is structured for different client groups, and at how diagnostic and reproductive risk information is understood and its implications are negotiated in the clinical context, is thus of direct relevance to these concerns.

Should we do his 22qs?

The diagnostic work described so far takes place within a framework of clinical perception and judgment, where the emphasis is on the visual observation of physical features, especially but not exclusively the face, in relation to other clinical signs and symptoms. Today, in addition to deciphering the 'classic' terminology for dysmorphic features (long philtrum, ptosis, etc.) and syndrome nomenclature (Williams, Kabuki, Seckel, etc), a novice clinical geneticist must also learn the vocabulary of molecular genetics, which increasingly features in the discourse of 'slides'. For example:

Extract 3: From a departmental meeting at which a consultant is presenting slides. [The slide shows the face of a male child, who looks unremarkable to the researcher].

Consultant: This boy is very severely retarded, but there is no motor delay. Should we do his 22qs, because this is one we get results on?

[The next slide shows the face of an apparently unremarkable-looking baby]:

Consultant: This is a girl of 14 months. Mum and Dad's chromosomes were normal and the FISH was normal.

The phrases 'doing the 22qs' and 'having normal FISH' refer to molecular tests using fluorescent *in situ* hybridization (FISH probes) to detect deletions of chromosome 22 as well as other sub-microscopic genetic differences. The constellation of features in Williams syndrome, for instance, was linked through molecular detective work with deletions on chromosome 7q, which can now be picked up in 'cyto' using FISH probes (Francke, 1999). 'Having normal FISH' refers to this test showing a negative result.

Attention to the discourse of 'slides' shows that the use of genetic tests is extending the diagnostic repertoire. Consultants, who ultimately shoulder the responsibility for diagnosis (Bosk, 1979; Good, 1994, p. 82), can test on colleagues ideas about using particular tests, or seek reassurance that they are pursuing the best line of investigation. It is also clear that the use of genetic tests is a matter of debate and negotiation which, in some cases, is re-shaping traditional diagnostic categories.

It may, for example, be worth doing a genetic test if you already have the blood sample and are not therefore subjecting the patient to an additional and possibly unnecessary procedure, even though the phenotypic features are not typical. Deletions of chromosome 22 are the most frequent deletions found in humans (Scambler, 2000), so testing for this deletion might get a result (show an abnormality). Thus, in extract 3, when showing the image of the boy who lacks the full range of features associated with chromosome 22 deletions, the consultant asks, 'Should we do his 22qs, because this is one we get results on?' Moreover, in these cases, the genetic characteristic (22q deletion) detected by the molecular test is becoming shorthand for phenotypic characteristics associ-

ated with the deletion: 'having a 22q nose' for example. A departmental meeting discussion of a collection of images of three babies and one mother, all shown on testing to have 22q deletions, concerned the question: Is there a 22q face? There is a distinctive nose, heart-shaped mouth, and, usually, small ears, and the conclusion was that there is a 22q face. Here, the genetic test re-focused attention on the phenotypic features important in classical forms of diagnosis.

A positive result from a molecular test might extend the range of phenotypic features associated with a particular syndrome. The photograph of a six-month-old baby diagnosed on the basis of a genetic test with Williams syndrome was examined during 'slides', because he had none of the usual features, except the heart problems. At this stage, it was too early to tell whether he would nevertheless develop the other features; the case will be followed up, and the deletion may prove to be atypical, a smaller deletion. This could lead to refinement of the category 'Williams syndrome'.

The value of molecular tests is therefore negotiated in relation to clinical observation and principles of clinical practice, in which consultants are concerned not to subject patients to unnecessary tests. But in their negotiations, clinicians also point to how pragmatic organizational issues influence the use of tests: clinicians have to consider how tests that produce clinically useless results can waste resources. Particular tests may cost at least several hundred pounds, so that there are criteria for requesting tests which are regularly reviewed. In other words, the use of tests is influenced by notions of efficiency.

For example, a recently developed test for telomeric rearrangements (alterations in DNA sequence at the end of chromosomes) was discussed on several occasions because of its 'poor hit rate' ('zero out of 65'), and because the cases so far picked up would have been detected by chromosomal analysis anyway. In terms of resources, this was not regarded as an efficient test. In contrast, at other clinical centres, telomeres may be 'done' more readily. The following extract illustrates how the value of doing such a test is negotiated in relation to certain criteria of clinical efficiency.

Extract 4: At this departmental meeting, Dr Grey is presenting slides from another centre:

Dr Grey: This girl is not very delayed. What tests would you do? [silence] She had her telomeres done. She had an unbalanced translocation, which her father and his mother had in balanced form.

Dr White: She would not have got into our telomeres.

Dr Brown: From a teaching point of view, you would never pick it up from her appearance.

Dr White: We are stringent here.

Dr Grey: There was a history of miscarriage in the family.

Dr White: That would not have made any difference here. With such

mild learning difficulties, she would not have come into our criteria. No test is perfect. You have to decide on what criteria you use it.

Dr Grey suggested expanding the clinical criteria for offering the test, but the two consultants present, Drs Brown and White, were not convinced. In subsequent discussion of the value of the telomere test in other cases of mild learning disability (rather than striking pathology), and where features do not appear to be dysmorphic, the consultants questioned the clinical value for the individual concerned, and for their family, of testing for a telomeric alteration, suggesting that it might cause unnecessary social problems. They were concerned about the potential for labelling a child's mild disabilities as genetic (or 'telomeric') in the absence of other clinical indicators, and did not think that the telomere test should be performed in these circumstances, even if a child's parents has requested it. In these ways, although the technology for a particular test may be available, the decision to offer or perform a test is located and adjudicated within the particular and complex context of clinical practice. Yet, as the above example also illustrates, clinical criteria and organizational complexities may well vary across different genetics centres.

Our observations also suggest that, even where tests are performed, consultants do not throw the full weight of proof onto the laboratory findings. They may make a diagnosis on the basis of dysmorphic and clinical features, or on the basis of physical signs alone, and if a genetic test is negative, they may question its sensitivity. A negative result in an otherwise typical case does not mean a diagnosis cannot or will not be made. For example,

Extract 5: Showing the slide of a girl's face, a consultant says:

This is going to be my star diagnosis of the year. The mother went to a special school. She does not cope with her daughter, who has fits. We think Angelmans is a possibility but the tests were normal. The mother's history of the child fitted Angelmans, but against that, the vision didn't fit. When we met her, we noted scissoring movement of the legs, and dystonic posturing. We wonder in retrospect whether this was seizure behaviour. We think she is going to have Angelmans when she grows up. She's had the standard test. So now we're doing UBE3A. I don't know what the pick up rate is. We can't make an easy clinical diagnosis because she moves the entire time.

Discussion

'Slides', the genetic slide show, is much more than a display of unusual facial and bodily features. On closer inspection, it gives a view into a world in which clinicians attempt to 'fix' clinical entities with diagnostic labels. This is not just a question of reconstructing the history of a disorder and applying knowledge of signs and symptoms. It involves the visual perception of subtle physical differ-

ences, which, like other forms of specialist knowledge and ability, is a skill acquired after long apprenticeship and experience. 'Slides' offers an insight into how junior clinicians and other participants are trained in the processes of diagnostic dysmorphology. It also develops, displays and affirms the particular skills of the senior clinical consultants, who adjudicate in the presentation, discussion and diagnosis of patients.

The very fact that diagnosis is 'performed' publicly through slides as well as individually in the consultation between clinician and patient draws attention to the social aspects of the production of a genetic diagnosis. 'Slides' is therefore, much more than a problem-solving exercise. In its structural form and its social and symbolic functions, it closely resembles the clinical round in contemporary medicine (see Atkinson, 1981, 1995; Latimer, 1997, 2000b; Sinclair, 1997), itself an element within a long tradition of transmitting medical knowledge visually and orally. In his analysis of "the liturgy of the clinic", Atkinson draws out the significance of the ritualized structure and ceremonial performance of the clinical round, in its different settings: the grand round, the teaching round, the clinical lecture (1995, p. 149). In a teaching round, the most familiar form of the clinical ward round, consultant and students examine and pronounce upon patients, and the consultant tests students' knowledge of the routine of history taking, examination, investigation and differential diagnosis. The round's liturgical structure, that is, its ritualized form and the element of performance, is significant because it enables medical work to be "accomplished in stable and predictable ways". These structural and performative elements are present even where the bodies of patients are absent. Today, in the complex social and technical organization of a modern hospital, medical 'cases' are frequently assembled away from the bedside, and in the patient's physical absence (Atkinson, 1995, p. 149). The patient is "repeatedly transmuted into objects of scrutiny and discourse" through a whole range of modern technological devices—images, scans, test results, "fragments of corporeal and other traces"—as well through older media of photographic representation. In such a context, rather than disappearing, the ritual presentation and performance of a case becomes critical to medical work:

The resulting narration of the case is one powerful way in which it is assembled as a case. It is a device whereby the diverse types and sources of knowledge, and actions derived from different time-frames, are brought together under the auspices of a single discursive organization and made available for the collective gaze of medical colleagues. One may metaphorically substitute the narrative for the body of the patient as the object of clinical scrutiny. (Atkinson, 1995, p. 149)

Conclusions

Specific molecular tests can now be used in the diagnosis of an increasing number of genetic conditions previously describable only in clinical terms. To

what extent, then, is genetic testing transforming clinical practice? The descriptions presented here suggest that, while molecular tests are undoubtedly supplementing the diagnostic repertoire, they are not supplanting traditional diagnostic techniques of history, observation and examination, investigation and diagnosis, at least with respect to the diagnosis of rare genetic conditions involving dysmorphic features. Molecular test results may challenge clinical classifications of dysmorphic syndromes, with the consequence that phenotypic classifications are being refined or extended, and elements of the terminology of molecular testing are being incorporated into systems of diagnostic classification, but clinicians do not necessarily privilege test results over other observations. Clinicians are reluctant to use molecular tests in the absence of good clinical indicators, and they are aware of the potential social consequences of unrestricted private demands for molecular tests. In the sub-speciality of dysmorphology within the clinical genetics service of the British National Health Service, there remains a general commitment to clinical judgment in the use of genetic tests.

Part of the explanation for this lies in the structural restrictions of cost and access to molecular tests, because funding does not permit the extensive use of molecular techniques for the diagnosis of rare disorders. The test for deletions on chromosome 22q may sometimes be used speculatively to assist diagnosis, because this is an 'in house' test that can be done on site in the hospital genetic laboratory at relatively low cost. Other molecular tests, however, are available elsewhere only on a research basis, and are not available on the NHS. In this case, access to such tests is generally informal, and tests may be performed as a 'favour' as a result of a particular link between a clinician and a research scientist. During departmental presentations, clinicians sometimes suggest particular research groups as possible recipients of a patient's blood samples: the research group gains the additional samples, while the clinicians obtain possibly useful test results. However, where there is no known relevant molecular research in relation to a particular constellation of clinical features, or where access to research is restricted, clinicians have no option but to rely on 'traditional' diagnostic techniques of visual inspection and clinical reasoning to gaining the assistance of colleagues in reaching a diagnosis. The cases discussed in 'slides' are on the whole cases of rare genetic disorders, of which there are thousands. To administer molecular tests for each of these possible diagnoses would be unworkable, expensive and time consuming, and in any case impossible on the basis of current knowledge.

How different is this situation from that of the the diagnosis of common genetic diseases? Down syndrome (trisomy 21) and fragile X (Xq 28, mainly affecting males) are two of the commonest single causes of intellectual disability, while cystic fibrosis is a relatively common recessively inherited single-gene disorder that does not involve any dysmorphic features or intellectual disability. Cases of these disorders are rarely presented in 'slides', because they are diagnosed routinely in other medical specialities. However, even in these cases, diagnosis is usually based on the observation of clinical signs and symptoms; diagnosis may be confirmed by genetic or molecular tests, but is not based solely

on the administration of such tests. Thus, even in the case of relatively common chromosomal and single-gene disorders, 'traditional' skills of clinical observation remain central to diagnostic processes. This is also true of common diseases such as breast cancer and heart disease, which are multifactorial (have many causes) and are polygenic (influenced by many genes).

Such a conclusion may be unsurprising to clinical geneticists, who are physicians trained to employ established techniques of clinical practice and to exercise clinical judgment in their diagnostic work. But it may be more surprising for social scientists to learn of the comparatively limited impact of molecular genetics on diagnostic processes, given the impact of molecular technologies upon many areas of basic genetics research, and given the press attention accorded to the medical potential of such research, in the development of new drugs, gene therapy, and so on.

It serves, perhaps, as a reminder that, in addition to the structural constraints of funding and access to research, "the most powerful restraint on the revival of eugenics has been nature itself": single-gene disorders explain "only a small fraction of human traits, disorders and diseases" (Kevles, 1985, p. 296), and most human characteristics are polygenic and their genetic components remain poorly understood, despite the considerable efforts of basic genetics research.

We have demonstrated here that, at least with respect to rare genetic disorders involving dysmorphic features, traditional observational clinical skills remain central to diagnosis, and clinical judgment is exercised in relation to the interpretation of genetic test results. We suggest that further research is needed to examine how requests for particular investigations are negotiated clinically and adjudicated by senior clinicians across a range of different institutional settings. Our conclusions at this stage are that the use of genetic tests is shaped in relation to principles of clinical practice and judgment, to clinically established criteria for requesting investigations, and to the constraints of auditing and budgets. Molecular tests have been put to work within the social structure of a clinical hierarchy with established methods of observation, investigation and decision making, and their use must be understood with reference to these processes.

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