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HISTORICAL & PERSONAL PERSPECTIVES

Paul Polani and the development of medical genetics

Peter S. Harper

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Abstract Paul Polani (1914–2006) was one of the key figures internationally in the beginnings and development of medical genetics. Best remembered scientifically for his highly original work on the basis of human sex chromosome disorders, notably Turner syndrome, he pioneered the application of basic biological research to clinical genetic problems. The unit that he founded in 1960, at Guys Hospital, London, provided an unparalleled model for combined research and service in medical genetics across a wide range of laboratory areas and helped to establish medical genetics as a specific discipline.

Introduction

With the death of Paul Polani on 6 February 2006, at the age of 92, the field of medical genetics has lost not only one of its founders, but one who did more to influence its development, especially in Europe, than almost anyone else. A number of obituaries have been written (Adinolfi and Alberman 2006; Crolla 2006; Harper 2006) but, understandably, these are unable to provide more than the shortest outline of his scientific work and influence. This article therefore covers his life only briefly, while concentrating on the scientific aspects of his work, particularly in the context of the overall development of medical genetics. The perspective I give here is inevitably a personal one, but sources are given at the end, as it is likely that other accounts will be written.

P. S. Harper (✉)
Institute of Medical Genetics, Cardiff University,
Heath Park, CF14 4XN Cardiff, UK
e-mail: HarperPS@cardiff.ac.uk

Paul Polani's life

Paul Polani was born on 1 January 1914 in Trieste, at that time part of the Austro-Hungarian empire, before it eventually became part of Italy. He already had become interested in genetics while at school, and this was further stimulated when he went to the University of Siena, by the influence of the biologist Umberto d'Ancona. His medical studies, including a research thesis on neurophysiology, were completed at the University of Pisa, but the possibility of a medical academic career in Italy was made unlikely for him by the growing dominance of the fascist regime, as he had refused to join the party, so in 1939 he came to Britain, which fortunately recognised Italian medical degrees, in the hope of receiving postgraduate training.

This hope was dashed by the outbreak of World War II, and on Italy's entry to this he, along with other Italian nationals, was interned on the Isle of Man, narrowly avoiding transportation to Canada on the *Arandora Star*, which was torpedoed en route, causing heavy loss of life among the Italian–British community. Instead, he was sent as a locum doctor to the Evelina Children's Hospital, in London's East End, where he was the only resident medical officer throughout the war.

He was fortunate that the visiting paediatricians from nearby Guy's Hospital noticed his ability, encouraged him to take the British postgraduate exams, and, in 1948, gave him a research fellowship at

Fig. 1 Photographs of Paul Polani: **a** in 1975, in Cameron House, Guy's Hospital, initial home of the Paediatric Research Unit; **b** in 1978, in the new Guy's Tower building; **c** in 1980, portrait by Leon Kelberman. Photographs reproduced by the kind permission of Professor Ellen Solomon and the Paediatric Research Unit

Guy's Hospital to investigate first cerebral palsy and then congenital heart disease. This allowed him, as described later, to develop his research skills and also to resume his interest in genetics by forging links with Lionel Penrose at the Galton Laboratory.

Polani remained at Guy's Hospital for the rest of his career, indeed for the rest of his life, for he kept close links and warm friendships with colleagues there throughout his long retirement of 25 years. After a series of research posts in the Guys Hospital paediatric department, he became head of the National Spastics Society's small research unit there, then spent a period in 1958 seconded to the World Health Organisation to co-ordinate a multicentre study of pregnancy wastage, and finally, in October 1960, was appointed director of the new Paediatric Research Unit, giving him the opportunity, as will be told in more detail, to create the first comprehensive medical genetics centre in Britain (Fig. 1).

Paul Polani not only encouraged his colleagues at this unit to achieve outstanding success, but also inspired great loyalty and personal affection from all grades of staff. Yet he was able to do this in a self-effacing way that ensured a smooth transition when he retired in 1982. His successor, Martin Bobrow, has noted that the structure of the unit was working so well at this time that he had to change almost nothing; and also, even more unusually, that having requested Polani to stay on for a transitional period (Bobrow was moving from Amsterdam), he never had the slightest difficulty with such an arrangement (Bobrow 2004). This surely must be an exceptional tribute to an outgoing head of department!

Paul Polani's bibliography illustrates how active he remained in retirement; not only are there valuable reviews of his own particular research areas (Polani 1985, 1996a) and of the early development of medical genetics generally (Polani 1996b, 1997), but also original work, particularly that on meiosis with John Crolla (Polani et al. 1979a, 1989). When I interviewed him at home, shortly before his 90th birthday, numerous recent textbooks and journals had to be cleared from the table to make room for the recorder. His 90th birthday was an occasion for celebration by his Guy's friends, with a notable address given by former colleague Hamerton (2004) (who himself died within a few days of Polani). His final and much enjoyed task was to open the new genetics laboratories at Guy's Hospital, just before his brief final illness.

Outside science, Paul Polani was a person of great culture, enjoying modern and classical literature, especially poetry, in several languages; his wife Nina was originally a professional musician and they also shared a love of horse riding. Her death in 1999, after a progressive neurological illness, left Paul lonely (they had no children), but welcoming all the more the links with Guy's Hospital and his contacts with visitors.

Early research

Although Polani's university education in Italy had included a period of research, he had no opportunity for using these skills during the next decade. Only in 1948, already aged 34, did his appointment to the research fellowship at Guy's Hospital allow him time and facilities to develop his research interests. The topic of cerebral palsy, in particular that resulting from kernicterus due to rhesus haemolytic disease, then a common problem in premature infants, set a pattern for the central theme of developmental disorder which would remain the basis of his life's work. His initial papers on this topic (Evans and Polani 1950; Polani 1954) show already how he would use both clinically based observations and experimental animal studies in tandem to approach a problem.

But Polani's early interest in genetics remained undimmed; in 1945 Lionel Penrose had been appointed to the Galton Chair of Eugenics (Penrose had it renamed as Human Genetics) at University College, London, and his unit rapidly became the world centre for work in this newly developing field. Polani's research fellowship gave him the spare time to become loosely affiliated with the Galton Laboratory over the next few years and to develop his knowledge of human genetics, though I suspect that in the details of this he was largely self-taught. As he noted in the 2002 interview:

> In practice I spent all my spare time at the Galton, shall we say 'sitting at his feet' if you like, but I mean you had to do that because Penrose was not a man who was given to a great deal of effusion, so you had to pick pearls as they dropped out of his mouth (Recorded interview with Harper 2006).

In 1950 Polani began a major study of the aetiology of congenital heart disease with Maurice Campbell, an outstanding cardiologist, whose Guy's Hospital Unit was closely linked with that of Helen Taussig in Baltimore. This gave full scope for a modern genetic approach and Polani used it to the full. Penrose's influence can be seen not only in the detail of the study, systematically recording consanguinity, maternal and paternal age, familial occurrence and associated abnormalities, but also in the fact that the initial and principal paper (Polani and Campbell 1955) was published in *Annals of Human Genetics*, edited by him. This general paper and subsequent ones in *Lancet* and *British Heart Journal* on specific heart defects (Campbell and Polani 1961a, b) are characterised by meticulous and detailed tabular recording of the full data. Again Penrose's influence can be seen here; when asked about reviewing papers, Penrose is said to have replied that he never looked at the text, just at the tables (I regret that I have been unable to confirm which former colleague of Penrose gave me this insightful information).

One element of this study proved to be the foundation for Polani's most original research finding—the chromosomal basis of Turner syndrome. In his overall series of congenital heart disease he had found, as previously known, that one defect, coarctation of the aorta, had a predominantly male occurrence, yet two of four female patients also had features of Turner syndrome, with ovarian agenesis. Puzzling over the possible reasons for this, Polani wondered if Turner patients might be sex reversed genetic males, analogous to the rabbits castrated in utero produced experimentally by Jost (1947).

Fortunately a way of testing this had become available through nuclear sexing, using the sex chromatin body discovered in 1949 by Barr and Bertram (1949). Polani practiced this technique and then, not entirely confident of his own accuracy, enlisted the help of Bernard Lennox, pathologist at Guy's Hospital, and provided some Turner samples (blind) for the unsuspecting Lennox to analyse.

> I collected, I think three or four bits of skin, sent them to Lennox and said, 'would you please tell me what you think about nuclear sexing of these bits of skin'; and time went by and nothing happened. So one day I rang him up and said, 'what have you done? What have you made out of those specimens?' He said, 'they are not very interesting, just ordinary males.' Exactly what I wanted! (Recorded interview with Harper 2006)

The findings were published in 1954 in *Lancet* (Polani et al. 1954) and matters might easily have been left at this point, but Polani was not satisfied that Turner patients were necessarily XY males.

> I started thinking really more seriously and I said, right, what is the evidence that they are males? Because we knew that we were testing only for the X through Barr body testing. And I just wondered whether they might be XO. In order to confirm that they had only one X chromosome at any rate, irrespective of whether the other one was missing or was a Y, I thought about using some genetic marker on

> the X; haemophilia was one which would be too rare to use, but colour blindness seemed to be OK; and when I discussed it with Penrose he said, 'oh yes, colour blindness would be fine, because its frequency is about seven per cent for males and 0.5 per cent for females, so you would be all right if you have enough patients'. So I got my 25 patients and out of those 25, three were colour blind. And there was a nice story there, a personal story attached to it, because I turned out to be colour blind myself, which I didn't know (Recorded interview with Harper 2006).

The finding of a male frequency of colour blindness certainly confirmed that Turner patients had only one X-chromosome, but it did not resolve the issue of whether or not they had a Y-chromosome. Polani's idea that they might be XO was completely against the accepted mechanisms of sex determination, which presumed that mammals were like Drosophila, in which the Y-chromosome plays no role in this. His raising of the possibility in the 1956 colour blindness paper (Polani et al. 1956) met with the strong disapproval of both Penrose and Lancet.

> Penrose would not have it. Penrose would not have it, I have to say. He was annoyed with me. He said 'Where do you get this stupid idea?' and I said 'well yes Professor Penrose, but see, the figures would suggest that there is something'. Well anyway, when I sent my paper into the Lancet in 1956 I had the audacity not only of suggesting that they might be XO sex, but also writing that, if they were indeed XO this would be unlike what happens in Drosophila. So perhaps sex determination in man was not correctly interpreted. And the Lancet wouldn't have this bit. [PSH: Do you think that Lancet might have got Penrose's views?] They certainly got some views and I know that they were quite determined for me to alter this bit, because the editor then rang up Phillip Evans, whose friend he was, and he knew that I was working for Phillip Evans, and said 'no, we can't have that sort of thing. Get him to modify it. Take it all out'. And I said 'no. I'm not going to take out the XO sex story' (Recorded interview with Harper 2006).

Polani's comment, possibly a little more cautious, indeed remained in the *Lancet* paper, but by now it was clear that only full chromosome analysis, just becoming possible with new techniques, would resolve the situation. Polani had already tried to analyse human chromosomes, with his colleague Gordon Thomas, in 1954, having little success, and after failing to interest others in London, he was able to persuade Charles Ford, then studying radiation effects on mammalian chromosomes at the Harwell Medical Research Council Unit, to collaborate, using the newly developed bone-marrow culture technique. This immediately confirmed that Turner patients were indeed XO, thereby completely vindicating Polani's unorthodox ideas on mammalian sex determination. The results appeared simultaneously in early 1959 (Ford et al. 1959a) with the work of Lejeune and colleagues showing trisomy 21 in Down's syndrome (Lejeune et al. 1959), and Jacobs and Strong's finding of an XXY basis for Klinefelter syndrome (Jacobs and Strong 1959). Polani had also been studying Klinefelter syndrome (Polani et al. 1958) and a sample sent to Ford proved to be an XXY/XX mosaic, published later in the same year (Ford et al. 1959b), the first example of human chromosomal mosaicism.

Polani's early Turner syndrome research is an outstanding example of how a clinical scientist can also contribute to fundamental biological advances; in his own case it also shows recognition of his own limitations of technique, and his ability to persuade others with the necessary skills to collaborate; he would develop this ability more fully with the founding of the Guy's Paediatric Research Unit.

The transition from this early work to what can be considered the established phase of Paul Polani's research is marked by the discovery of translocation Down's syndrome. Already, in 1958, he had planned to include Down's syndrome in the cytogenetic collaboration with Charles Ford, but Lejeune's discovery of trisomy 21 caused a switch to concentrating on those Down's children born to younger mothers, already identified as a special group by Penrose. The 1960 report of a 10-year-old Down's girl with 46 chromosomes (Polani et al. 1960) was followed later in this year by the analysis of translocation in a three generation family, also containing balanced translocation carriers (Carter et al. 1960), and showing for the first time the usefulness of chromosome analysis for genetic counselling.

In the short interval between these two 1960 publications on Down's syndrome, major changes had occurred for Polani. He had recruited John Hamerton as cytogeneticist (originally trained by Charles Ford) and so now had a chromosome laboratory directly available on site, rather than being dependent on others; he had also been appointed in October 1960 as director of the new Paediatric Research Unit at Guy's Hospital, with the specific remit of developing medical genetics research on a broad front in relation to the prevention of developmental disorders. It is understandable that both Penrose (with no cytogenetics facility until 1960) and Ford (isolated at Harwell from clinical links) should have felt some chagrin in seeing this previously junior colleague becoming fully independent and successfully established; had the natures of all three been less generous, differences might have become more marked.

Looking back at this first decade (1950–1960) of research, there can be no doubt that it contains Paul Polani's most unique discoveries. Certainly, when in my 2002 interview (Recorded interview with Harper 2006), I asked him which he himself considered were his most important contributions, he named the Turner research first, and then also the translocation Down's discovery. The work on Turner's syndrome in particular represents a clearly thought out progression, from initial clinical observation, through experimental verification, to a hypothesis of general biological importance, ending in its definitive confirmation. The fact that he did not personally undertake the final chromosome analysis in no way diminishes this.

Later research

The creation of the Paediatric Research Unit (see below) did not in any way diminish Polani's commitment to his personal research interests. Once the initial burst of activity on the identification of new chromosome disorders had subsided, these activities again became more biological, with two in particular remaining lifelong interests, X-chromosome biology and the underlying mechanisms of meiosis.

X-chromosome research in the 1960s had been greatly stimulated by the fundamental work of Ohno on X-chromosome evolution and of Lyon on X-inactivation; Polani was able to bring his resource of cell lines with rearrangements of the X together with genetic linkage, sex chromatin analysis and autoradiographic approaches, to bear on these problems. A notable example is given by his 1970 *Nature* paper on the localisation of the Xg blood group and its inactivation status in structurally abnormal chromosomes (Polani et al. 1970), which combines the testing of clear hypotheses with presentation of detailed tabular data on each individual studied.

In the field of meiosis, he was again interested primarily in discovering the basic mechanisms, highly relevant to the occurrence of non-disjunction and other forms of chromosome abnormality, including the effects of maternal age. Again this research, first with Georgiana Jagiello (Jagiello and Polani 1969; Polani and Jagiello 1976), later with John Crolla (Polani et al. 1979a, 1981; Polani and Crolla 1991), involved highly sophisticated techniques, such as the study of chiasmata at successive stages of human meiosis and the use of ovarian transplantation in mice to test the 'production line hypothesis' under which the earliest formed ova are also those first to be ovulated. As has already been noted, this last field was one in which he continued active research well after his retirement. Indeed it can be considered remarkable that a high proportion of his significant research was undertaken after the age of 40, when the activity and originality of many research workers is starting to decline.

As leader, from 1960, of a large research unit containing other senior staff, there were inevitably areas of work where Polani was not directly involved, but which were nevertheless of special interest to him. The development of prenatal diagnosis was one of these, while another was research into the basis and prevention of neural tube defects, where work in his unit included experimental studies of the 'curly-tail' mouse model (Embury et al. 1979; Seller et al. 1979), prenatal diagnosis, and prevention by preconceptional vitamins (Seller et al. 1981; Wald and Polani 1984). His most important role in these areas was perhaps to help bridge the work of the specific groups involved. During this time, he also provided laboratory space for a young postdoctoral worker Andy Copp, who had recently completed a PhD in Oxford and had been accepted as a medical undergraduate at Guy's Hospital Medical School. Paul Polani provided essential support and encouragement for Copp's pioneering work on primordial germ cell migration in the mouse (Copp et al. 1986) as well as for establishing the in vitro model for studying neuropore closure in the curly tail mouse (Copp et al. 1982), which was to become a strong focus of his future research interests.

A broader role in the development of medical genetics

Human genetics, as a specific scientific field, can be considered as having begun almost immediately after the end of World War II. Medical applications, though, were at this time minimal, while the abuses of eugenics had made both scientists and clinicians realise that efforts had to be put into the development of the basic science of the field before there could be any hope of fruitful applications. An impetus was given, both in America and Europe, by the genetic risks posed from human radiation, as a result of the atomic bomb explosions and subsequent nuclear testing. In the UK, the Medical Research Council established units at both

Harwell and Edinburgh, which developed strong research programmes in radiation genetics, later with a notable emphasis on cytogenetics. Penrose's appointment as head of the London Galton Laboratory provided, as already noted, a focus for broad-based human genetics research, especially that with a theoretical and quantitative basis.

Until 1960, though, the UK had no centre that could be considered to focus on medical genetics, as opposed to basic human genetics research. The small MRC unit of John Fraser Roberts and Cedric Carter at the London Institute of Child Health had no laboratory facilities to back its family studies, while the Galton Laboratory was (and remained under Penrose's successors) largely non-clinical. Perhaps the closest in aim, if not in outcome, was the Oxford MRC Population Genetics Research Unit under Alan Stevenson.

The establishment of the Paediatric Research Unit in 1960 was therefore a major innovation, both for the UK and worldwide. Despite the general nature of its name, its remit was specifically to undertake research in development using genetic approaches, and its blueprint was drawn up by Paul Polani himself. With hindsight it seems truly remarkable that it should have been created and funded by a relatively small children's charity, involved with cerebral palsy (the then National Spastics Society), without government aid, and even more that it should have been planned as a broad-based research institute without immediate commitments to clinical application. There is no doubt that the society's trustees and their research advisory committee would not have backed such a major venture had not Paul Polani already been established in research at Guy's Hospital and available to be director. But it also shows their remarkable prescience in recognising the talent and potential of someone who had never been part of the British medical or scientific establishment.

An important factor must have been not just Polani's own research but his international links and reputation, initially with formed with America through his congenital heart disease study, but strongly developed with both USA and Scandinavia as a result of his 1958 secondment to the World Health Organisation. Some of the background to the establishment of the unit is given in the 'Festschrift' volume on Polani's retirement in 1982 (Adinolfi et al. 1982; Evans 1982; Smith 1982), but whatever doubts there may have been over the scale of the venture and a relatively untested director, Polani's achievements rapidly set them to rest.

The initial structure of the unit, as set up in 1960, consisted of five research groups, each led by a senior scientist; these were cytogenetics, biochemical genetics, experimental biology in relation to development, developmental immunology and clinical genetics with genetic counselling. An already existing group working on the epidemiology of malformations was also linked in. The key to success in such a broad initiative was to attract able senior staff to lead the groups; here Polani was outstandingly successful, as he was in the difficult task of encouraging independence while retaining contact and ensuring a unified approach for the unit as a whole. He could also be opportunistic, attracting as clinicians both John Fraser Roberts on his retirement from the MRC, and Caroline Berry, whose family commitments initially necessitated that she worked part time, not then a usual practice.

A key element to the unit from the beginning was the provision of strong support services, notably an outstanding library, animal facilities and good administrative staff. Initially the unit was housed in temporary accommodation, but this allowed detailed planning for the later definitive facility in the newly constructed Guy's tower block.

Despite the remarkably generous funding for the unit (£2 million in 1960 represents at least ten times that amount almost 50 years later), it was clear from the outset that substantial extra funds would be needed if it were to be sustained and to grow. Here the ability of senior research staff to attract research council and other funding was complemented by Polani's own entrepreneurial talent in interesting individual and corporate sponsors, long before this became a generally accepted activity. This was the origin of the *Generation Trust*, which provided major funding for the Unit over a long period. Also of particular importance was the transfer of areas that were initiated as research into diagnostic services that could be funded by the rapidly developing National Health Service. This close linkage of research with service was to become a model for medical genetics units generally, but especially in the UK, and it represents the next key element of Paul Polani's legacy to medical genetics.

Medical genetics services

While human genetics in 1950 could not claim any significant applications of medical value, apart from a limited scope for genetic counselling, the situation had changed radically by 1960, largely as the result of the possibility of diagnostic chromosome analysis. Most existing cytogenetics laboratories, though, were neither interested in nor set up for such diagnostic work, nor did human cytogenetics have a high academic profile in the few medical genetics departments already established around the world.

Polani's attraction of John Hamerton in 1960 to head the new Paediatric Research Unit cytogenetics laboratory allowed service funding to support the increasing volume of diagnostic work while at the same time providing a large flow of material, which could identify new chromosome anomalies. It also permitted their epidemiological study in spontaneous abortions and later in prenatal diagnosis, an area in which Polani took a particular and continuing interest. This laboratory activity at the same time increased the demand for expert genetic counselling and syndrome diagnosis that would form much of the basis for the new field of clinical genetics. Links with clinicians were strengthened by providing clinical genetic services not just in central London but also in the south east region of England, linked administratively with Guy's Hospital. Again, this regional approach was to become one of the hallmarks, and strengths, of UK Medical Genetics generally. Polani documented the clinical genetics service activities of his unit over its first 16 years in 1979 (Polani et al. 1979b).

Parallel to, though somewhat later than cytogenetic diagnosis, was that of biochemical genetics, where specialist health service funding was used to provide a supra-regional service for rare enzyme defects, including their prenatal diagnosis. Finally the same approach was used after Polani's retirement, by his successor Martin Bobrow, to develop diagnostic molecular genetics. Thus Paul Polani was able to see during his lifetime a flourishing and comprehensive medical genetics service established alongside the research institute that had been his primary creation.

This model of closely linked research and services has had a much greater influence than is often recognised. Had Polani's Paediatric Research Unit, and the comparably structured UK units that followed it, (such as those in Glasgow, Manchester and Cardiff), not adopted this integrated approach, it is likely that medical genetics services would have developed in a much more fragmented way, with laboratory genetics, including molecular genetics, becoming attached to general pathology and biochemistry units, clinical genetics perhaps remaining part of paediatrics, and both probably lacking in the strong academic links that have characterised the development of medical genetics over the past 40 years. The UK model has also had a strong influence on developments in many continental European countries and in Canada.

The history of the development of medical genetics services has yet to be fully studied and written, though some beginnings have been made. When interviewing Paul Polani I was keen to see if he could identify key individuals in the Department of Health and elsewhere who had been especially influential in promoting policies and service developments in this field, but he was unable to name any such person. Rather it would seem that he and a small number of others were alert to the possibilities, and able to attract health service funds by the initiatives which they had already set up, and which were clearly likely to be of clinical value; their own enthusiasm and persistence also being a strong factor.

Other influences

Although the primary factors underlying Paul Polani's profound influence on the development of medical genetics were, as already noted, the originality and importance of his own research, his creation of the first definitive medical genetics institute in Britain, and his commitment to the parallel development of genetics services, his influence extended beyond these. A glance at his curriculum vitae shows the range of medical and scientific bodies, committees and working groups of which he formed part (MRC Subcommittee to Review Clinical Genetics 1978; Polani et al. 1979c), especially during the period 1965–1980, when medical genetics was developing rapidly across Britain. It is perhaps characteristic of UK medical genetics, as well as of Polani's quiet and collegiate approach, that, in contrast to some other countries, no single unit attempted to become the dominant centre in terms of either resources or influence, the main leaders rather working together to advance the field as a whole across the country.

One surprising gap when we look at Polani's influence is that he trained very few of the younger clinical geneticists of the next generation, by comparison with the other units of the time, notably that of Cyril Clarke in Liverpool. I suspect that this was mainly due to the fact that substantive training posts in clinical genetics only became available towards the end of his career, and that in the earlier years few paediatricians saw this as a viable career option. Regardless of this, it is unfortunate that few young British clinical geneticists outside the Guys Hospital orbit, in contrast with research scientists, had direct exposure to Polani's thought and enthusiasm through working in his unit.

Polani's international background and continuing links ensured a strong influence on developments across Europe, especially in Italy, despite the problems of medical and scientific funding and research there until more recently. A series of able Italian workers came to study with him in London, several of whom remained permanently, while he received a long series of scientific and medical honours from Italy.

It is worth asking who were the main influences on Polani himself? I greatly regret that I did not directly ask him this myself during my interviews with him, but it is clear that he owed much in a general way to his early mentor in biology Umberto d'Ancona, and notably to Lionel Penrose for his inspiration in human genetics. I suspect, however, that his own vision for medical genetics was largely self-inspired, just as it was self-realised, without any clear model from elsewhere to act as a basis. In fact no such model existed at the time; Penrose's Galton Laboratory, despite the genius of Penrose himself, was in no sense a practical model to emulate, while elsewhere in Europe, notably in Scandinavia and later Germany, most institutes were related to basic human genetics. The closest in spirit was perhaps that of Maurice Lamy in Paris, which was also strongly paediatric in its orientation, as was that of Clarke Fraser in Montreal, contrasting with the adult genetic disorder focus of the other two early American units of Victor McKusick in Baltimore and Arno Motulsky in Seattle.

Conclusion

Paul Polani's life and career spanned the entirety of the first half century of medical genetics, and the centre that he created at Guy's Hospital, London, stands as a rare example of a wide ranging vision for a new field that was actually turned into reality. Medical genetics has now long passed the time when a single individual, however able, could be responsible for such an achievement; Polani's recognition of this, with the broad structure of his unit, and its embedding in UK and international medical genetics, ensured that his creation would last and prosper. This, together with his own fundamental research and his wider contributions to the field, give him a lasting place among the small numbers of key founders of what has become, 50 years on, a central part of both modern medicine and scientific research.

Sources

Paul Polani wrote a series of unpublished documents, updated in 2003, to cover his life, family background, establishment of the Paediatric Research Unit, and his discoveries around the year 1959, along with a full bibliography. He kindly made these available to me when I did a recorded interview in November 2002 (Recorded interview with Harper 2006). Two earlier recorded interviews have also been made (Videotape 1987; Audiotape 1992). Some biographical material also appears in the 1982 'Festschrift' volume.

His extensive personal library of scientific books is now housed partly at the Polani Research Library, Guy's Hospital, and also as part of the Human Genetics Historical Library at Cardiff University. A catalogue is available from Lesley Exton at the Paediatric Research Unit, (*lesley.exton@genetics.kcl.ac.uk*) and details are also on the Genetics and Medicine Historical Network website (*genmedhist.info*). The listing under Polani's name on *Pubmed* contains most of his published papers in journals but not all reports or book chapters.

Almost no personal scientific correspondence or other unpublished documents seem to have been preserved. Thus if other workers have relevant correspondence, this would be an important addition to the present limited material, which is housed at the Polani Research Library (Contact, Lesley Exton, email as above).

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