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HISTORICAL AND PERSONAL PERSPECTIVES

Fiftieth anniversary of trisomy 21: returning to a discovery

Marthe Gautier · Peter S. Harper

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"In reality, discoveries are due to people at the edge of the formalised groups of researchers"

Pierre Laszlo

Fifty years ago, I was the co-author[1] of the first paper that showed the presence of an additional chromosome (Lejeune et al. 1959) in the syndrome identified by Langdon Down in 1866 and commonly known as "mongolism" in France at the time. This, the first autosomal chromosome aberration recognised in the cells of the human species, was named trisomy 21. I thought it would be of historical interest to bring my own personal testimony as an actor in that discovery.

A historical background

Going back to 1958 involves rediscovering the context and the firmly held beliefs of that period. Although it had been accepted for decades that human beings possessed 48 chromosomes, Tjio and Levan (1956) demonstrated in 1956 that there were in fact only 46. This did not affect many people, apart from a few geneticists, and for a long time 48 was still the figure taught in schools. This stage, which seemed simple, was followed by other more important stages that brought us closer to finding the origins of life; however, this did not create such a stir in the media as the launch of the first artificial satellite Sputnik (meaning "fellow traveller" in Russian) a few months later, which drew us closer to finding the origins of the universe. Science advances on different levels, depending on the disciplines.

It had been necessary to wait 30 years before the genetic laws of peas, as observed by Johan Mendel or 'Brother Gregor' of the Augustinian Monastery of Brno, was recognised by biologists. Soon after this, Nettie Stevens revealed the existence of sex chromosomes in a certain species of beetle (Gilgenkrantz 2008). In about 1910, Morgan's work on *Drosophila*, the providential fruit fly with its amazingly fast reproduction rate and giant chromosomes, laid the first foundations of cytogenetics (Morgan et al. 1925). Had it not been for the attitudes of Alexis Carrel (1912 Nobel Prize winner) during the Occupation (Gilgenkrantz and Rivera 2003), his cell culture experiments would have been widely used. However, a long sequence of errors and failures discouraged the researchers. And it was not until 1949, and then only on cat neuronal cells, that Barr and Bertram (1949) discovered the existence of a body only in the female nucleus; this in fact proved to be a general phenomenon that indicated the presence of two X-chromosomes. The cytological explanation for this (lyonisation) fell to Lyon (1961). Simple swabs of the mucous membrane in the mouth then allowed inter-sexual states to be diagnosed.

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M. Gautier
6 Rue de Douai, 75009 Paris, France
e-mail: marthe.gautier@free.fr

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

[1] By a slip of the pen that I dare not interpret, my name was wrongly entered as "Marie Gauthier". The error was corrected in subsequent publications.

The discovery of trisomy 21, as I lived through it…

The beginnings

I arrived in Paris in 1942, in the middle of the war, to stay with my elder sister Paulette, an intern at the Gustave Roussy Institute nearing the end of her medical studies. She introduced me to the mysteries of the student world, and warned me: "If you're a woman, and you're not the boss's daughter, you have to be twice as good to succeed". I started on a PCB (first medical degree): easy enough. In 1944, Paulette was killed by the Germans in a showdown at the time of the Liberation. For my grieving parents I, from that moment on, had to be both her and myself: not at all easy. I aimed at the competitions that opened the doors. After my medical clerkship, I was awarded an IHP, an internship at the Paris Hospitals, a post often sought after but rarely gained by women (no woman actually got one until 1885). In my promotion, out of 80 appointed interns, there were only two girls.

After 4 years of wonderful clinical apprenticeship in paediatrics, one of my tutors, Prof. R. Debré, the father of paediatrics, put me forward for a 1-year scholarship at Harvard, offered by a patron who had just founded the SESERAC.[2] The subject was child cardiology with the following aims. (1) Eradicating Bouillaud's Disease (also known as acute rheumatic fever) with penicillin and treating sometimes fatal cases of carditis with cortisone, still scarce in France. I dedicated my thesis to the clinical and anatomopathological study of the lethal forms of this disease caused by attacks of beta-haemolytic streptococcus A, an organism that was still very sensitive to low doses of penicillin, which did not arrive in Europe until a late stage, after the war. (2) Creating a department for the diagnosis and surgical treatment of congenital heart conditions in newborns and infants. These were new and fascinating perspectives: learning in order to provide better care and recovery for children…

After some hesitation, I agreed, not without reluctance, to leave family, friends and love for a year, without being able to see them or even telephone (too expensive then). However, my mind was made up, and in September 1955, I took a tearful train journey from Paris to Le Havre and a cabin on the Cunard line's *Mauritania* (air travel was much too expensive for mere scholarship holders). By chance, two IHP colleagues from the Robert Debré School, paediatricians Jean Aicardi and Jacques Couvreur,[3] Fulbright scholarship holders, were also on the voyage and also based in Boston. We were the first IHPs to benefit from a scholarship to study in the United States. After 5 days at sea and a slight storm, we sailed in slowly at crack of dawn. The propellers gently fell silent. The skyscrapers of Manhattan stood out stark against a gloriously blue sky. We were the guests of Uncle Sam. Although not exactly bilingual, we were not "immigrants without papers"; we had a 1-year visa.

"As a pilgrim" I am in Boston

I had 24 hours to find a shared apartment and buy a bed, chair and table at the local flea markets. Prof. David Rutstein had put together a perfect programme: with Prof. Alexander Nadas, pioneer in the diagnosis of congenital cardiopathy before surgery and with Prof. Benedict Massell, responsible for acute rheumatic fever (ARF). I was also to visit several centres that specialised in ARF: Cleveland, Chicago, San Francisco, Seattle, New Orleans and Washington. The dose of cortisone to be prescribed, and the duration of treatment, was in fact far from being agreed upon. People were also asking whether this "miracle" drug could prevent the onset of heart conditions. The heads of each centre shared their experience and opinions with me, and I learned a great deal, even from the differences. Travelling alone on Greyhound buses (more than ten nights to save on hotel bills) was a brave step; but buses were miles better than planes for appreciating the landscape.

I was given another "job" that I knew nothing about, working as a technician in the cell culture laboratory with fragments of aorta. This was a plus: I worked part time, as I chose, on Sunday if it suited. Who would not want that? A delightful lady technician taught me everything there was to know about cell culture, and even taught me American slang. Everything was at my fingertips in the freezer. I came to know how to examine cultures under the microscope, photograph them and develop the photographs. I compiled dossiers for biochemists working on comparative studies of cholesterol levels in child and adult fibroblasts. I replaced the laboratory manager who was on maternity leave. I spent hours in the great library on the upper floor. I explored the various techniques of cell culture, and recent cardiology data. But at the time, I was not asked any questions on genetics.

[2] One of his children had just died from Bouillaud's Disease because of a lack of cortisone in France and he had founded the Society of Study and Care for Children with Acute Rheumatic Fever and Congenital Cardiopathy.

[3] Jean Aicardi went on to pursue a brilliant national and international career establishing child neurology, and one syndrome is named after him. Jacques Couvreur, meanwhile, divided his life between hospitals and private clients and was the national reference point for the treatment of congenital toxoplasmosis.

The library was a place for meetings and exchanges. We French were seen as natives of a country that always needed help with ending its wars and which at the time was meddling in Algeria! Ever since then, I have pleaded for and defended all the immigrants of the world.

My visa finally expired and I returned on the *Flanders*. I honoured my debt to my patron, coming back full of enthusiasm and plans. I arrived early in the morning at Le Havre. They were waiting for me on the quay… And in Paris, it was time to come down to earth.

New décor

The post of head of clinic with Prof. M. Lelong, promised before my departure, had been given to a colleague in my absence. The only posts available were at the Hôpital Trousseau, with Prof. R. Turpin, with whom I had never been a trainee, extern or intern. We did not know each other; I was not a pupil of his house! With my friend Jean Aicardi, who also returned from Boston, there we were as "heads" (chef de clinique) in September 1956 (Fig. 1). The clinic offered a poorly paid part time teaching post, but I needed it to become an assistant and eventually an established paediatrician. The atmosphere was like a hospital department, with its typically French rigid hierarchy, and the supervisor was a very distant and laconic figure. What a contrast to the laid-back atmosphere in the United States! But you have to "work with" before you can flourish and advance in life.

As experienced paediatricians, we knew that this supervisor was interested in malformations, and attempting to draw a distinction between innate and acquired. In 1937, he had mentioned that mongolism might be due to a chromosome abnormality similar to that of the Bar mutation in the fruit fly (Turpin et al. 1937). He was not the first or the only one to put forward this hypothesis, but he had gone no further at that time. He turned to fingerprint patterns, for the want of anything better, in his research into the hereditary nature of mongolism. In 1950, in London, Penrose (1950) leaned more towards a triploidy than a trisomy or monosomy. He had the chance to obtain a testicular specimen, from a patient, which he gave to Ursula Mittwoch. The technique and results were uncertain; she concluded that the cells had "47 or 48 chromosomes" at a time when the normal number for a human was estimated at 48. However, at least triploidy was excluded.

Fig. 1 Professor Turpin's Department in 1957. *First row: first on left*, Marthe Gautier, *third*, Jacques Lafourcade, *fifth*, Professor Raymond Turpin. *Second row*, *first on left*, Jean Aicardi

The turning point

Then, at the 1956 start of the University Year, the Chief, returning from the International Human Genetics Congress in Copenhagen, informed us that the number of chromosomes in the human species was not 48, but "46". He then voiced his regret that there was nowhere in Paris to produce cell cultures to count the number of chromosomes in Mongolism. I was greatly surprised at that remark and, armed with my American experience, offered to "do what I could, if I was given some premises". I knew that I had to act quickly, without getting it wrong, and succeed at the first attempt, because the international teams were already in competition, or about to be, with the rivalry found in the field of research just as elsewhere. I entered the Sorbonne to study for a Cellular Biology Certificate. I realised that I should not count on the support of the research organisations, as France had not yet recovered fully from the war, especially in the restructuring of the INH.[4] Ultimately, science and politics only go together well when there is money, which was not the case here. The role of the university was one of clinical teaching; it was not equipped for cutting-edge research. The elite of the hospitals did not yet realise that the initiative had to come from them.

I finally found premises, in the form of an empty former laboratory with three magnificent pieces of furniture: a refrigerator, a centrifuge and an empty cupboard with a low-definition microscope. Water, gas and electricity, and only me to organise everything; it was the stuff of dreams! I was not fortunate enough to be offered any finance, and therefore, at my own expense, I took out a loan to equip myself with glass items, distilled-water apparatus, and so on. None of the products needed for culturing was marketed in France. Determined, however, I did not give up hope. Each week, I prepared the fresh embryo extract, obtained from 11-day fertilised eggs obtained from the Pasteur Institute. For the plasma, I used punctures to take

[4] Although the National Institute of Hygiene was created in 1941, reforms were not made until 1958.

blood from a cockerel that I had purchased, raised in a garden at Trousseau. And the human serum was from me—an economical and reliable procedure. All this has been reported (Lejeune et al. 1960). I had no desire to use foetal lung or bone marrow cells; instead, I used connective tissue explants in which I examined the very young cells in situ, transplanting the explant when I felt it was sufficiently grown. There were never any antibiotics or colchicine, as I feared a possible adverse effect on the integrity of the karyotype. And there were no subcultures after trypsin treatment, to prevent anomalies occurring in vitro through transformed cells. I believe that to be essential to avoid any form of artefact, such as erratic or induced chromosome changes. There was a need for proof of initiative, imagination and discernment in case of failure.

Finally, with adaptations, I used the principle of hypotonic medium that had produced the results for Tjio and Levan (1956), but using a serum base in order not to break the cell membrane, and finally allowing the slides to dry before staining them (Rothfels and Siminovitch 1958). Never any squash, as some recommended (Hsu and Pomerat 1953). Thus, my best preparations were in prometaphase, without cell membrane breakage, and so produced an exact figure and beautiful elongated chromosomes, easy to pair and unbroken. These results were not accomplished until after a few failures. I had no bibliography, only my notes taken in Boston. The controls, given to me by the neighbouring surgical department, came from planned surgical procedures on normal children; and they had *46 chromosomes*. I now had two AP (Assistance Publique) technicians who, under my instruction, proved quite remarkable.[5] I passed on my skills and experience to them.

A new arrival at the laboratory

I do not remember any visits from the Chief at the beginning. On the other hand, his assistant Jacques Lafourcade came to see me, somewhat intrigued and initially sceptical of the adventure's success, especially given the precarious conditions in which it was undertaken. No doubt he reported on how my work was going. However, I soon began receiving regular visits from J. Lejeune. J.L., whom I did not know, was a trainee at the CNRS and a student of the supervisor, as witness their joint publications on fingerprints and the adverse effects of ionising radiation (Turpin and Lejeune 1954; Turpin et al. 1955; Turpin and Lejeune 1955; Turpin et al. 1957). I quickly recognised his interest in the cell cultures, abandoning his magnifying glass and his statistics on the frequency of the median palmar crease.

[5] Mmes Macé & Gavaïni.

At last, some tissue from Mongol children was obtained.[6] In terms of mitosis, the cells of the Mongol children had an unmistakable difference: all had 47 chromosomes, while the controls had 46. My gamble, which was that I would succeed alone with my laboratory workers at my technique and above all discover an anomaly, had paid off. It is a French discovery, something that was not apparent at the start.

The additional chromosome was small, and the laboratory did not have a photomicroscope that would confirm its presence and establish the karyotype. I entrusted the slides to J.L., who had the photos taken but did not show them to me; they were, he said, with the Chief and therefore under lock and key. The chromosome appeared to be number 21, but it was not christened as such until the Denver Conference in 1960.[7]

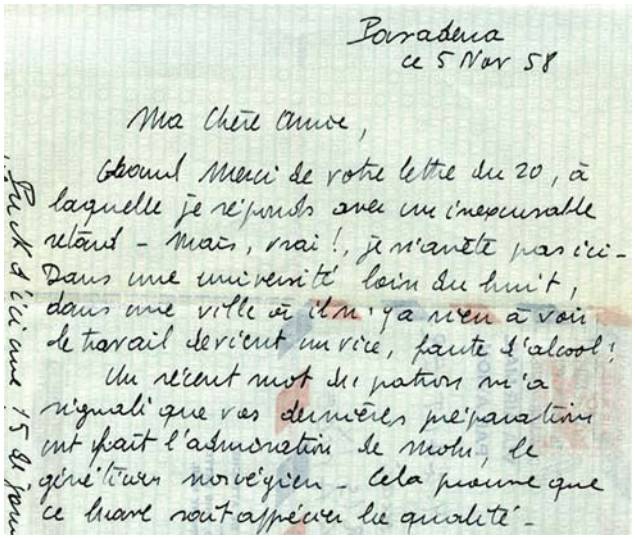
I am aware of what was said on the side, but I did not have enough experience or authority in this medical world, whose mechanisms I did not yet understand, to deal with it. I was too young to know the rules of the game. Kept apart, I had no idea why they did not publish earlier. Only later did I understand that J.L., anxious and inexperienced with cultures, feared an artefact that might wreck his career, which up until then was nothing special, but would have suddenly become glittering had the results been revealed. I suspected political manoeuvring, and I was not wrong. On the other hand, I had no personal intention of "exploiting" this additional chromosome, my professional life was then working towards the clinic.

J.L. was now presenting himself as the discoverer of trisomy 21. Reporting for the CNRS at the Ionising Radiation Congress in Canada, and without planning anything with Turpin or indeed with me, he mentioned the discovery at a McGill seminar in October 1958 as though he were its author. I, however, received this letter dated the month following that when he visited laboratories in the United States (Fig. 2).

At that time, J.L. was brought up to date with the work of Patricia Jacobs, who had just found an additional X-chromosome in Klinefelter's syndrome (Jacobs and Strong 1959; Harper 2006). On his return, we finally published with the Academy of Sciences as a matter of urgency, in order to overtake the Anglo-Saxon teams (Jacobs et al. 1959) rather clumsily, without me being able

[6] I was very busy at the time, with part time work at Hôpital Bicêtre in the CC (congenital cardiopathy) nursery departments, ARF consultations, and the start of my private practice.

[7] It was an irony of cytogenetic history that after the Denver classification of 1960, it was subsequently noted that this chromosome was smaller and therefore corresponded to the 22nd pair, but everything remained in that order in order not to confuse the wealth of literature already available on the subject.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Ma Chère Amie,

Encore Merci de votre lettre du 20, à laquelle je réponds avec un inexcusable retard - Mais, vrai !, je n'arrête pas ici - Dans une université loin de tout, dans une ville où il n'y a rien à voir de travail devient un vice, faute d'alcool ! Un récent mot de Watson m'a signalé que vos dernières préparations ont fait l'admiration de Moh, le généticien norvégien - Cela prouve que ce brave sait apprécier les qualités -

Fig. 2 Photocopy of a letter sent by J.L. during his voyage to the United States. His reference to "your preparations…" refers to the slides that I had obtained with the first 47 chromosome mitoses

to see the photos or be informed about anything. The text was read to me at mid-day one Saturday for presentation on the Monday. This is exceptional in France, as one could, in fact, publish within 3 days in the CRAS (Academy of Sciences reports) in Paris, while a period of 2 months was needed in the international journals. We were therefore the first to publish this discovery in the international scientific world, after talking about it at the McGill Seminar. Contrary to standard practice, J.L. signed first and my name only appears second. As usual, Prof. Turpin, the leader responsible for the initial hypothesis, signed last. I was hurt and suspected a degree of manipulation, having a feeling of being the "forgotten discoverer". J.L. then whipped up a great storm in the media, being interviewed by all the papers. A great French discovery…

J.L. was then showered with all kinds of rewards, being promoted from CNRS trainee to master of research and winning a gold medal. Without going through the university channels, he was subsequently named professor of cytogenetics, a title created by Prof. Turpin for his student. This chair ushered in the age of cytogenetics in France, while the discipline was developed right across the world and the fame of J.L. increased. He was awarded the Kennedy Prize without asking for me to be associated with it. Progressively, through his participation in numerous congresses, he was hailed as the only discoverer and ended up convincing himself of that, to such an extent that Prof. Turpin's descendants kicked up a fuss through their lawyers. In addition, they lodged in the Pasteur Institute's archives their father's articles certifying his seniority in the chromosome-based hypothesis concerning mongolism, which was finally verified. Now, however, "the father of trisomy 21", as he is hailed in the media, was becoming a kind of miracle worker[8] whose efforts at treating trisomy 21 left numerous scientists sceptical for not being based on the credible biochemical mechanisms. Subsequently, and in a very coherent continuity, it became possible to make diagnoses before birth in the late 1960s, and then, in 1975, came the voting of the abortion laws that roused JL, a strong believer, to indignation, polemics and battle cries. The laws sparked serious arguments in society and caused a real split amongst cytogeneticists, some of whom wanted prenatal diagnosis to be practised in France. At that time, as André Boué notes,[9] the Nobel Committee had considered rewarding the discovery of the origins of mongolism. Is it because of the position he adopted that the Nobel Prize was not awarded to Jérôme Lejeune, the only name that the trumpets of fame had sounded?

Epilogue

The first human autosomal anomaly or the first gonosomal anomaly, in Paris or in Edinburgh? These discoveries were made at the same time, as is often the case when certain scientific and technological levels are reached. If I had not been the first, others would have got there. Whatever happened, I have no happy memories of that period, as I felt cheated in every respect. However, in the history of "discoveries", many others have also gone unnoticed, like Johann Friedrich Miescher of Basle or Rosalind Franklin of Great Britain, and that in the field of DNA alone.

Since then, molecular genetics has quickly caught up and overtaken cytogenetics. We now know the physical map of chromosome 21—it has 225 genes, of which only 127 are currently identified—and its sequence, produced in 2000.

Since then also, the respect for women scientists has undoubtedly progressed, as in 2008, the Nobel Prize was awarded not only to Luc Montagnier, but also to Françoise Barré-Sinoussi, for their work on the discovery of the retrovirus responsible for AIDS (Costagliola 2008). There is hope for the future.

Acknowledgments

I would like to thank Joëlle Boué and Simone Gilgenkrantz, who encouraged me to revive these very old memories.

[8] Or at least, one who claims to be a miracle worker.

[9] See interview with André Boué, January 2001. History of INSERM: http://infodoc.inserm.fr/histoire.

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Commentary

Fifty years of human chromosome abnormalities

The fiftieth anniversary of the discovery of the first human chromosome abnormalities marks not only a key point in the development of human cytogenetics and the birth of clinical cytogenetics, but it is also a landmark in medical genetics as a whole, providing laboratory foundations for what had until this time been principally a theoretical area of medicine. The increased demand for genetic counselling and the overall development of medical genetics during the following decades were largely based on these initial discoveries and the technical advances that rapidly followed to make them suitable for use in a medical diagnostic context.

Fifty years on, we have reached the point where human cytogenetics and human molecular genetics have largely fused, so this year, 2009, is an appropriate point for historical perspectives on how these early discoveries were made and how the field developed. Hopefully there will be a number of such articles in both the genetics and the history of medicine and science literature, which will collectively allow this important period to be assessed critically in a way that was not possible at the time of the events.

The accompanying article by Dr Marthe Gautier in this issue of *Human Genetics (*Gautier 2009), translated directly from that written in French and published earlier this year, makes a valuable and unusual contribution to the history of one of the key discoveries—that of trisomy 21 as the chromosomal basis of Down's syndrome. It is valuable as coming directly from the worker most involved in the actual discovery, and unusual in that it brings into the public domain facts concerning the discovery which, while widely recognised in France (Gilgenkrantz and Rivera 2003) are little known internationally, and which will prompt a reassessment of the respective roles and contributions of those involved in the work.

To place this article in context, it is important to recognise that Down's syndrome had been proposed as a possible human chromosome abnormality as long ago as 1932 by both Davenport (1932) and Waardenburg (1932), but establishing or refuting this was prevented by the

limitations of cytogenetic technology and the uncertainty of the normal human chromosome number until the publication of Tjio and Levan (1956), (Harper 2006b), in 1956. Once these obstacles were overcome, multiple groups across Europe (but not initially in America) began the search for chromosome abnormalities in both Down's syndrome and the possible sex chromosome disorders.

By the end of 1958 at least four groups were actively studying Down's syndrome, including those of Marco Fraccaro (then in Uppsala) (Fraccaro 2004), Patricia Jacobs (Edinburgh) (Jacobs 1982), and Paul Polani (London) (Polani 2003) in collaboration with Charles Ford (Harwell). As Gautier makes clear in her paper, the Paris workers were keenly aware of this, and of the greater cytogenetic experience and technical resources of the other groups. In the event, the initial, exceedingly brief, paper on trisomy 21 appeared in the *Comptes Rendus* of the French Academy of Sciences for January 1959 (Lejeune et al. 1959), virtually simultaneously with the two other landmark papers, both on sex chromosome abnormalities, by Jacobs and Strong (on XXY Klinefelter syndrome, January 31) (Jacobs and Strong 1959) and by Ford et al. (on XO Turner syndrome) (Ford et al. 1959). Any attempt to assign priority to one or other of these contributions is meaningless, especially when the minimal peer review process of the French Academy of Sciences is taken into account (Harper 2006a). But there is no doubt that the Paris workers can claim the credit for discovery of the first autosomal chromosome abnormality and it is wise of Gautier to restrict their claim to this.

It is of interest to consider briefly the other initial studies on the chromosomal basis of Down's syndrome that appeared in 1959. That of Patricia Jacobs, with her clinical colleague John Strong appeared in Lancet in April 1959 (Jacobs et al. 1959), while the study of Fraccaro, with Jan Lindsten and Jan Böök, was published in *Acta Paediatrica* in September 1959 (Böök et al. 1959). Polani and Ford did not continue their overall study of Down's syndrome, but rather focused on the group born to younger mothers, leading to their discovery of translocation Down's syndrome, published the following year (Polani et al. 1960). A wider account of this rapid succession of discoveries is given in the author's book, *First Years of Human Chromosomes* (Harper 2006a).

It can be seen from Marthe Gautier's article and from a previous review of early human cytogenetics in France by Simone Gilgenkrantz (Gilgenkrantz and Rivera 2003), that the widely perceived role of Jérôme Lejeune as discoverer of trisomy 21 requires revision, preferably also in the light of other evidence and documentation from those in Paris at the time but not directly involved in the discovery, since neither Lejeune nor Raymond Turpin, head of the department, are still living to give current personal accounts. It is of relevance that Gautier herself has kept silence on the exact circumstances of the discovery for the past 50 years, having subsequently made a distinguished career in paediatric cardiology, not in genetics. In addition to the 50th anniversary, a further factor making this subject a topical one has been the recent initiation by the Roman Catholic Church of proceedings for making Lejeune a saint, a process requiring testimony from those involved.

Regardless of the significance of Lejeune's own contribution to the discovery of trisomy 21, there can be no doubt as to his key role as the leader of the Paris school of human cytogenetics, which over the following decade made a series of major discoveries of human chromosome abnormalities (Lejeune et al. 1963; Lejeune and Lafourcade 1968) and developed important new cytogenetic techniques (Dutrillaux and Lejeune 1971), giving France a world leading role in this field. It is perhaps this for which he should be remembered, rather than for his association with the trisomy 21 discovery.

What general historical conclusions can be drawn from this work and from the reassessments by Gautier and by Gilgenkrantz and Rivera? First, and perhaps most important is the need for close collaboration and mutual respect between clinical research workers and basic scientists involved. The mutual roles of Paul Polani and Charles Ford, and of Patricia Jacobs and John Strong provide examples, in the first instance allowing distinction of translocation Down's syndrome by focusing on those born to younger mothers—none of the early series contained such cases; the Edinburgh study increased the rigour of its series by inviting Lionel Penrose, world authority on Down's syndrome, to examine the patients, resulting in exclusion of a number that would otherwise have been misdiagnosed. The Paris group was perhaps unusual in that all three of the workers were paediatrically trained, but it also ensured its diagnostic accuracy through the long-standing experience of Down's syndrome of Raymond Turpin, head of the Paediatric unit at Hôpital Trousseau.

A powerful impression from Gautier's article is the lack of appreciation or respect for the work of women in science, even in relation to their key discoveries. This certainly seems to have been present strongly in the Paris group, and the situation is reminiscent of that experienced by Rosalind Franklin in relation to the discovery of the structure of DNA (Maddox 2002). In contrast, Patricia Jacobs received both encouragement and full credit for her work, and is specific that she never encountered prejudice as a woman in science, in Edinburgh or elsewhere (Jacobs 2004). Before concluding that the UK record was better than that of France, however, one should remember that Rosalind Franklin received full encouragement and respect while in Paris, only to encounter such prejudice after her return to Britain.

A final lesson to learn is that the initial publications concerning a major scientific discovery may not always contain the full truth, especially when this concerns the relative contributions of those involved. It is salutary to note that it may take 50 years or more for all the necessary facts to come into the public domain, by which time not all the participants are likely to be living. In this respect, the situation for the discovery of trisomy 21 is perhaps comparable with that of the work and individuals concerned with study of the normal human chromosome number in Lund, where again 50 years elapsed before the first preparations demonstrating 46 human chromosomes were published (Harper 2006b).

The paper by Marthe Gautier published here in English translation will be read with interest by both those working in genetics and by historians of science and medicine. It will form a valuable strand of the definitive history of this chapter of work, along with accounts from different perspectives, and we should be grateful to Dr Gautier that, after 50 years, she has set on record her own perspective as one intimately involved with, and responsible for, one of the most important advances in human genetics.

Peter S. Harper

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