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EXOTERIC KNOWLEDGE AND ESOTERIC KNOWLEDGE. LUDWIK FLECK, PEDIGREES AND THE VISUALIZATION OF PATHOLOGICAL HEREDITY

JEAN-PAUL GAUDILLIÈRE
Centre de Recherches Médecine, Sciences, Santé et Société
INSERM-EHESS, Pans, F.

SUMMARY

In Genesis and Development of a Scientific Fact*, Ludwik Fleck uses the concept of an "ideogram" to designate the representation of a thought style through an image, which condenses its features in graphic properties. Pedigrees are such ideograms used by scientists and health professionals on the one hand, patients and lay persons on the other hand. Building on Fleck's analysis of the relationships between esoteric circles and exoteric circles, this paper traces the transformation and uses of pedigrees in 20th century medicine. It suggests that pedigrees in eugenics, clinical medicine, human genetics, and molecular genetics have presented distinct and relatively stable characteristics, reflecting the changing boundaries and roles of esoteric and exoteric knowledge.*

Introduction

Genesis and Development of a Scientific Fact is a book on experimental words and work, but it is also a book on images and visualization. In fact, the iconography played a specially important role in the reception of the book, in that the anatomical plates reproduced in the second part of the volume inspired Kuhn to read it then to press for its

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translation into English, thus leading to the appropriation of Fleck's book by the Anglo-Saxon world. In *Genesis and Development of a Scientific Fact*, Fleck uses anatomical images to clarify the concept of an "ideogram", *i.e*. the representation of a thought style through an image, the significance of which is condensed in its graphic properties.

Geneticists' pedigrees are obviously this type of ideogram.

When examined, this very common example published in the *Journal de génétique humaine* in 1952 can be easily associated with four levels of significance, each referring to specific worlds. First, it is a family tree, a summary of family history linking couples and progeny, with dates of birth and death, and prominent events in the trajectory of a unit of life and relationships. Next, this pedigree is a part of a medical record. Some of the individuals whose existence is represented by a circle or square are patients identified as having suffered and possibly died of a disorder of interest to the author of the publication, who collected enough data to make it possible, or not,

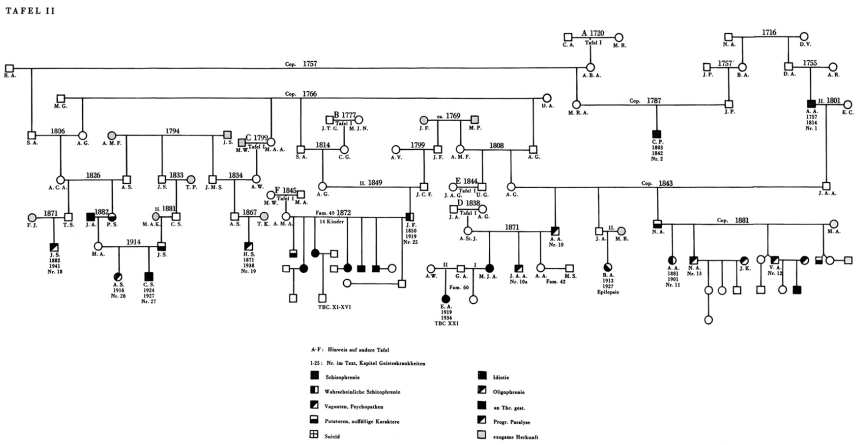


Fig. 1 - Pedigree of a psychiatric family. Source: *Journal de génétique humaine,* vol. 2, 1952.

to assign this or that characteristic to this or that member of the tree. As a summary of medical information, this pedigree is a tool for diagnosis that could reveal the existence of transmission. As such, it could also be used, for instance, for prognosis purposes: to define the probability of the pathology's occurring in the future and thus assess the future of certain family members. Third, this is a scientific fact published as an observation in an academic journal after critical reading. This example was judged as interesting enough to be circulated and integrated into the informal collection of pedigrees used by the community of geneticists, and it might even have found its place as an illustration in a manual. Finally, this representation belongs to the sphere of politics. It is an element of proof used in all kinds of public arenas concerned with human heredity, its nature and its problems: exhibitions, journals, and parliament.

For an analysis of this diversity, the interest of Fleck's book lies less in its approach to representation, which is relatively conventional, than in its vision of the interactions between the significances of the ideograms, the conditions of their production and the concept of "thought collectives". The changes in thought styles of the modern period are particularly revealed in the corresponding anatomical plates, which, as representations of the body, carry power of conviction. They give the impression that access to reality is a simple matter of observation. Yet when examined, they also immediately convey the feeling of stemming from a world that is no longer ours: even "normal" bodies seem to have changed. Generally speaking, examining ideograms is therefore a good way to identify thought styles. Just as thought collectives that share thought styles and make them live are also action collectives, ideograms are also the productions of various forms of work. The plates in *Genesis* are thus the outcome of an examination of diseased bodies, autopsies and drawings.

A first "Fleckian" approach to pedigrees could therefore consist of following their process of production by looking at how the data was

collected, recorded and written up, *i.e.* at the practices specific to places where medical genetics are practiced[1]. The exercise proposed here stems from another Fleckian probe: the analysis of the relationships between esoteric circles and exoteric circles.

Contrary to what might be believed, this picture of a scientist commenting on a pedigree drawn on a blackboard was not taken from a researchers' seminar or a classroom. The photograph illustrated an article, published in the journal *Vaincre la myopathie*, on a visit to what was in the 1990s the INSERM's Unit 12 (U12), located at the Hôpital des Enfants Malades in Paris, by families with children affected by spinal amyotrophy and members of a collective of the French association for the fight against myopathies, the Association Française de lutte contre les Myopathies (AFM). The AFM became famous as the organizer of the French fundraising Telethon and as a prime player in French genetics and genomics research[2]. The fami-

Fig. 2 - Molecular geneticist explaining the transmission of Spinal Muscular Atrophy, Paris, 1994. Courtesy of AFM.

lies invited that day were all the more interested in what was being done in U12 that their organization is the main fund provider for the U12 geneticists' research on this disease.

At first glance, this is a scientific area in which pedigrees exist and are used and where social studies have a lot to say: hybrid forums, the role of users, joint production of knowledge, lay expertise, technical democracy, etc. All of these themes have been extensively explored in the past 15 years by "science studies, "with a perspective on the idea that we are currently witnessing major changes in the status of science, whereby the ways in which scientific knowledge is produced are becoming more diverse[3]. The purpose here is not to claim that Fleck had already foreseen it all and that he had provided the theory to understand the therapeutic activism of the AIDS years or the emergence of the Women's Health Movement, but, more modestly, to see whether certain features of *Genesis and Development of a Scientific Fact* help in reflecting upon the involvement of laymen in the production of knowledge and in taking a critical approach to its history.

Indeed, in *Genesis*, the value of the ideograms and their role in the stabilization of a thought style is not only their value as a summary or digest, but also that of the multiple significances that they assemble and convey. The ideograms are therefore not only entities that are separately part of heterogeneous worlds, they can also circulate among these different worlds, and in particular between what Fleck calls (on p.105) esoteric circles and exoteric circles.

> *There are also structural characteristics shared by all such communities of thought. The general structure of a thought collective consists of both a small esoteric circle and a large exoteric circle, each consisting of members belonging to the thought collective and forming around work of the mind, such as a dogma of faith, a scientific idea, or an artistic musing. A thought collective consists of many such intersecting circles. . . . There is a graduated hierarchy of initiates, and many threads connecting the various grades as well as the various circles*[4].

For Fleck, the worlds of specialized knowledge and lay knowledge are not separate entities. On the one hand, there are multiple forms of communication: from the expert toward the layman through a communication or "popularization" process, but also from the layman toward the expert ("syphilitic blood", for instance, was part of common knowledge). On the other hand, these relationships combine two dimensions. First, there is the trust placed in the work and the competence of initiates. Second, initiates are also somewhat dependent on opinion, which can lead to the technicization of such or such an element of exoteric culture ("syphilitic blood" was then used in the construction of the Wassermann reaction used to diagnose syphilis).

In addition, for Fleck, the question of the relationships between the esoteric circles and the exoteric circles is related to the question of democracy. For him, the existence of a "hard core" of practitioners and of a wider circle is a highly general sociological phenomenon that is not specific to the world of science. It is found in the worlds of sports, religion, fashion and politics, for instance. The separation claimed between initiates and laymen may well be a guarantee for efficiency in knowledge production, but is also a political and ethical problem that can be managed in two different ways: democratically (the way of science) and through dogmatic authority (the way of religion). There is an ambiguousness in the discussion in *Genesis*, which comes from Fleck's vagueness regarding the limits that should be applied to the world of science. The two circles can be perfectly interpreted as being part of the territories of the professional genesis of knowledge. In that case, the reference to public opinion is to be taken as a metaphor. This reading is in keeping with the epistemology of the demarcation to which *Genesis* was opposed. For us, and perhaps also for Fleck, it is more interesting to consider that the analogy between scientific legitimacy and political legitimacy is not limited to recalling the importance of peer criticism. In Fleck's open epistemology, esoteric enclosure, a pledge of the stability of

knowledge and of "the harmony of illusions", needs correctives and contributions that can only be provided by participants from outside, but concerned circles[5]. This cautious joint construction, with much partner mediation and intervention (Fleck was originally thinking of the *Geisteswissenschaften*, the social sciences, but the scope can be enlarged), is specially well-adapted to the objects of biomedicine, particularly those that circulate extensively within and beyond the borders of laboratories and hospital services, such as physiologists' animal models, the clusters in epidemiology or geneticists' pedigrees.

Starting from this view of the articulation between exoteric knowledge and esoteric knowledge, I would like to propose a typology of pedigrees that is based on what we have recently learned from a very small part of their usage: that associated with the management of pathological heredity and the practice of medical genetics, including genomics.

1. *Eugenic pedigrees*

The history of eugenic pedigrees has been discussed in detail by Pauline Mazumdar in her history of the British Eugenic Society[6]. They are also found in the French context, albeit more rarely because of the country's eugenics history[7], but they were massively used in the same type of places: the *Société Française d'Eugénique* and societies that fought against tuberculosis or syphilis. Eugenics societies are institutions that are emblematic of the intersecting of exoteric and esoteric circles. It is true of their composition: they comprise experts in demography, clinicians, geneticists, administrative officers, and citizens with no biomedical competence but concerned with the fate of the nation, usually from the economic or political elite. It is also true of their activities, which are as much involved with communication, mainstream education and political lobbying as with doing research or conducting surveys[8].

The way contemporary pedigrees are designed thus owes a lot to the standardization of the forms of representation developed by the British and American eugenics societies[9]. This is in particular the case for the squares and circles used to indicate male and female individuals, or again for the vertical organization of the lineage starting from an initial couple, which was the outcome of discussions by a special committee set up by the Eugenics Society in 1911, chaired by Edward Lidbetter, an expert hired by the eugenics society to organize research on the heredity of poverty, diseases and mental illness. For Lidbetter, this standardization was indispensable to be able to carry out large-scale research projects, which were conducted by researchers specially trained to transform the records of the history of complex families, in which relationships and individuals were reported in a variety of manners, drowning the data in masses of details, into a system that made it possible to visualize sanitary and social disasters, and the accumulation of defects through the passing generations (Fig. 3 and 4).

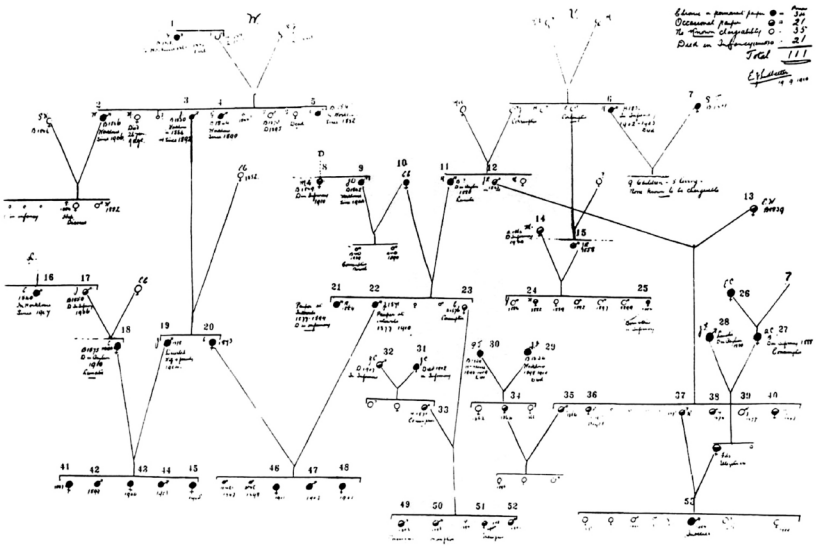


Fig. 3 - Lidbetter's pauper pedigree in original form. Source: *Eugenic Review*, vol. 2, 1910-1911.

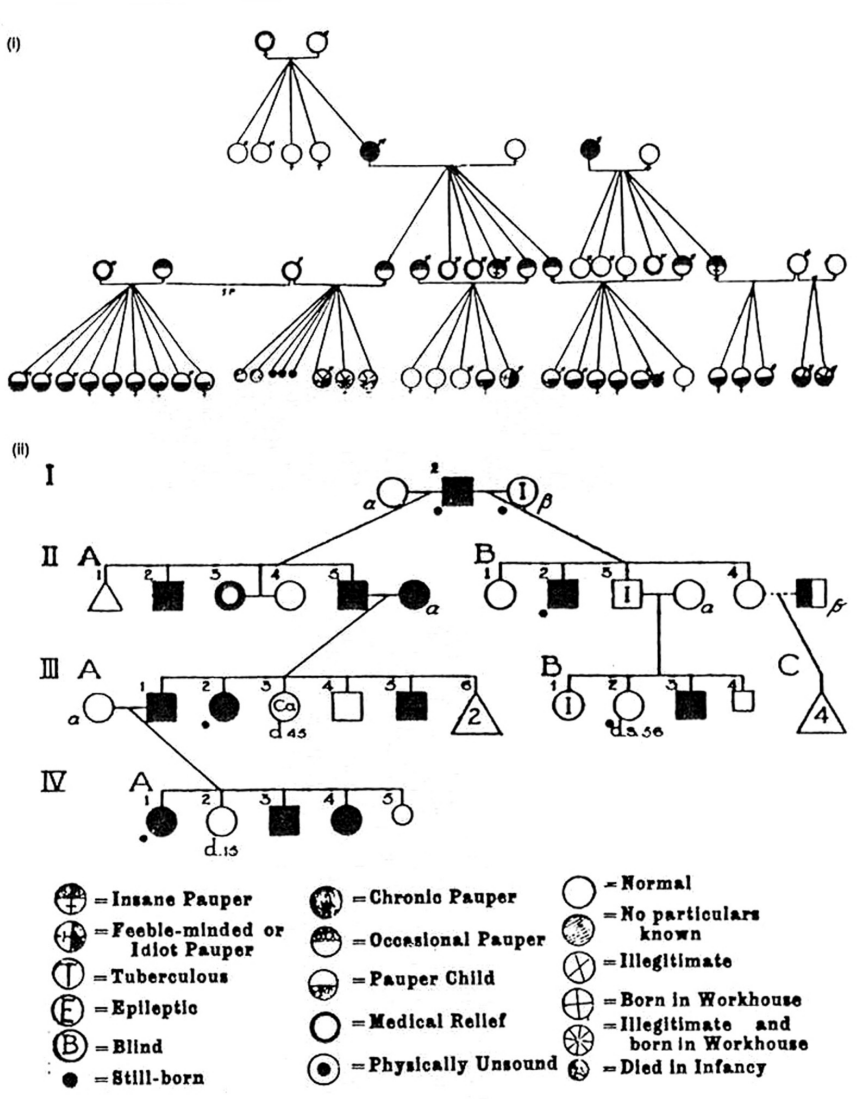


Fig. 4 - Lidbetter's standardized pedigree. Source: *Eugenic Review*, vol. 4, 1912-13.

More generally speaking, eugenic pedigrees came into existence at the same time as ideograms to depict degeneration. A lot of emphasis has been put on the role of family trees in the dissemination of Mendelism among physicians and hygienists[10].Trees typical of recessive or dominant diseases were presumably the main vectors for this dissemination. The mass of eugenic pedigrees, however, is not this type of tree. The problem that they record is not one of transmission mechanisms, even less so that of the number or the nature of the genes involved, but that of the effects of pathological transmission: a degradation in the quality of the population and a weakening of the nation as a direct outcome of pauperism (Great Britain), the declining birth rate (France) or the degeneration of the race (Germany). The purpose of this visualization was therefore to link family lineage with the distribution of ills previously identified by clinical medicine, psychiatry, anthropology, demography or sociology. In this perspective, eugenic pedigrees acquired two specific qualities: a) the fact of being pedigrees of social groups rather than of individuals' genealogies; b) the ordering in space and time of degradation.

A last feature of eugenic pedigrees is that they were eminently public objects. Not only because they were about drawing from more-or-less formally organized collections[11] for publication in journals published by these same eugenics societies, but also because communication of pedigrees became part of an effort of continued education of the middle classes through the press and through exhibitions (starting with the big eugenics exhibition of Dresden in 1911). Present in places as diverse as local organization meetings, eugenics conventions, international exhibitions or parliamentary chambers, this "lay" eugenics culture corresponds to an authoritative form of the expertise which leads to a display of exemplary histories of pathological families whose reproduction threatens the natural order (Fig. 5).

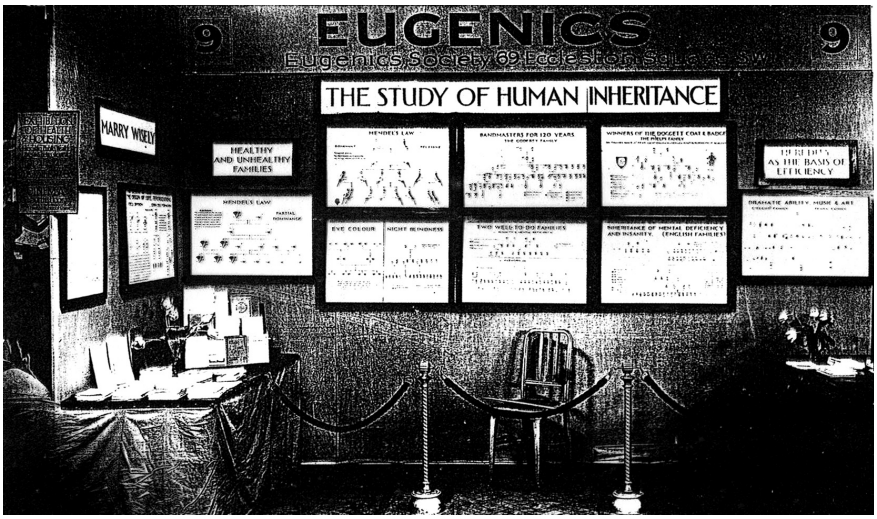
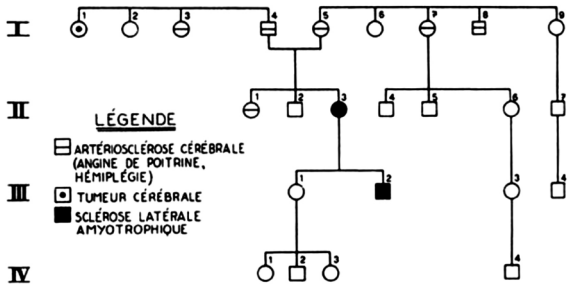


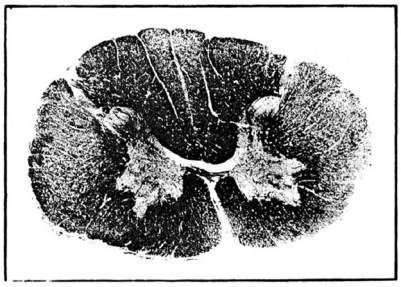
Fig. 5 - Exhibit of the British Eugenic Society, ca. 1920.

2. *Clinical pedigrees*

Clinical pedigrees are not the outcome of the traffic between experts in biology, medicine or demography, and laymen belonging to a social and economic elite, but of the talks between medical professionals and "their" patients. Here again, this type of communication is highly ordered, with the symptoms, signs and experience of disease translated into classification, nosography and diagnosis while, in the opposite direction, the clinician's knowledge is supposed to determine the care to be applied.

Clinical pedigrees reflect a vision of family illness where the "medical collective" works on constructing and taking responsibility for "cases". These proceed from a combination of biographic narration, anatomical and pathological observations or, exceptionally, from biological analyses (Fig. 6). The pedigrees entered into patients' records are meant to complete clinical observations with a visualization of transmission, which helps to identify – or label – a genetic disease.





Coupes médullaires du cas 1.

2 a) au niveau de la région cervicale C_5-C_6

2 b) à la hauteur de C_8-D_1

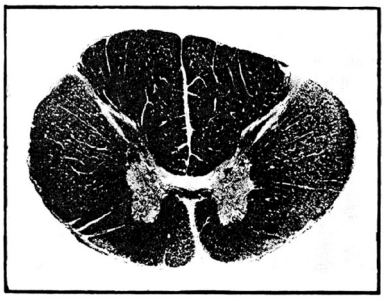


Fig. 6 - Histological photographs accompanying pedigrees in a study of lateral amyotrophic sclerosis. Source: *Journal de Génétique Humaine*. Vol. 4, 1955.

Pedigrees became part of the arsenal of clinical instruments starting in the thirties. But it is specially in the post-war period that they spread, as universities began building from the ruins of state eugenics by offering medical genetics as a speciality. Part of these pedigrees was therefore published in genetics journals and came from hospital services bearing the same name. The majority, however, is found in so-called clinical journals and came from paediatrics, ophthalmology, oncology, etc. services.

These products of clinical observation constitute the family as a collective patient in a form aimed for neither genetic analysis (focused on the transmission and assignment of genotypes) nor aggregation (through the computation of frequencies), but the purpose of which is to be able to compare a set of cases. Their interest is that they are attributable to a single pathological entity. They open the way to exploring borders and variability, with particular interest in the states previous to the appearance of symptoms so as to be able to pick up forewarning signs that could warrant early intervention.

3. *Pedigrees of human genetics*

To understand how pedigrees of human genetics differ from clinical pedigrees, we can refer to the work of Lionel Penrose in Great Britain. In the thirties, Penrose was in charge of a mission to study the heredity of mental illness by focusing on the observation of the inmates at the Colchester mental institution[12]. The survey reports combine clinical pedigrees and "Mendelian" pedigrees, *i.e.*, pedigrees collected as proof of a recessive or dominant genetic transmission. The construction of phenylketonuria as a hereditary disorder is of this type of configuration[13]. Penrose's finding of a particular form of amaurotic idiocy leaned on the conjunction between the performance of a biochemical test performed on the patient's urine, the collation of trees indicating recessive transmission and the statistical calculation of transmission probabilities on the basis of the observed incidence of the disease.

The production of medical-genetics pedigrees was based on talks between esoteric circles and exoteric circles comparable to those that were at the source of clinical pedigrees in that they involved the contribution of patients and their families. But in the first case, the purpose was health care. Here, it was about managing reproduction. Moreover, expert "geneticists" are not necessarily physicians. Finally, the privileged mediation space is no longer that of a hospital service, but a new form of consulting, first called "eugenic consultation" then "medical genetics consultation"[14]. It was these consultations that turned obtaining and analyzing pedigrees into a privileged medical activity (Fig. 7). This can be illustrated by the way in which in the mid-fifties, Maurice Lamy and his colleagues at the Necker hospital changed the aetiology of myopathy in order to divide it into two distinct forms according to the form of genetic transmission[15].
A so-called genetics consultation is focused on the relationship between signs and transmission, the idea being to collect testimonies from all the family members on their medical trajectories, if possible attested to by records transferred by colleagues. A genetics consultation aims to provide an etiologic analysis where clinical signs override genetic signs in case of conflict between the two. But its purpose is also to provide counselling, *i.e.*, a very particular form of medical interaction where the diagnosis is expressed in terms of a transmission or recurrence probability that needs to be "explained", in other words, to be contextualized so as to be able to offer reproductive counselling. Here is where a lay culture of genetic pedigrees was constituted, whereby people's trajectories are juxtaposed and articulated with the different levels of expert discourse, and which is not limited to "the" significance that geneticists intend to convey[16].

4. *Molecular pedigrees*

Molecular pedigrees are no longer tools for making diagnostic or reproductive decisions. They are associated with inscriptions that

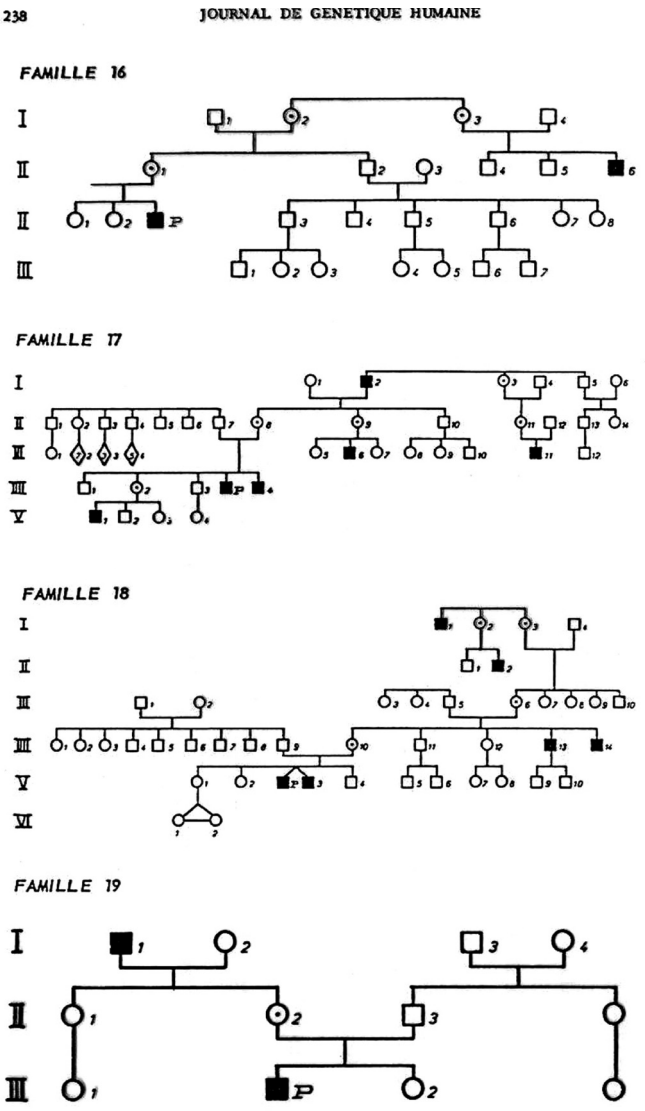


Fig. 7 - Pedigrees illustrating the mendelian transmission of muscular dystrophy. Source: *Journal de Génétique Humaine*, vol. 3, 1954.

make of the gene not a transmission unit but a molecular entity that is isolable, chemically characterized, and possibly machine reproducible. Such inscriptions bring about a reversal of the hierarchy between clinical knowledge and biological knowledge. When there is contradiction or difficulty, the molecular analysis overrides both the clinical observations and the pedigree showing family transmission. Historically, this reversal appeared in the early seventies, just as another visualization of the gene, through the microscopic observation of chromosomes and the karyotype, became a means of medical intervention. Combined with amniocentesis, the karyotypes enable a prenatal diagnosis of chromosomal abnormalities[17]. A hierarchy favourable to molecular analysis is therefore certainly linked to the acceptance of a genetic determinism of disease, but it also has to do with the coupling of a genetics consultation with a "therapeutic" termination of pregnancy accepted as an emergency solution starting in the late fifties, and it was generalized in the context of debates on abortion.

As can be guessed from Figure 2, molecular pedigrees are pedigrees with no biographical or clinical indications; they are the minimal expression of pedigrees where what is essential is the distribution of DNA sequences used as markers to track mutations (Figure 8). They are linked to the "DNA machinery" (sequencers, blotters, PCR kits), coupled with the statistics-processing software that makes it possible to compute co-transmission scores and calculate the risks. The first function of genomics pedigrees was in fact to produce statistical associations between markers and incidence in order to localize the genes responsible for disease and to build molecular etiologies. This is what, for instance, the above-mentioned U12 geneticists did for spinal amyotrophy[18]. They localized possible genes on chromosome 5, isolated a sequence transferred in all families from which they had collected the DNA and finally reduced the diversity of spinal amyotrophies to a single molecular disease, whereas previously the

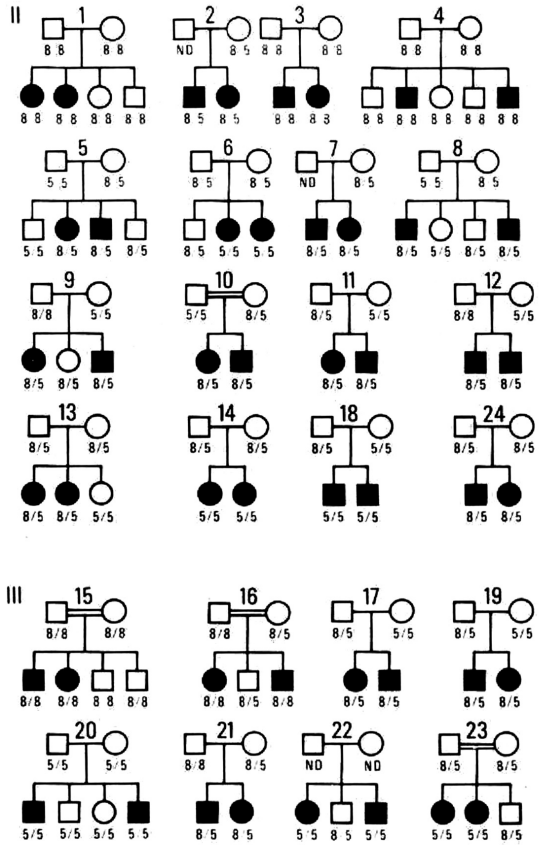


FIG. 1 CP-SMA pedigrees. Genotypes at the D5S39 locus are shown for each individual in affected families: type II (first four rows) and type III (the last two). RFLP detected with D5S39 was determined by hybridizing the DNA probe to Southern blots containing genomic DNA. ND, not done.

Fig. 8 - Molecular pedigree showing the transmission of DNA markers in families affected with spinal muscular atrophies, 1990. Courtesy of Nature.

heterogeneity of the clinical tables had warranted a nosologic classification into two types of amyotrophy: a critical form bearing a very rapidly fatal prognosis and a form with a slower evolution.

Apparently, nothing is further from exoteric circles and families than a molecular pedigree. Laboratory work is however always connected to a genetics consultation, which is one among other fields of application. In the case of spinal amyotrophy, as in the history of Down's syndrome, the stabilization of the molecular hierarchy, which amounts to the acceptance by clinicians of the fact that there is only a single form of amyotrophy, owes a lot to the practical use of the DNA sequences identified by the U12 geneticists to carry out prenatal diagnosis. This latter was in fact offered to all families having had a child affected by amyotrophy, whatever its type. Without the mediation of the consultation, without the families' collectively demanding its practice (Fig. 9), stabilization of this knowledge would have probably been a lot more difficult to achieve.

This leads to a final remark, which concerns the specificity of the interactions between esoteric circles and exoteric circles when these latter include patients and their relatives, as well as family collectives and associations. In its leaders' rhetoric and in its publications, the Association Française de lutte contre les Myopathies (AFM) first highlights its role as initiator and fund provider of the research in human genetics. But involvement in research also has to do with the constitution of persons' identities[19]. The spinal-amyotrophy group is a group where the common identity built around the experience of the disease is expressed in terms of molecular genetics. Previous to the etiologic unification achieved by the U12, there is also the unification of the families with a child affected with spinal muscular atrophy within the AFM and the campaigns to enlarge it, which aimed as much to reinforce self-support practices as to collect more DNA. Even though molecular pedigrees belong to the culture of these collectives, it should be noted that in its activities as a grouping of patients, the SMA group mostly used the pedigrees and figures of the transmission of pre-molecular genetics.

Amyotrophie Spinale

LE Pr MUNNICH INVITE LES FAMILLES À FAIRE LE POINT

Le Pr A. Munnich répond aux nombreuses questions des familles venues s'informer de l'avancée des recherches sur l'amyotrophie spinale.

Fig. 9 - Visit of Spinal Muscular Atrophy families at Necker Hospital, ca. 1994. Courtesy of AFM

Conclusion

The above can be summarized by specifying (see Table 1) for every type of pedigree the following categories: type of ideogram, idea conveyed by it, form of scientific work, nature of the esoteric and exoteric circles, forms of articulation between these circles, type of expertise.

	Eugenic pedigrees	**Clinical pedigrees**	**Genetic pedigrees**	**Molecular pedigrees**
Idea	Degeneration	Family illness	Transmission of Mendelian factors	Molecular mutation
Form of scientific work	Social surveys, reports	Anatomic-pathological exams, nosologic classification	Clinical diagnosis, statistics, etiologic classification	Diagnosis, DNA analysis, computation (models)
Ideogram	Group family tree	Case family tree	Collection of transmission trees	Family tree with markers
Esoteric/ exoteric circles	Eugenics societies, journals, exhibitions, political assemblies	Medical specialties, family, hospital consultation	Geneticists' societies, counsellors' associations, family-patient collectives, genetics consultation	Idem + biology laboratory, support group, organization
Articulation procedures and type of expertise	Administrative expertise, education and legislation	Professional expertise, biographic recording, care	Professional expertise, counselling and managing reproduction	Distributed but top-down expertise, risk management

This typology is interesting for two reasons. On the one hand, the choice of classification criteria refers us to the fact that Fleck's approach is still relevant for the history of medicine. On the other hand, it helps in taking into account the diversity of forms of visualization of pathological heredity. It can thus help to put into historical perspective the Science and Technology Studies (STS) analyses on the recent transformations of biomedicine. This leads to a number of remarks.

First, the twenties and thirties, and fifties and sixties are two periods of particular visibility of the pedigrees that can be related with the metamorphoses of biopolitics in the course of the twentieth century, which moved from a biopolitics of populations, focused on more-or-less authoritative state intervention, to a biopolitics of individuals, focused on the biomedical objectivation of risk and its management through people's "informed" choices.

Second, although the role of pedigrees is no longer crucial in the technical management of genetic illness, family trees and the representations associated with them have not lost their importance in the production of the illness as a *family disease*. They remain mediation instruments among geneticists, clinicians and families, characteristic records of the grey zone in which exoteric and esoteric circles mingle.

Third, the changes associated with gene molecularization have turned pedigrees into an appendix of "biomedical platforms"[20], which multiply technological inscriptions. At the same time, molecular pedigrees are assembled by "lay" collectives (organizations, support groups, family associations), which are highly involved in their production. This joint construction reflects the redistribution of expertise, which has shifted both the experts' and the laymen's roles and competences, but has affected neither the asymmetries in knowledge, nor the power orders.

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Correspondence should be addressed to:
gaudilli@vjf.cnrs.fr