Medical pedigrees: Typography and interfaces

Boris Veytsman and Leila Akhmadeeva

Abstract

We discuss the history of medical pedigrees and its importance for the design of the modern pedigree drawing software.

1 Writing on the wall

The participants of TUG 2009 could see on the wall of Room 126, DeBartolo Hall, University of Notre Dame, a poster 23 feet wide. This poster depicted a pedigree of one of the authors of this paper (Leila). The pedigree included 13 generations (since the beginning of the 17$^{\text{th}}$ century), about three hundred persons in total. It was created in the following way: Leila did research in the National Archives of Bashkir Republic, interviewed her aunt and other relatives and deciphered the notes about family history dictated by her grandfather at mid-1980s. She put the data into an Excel file and periodically e-mailed the updated file to Boris, who then run it through a custom-made Makefile, getting as the result a PDF file. This file was e-mailed back. The final version was printed on two 16 foot sheets, which were taped together by Leila and her cousin in Ufa.

This project became possible due to the suite of programs for automatic drawing of medical pedigrees we have been developing since 2005 (Veytsman and Akhmadeeva, 2007a; Veytsman and Akhmadeeva, 2007c). Their previous versions were discussed at TEX meetings (Veytsman and Akhmadeeva, 2006; Veytsman and Akhmadeeva, 2007b; Veytsman and Akhmadeeva, 2008) as well as conferences on genetics (Akhmadeeva, 2007). Now that the programs are no longer at the proof of concept level, we became more interested in improving them and making them of practical use for physicians, other health care specialists, geneticists, researchers, educators, and students.

There are basically two ways to improve a typesetting program. First, we can improve its output, making the result more beautiful and clear. Second, we can improve its interface, making it more convenient, user-friendly and adding new features. In this paper we discuss both these approaches.

2 A (very) short history of pedigree typography

A usual approach to beautiful typography is the study of history. The aesthetics of a printed page is based on the tradition. Thus it was natural for us to turn to the history of pedigrees in our quest to make them beautiful. We were fortunate to find the seminal paper (Resta, 1993) discussing just that topic. Resta unearthed many early pedigrees, and this section is based primarily on his research.

One of the biggest surprises for us was the fact that pedigree drawing is a relatively modern art, started as late as the middle of the 19$^{\text{th}}$ century. One would think that people drew genealogical trees for ages, and thus pedigrees should have long history with venerable traditions. Still, this is not the case. While both genealogical trees and pedigrees are a graphical depiction of a family history, the goals of these two are completely different. A genealogical tree is intended to show the lineage of an individual, while a pedigree is used to show genetic traits. This difference in goals leads to a considerable difference in results. As an illustration of this difference, we show in Figure 1 a very nice genealogical tree created with PSTricks (Coustillas and Girou, 2004). The corresponding pedigree is shown in Figure 2. Note that the data of Figure 1 are actually not sufficient for the medical analysis, so we guessed that the marriage of Paul Joannon and Laure de Mortillet was childless. We also could not guess the relationship between the first and the second husbands of Élise Vidal; were they brothers? an uncle and a nephew? — so we decided against putting them on the chart.

Even a casual glance at these two pictures shows the difference between the presentations. Clearly, the typographical traditions of genealogical trees is not very helpful for pedigrees.

One of the first known medical pedigrees was published by Earle in the middle of the 19$^{\text{th}}$ century. He studied cases of color blindness in his own family. The pedigree included only females. Earle found out that his printer used to typeset musical sheets, so taking musical notes for symbols was a natural decision. Unaffected females were represented by half note symbols, while affected ones were represented by quarter-notes. Figure 3 shows the result.

This nomenclature was apparently not used by anybody but Earle himself. Other scientists chose other ways to represent pedigrees. An influential researcher of the latter part of the century, Francis Galton, in his books and papers published in 1869–1904 dispensed with drawing pedigrees, and used intricate tables instead (Resta, 1993).

The rediscovery of Mendel's seminal works on plant genetics might be the cause of the adoption of the symbols of Mars (♂) and Venus (♀) for males and females. A typical (hand-drawn) pedigree using this nomenclature is shown in Figure 4. It was

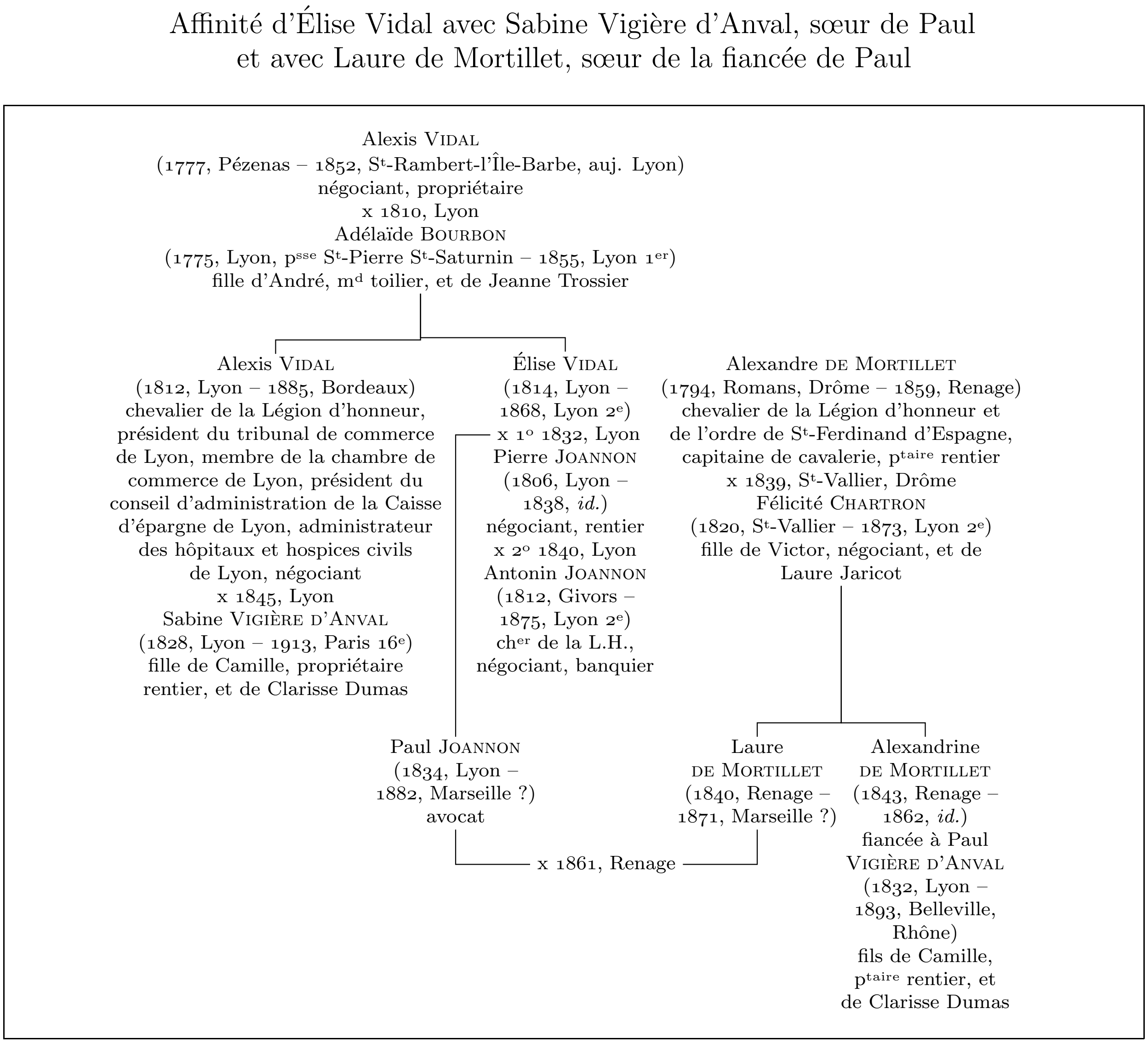


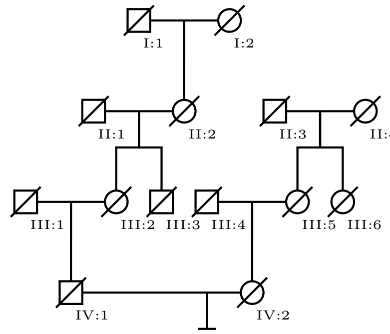
Figure 1: A genealogical tree from Coustillas and Girou, 2004

proposed by Pearson based on Galton's ideas. Karl Pearson, widely known now for his works in mathematical statistics, was a student of Galton, and later took his position as the director of the Laboratory for National Eugenics, UK.

It should be said that the relationship between eugenics and modern genetics resembles the relationship between alchemy and chemistry or astrology and astronomy. We no longer believe that we can breed a better human like we breed better dogs or chickens: people are more complex beings. We also do not believe that stars can be used to predict one's fate or that base metals can be transmuted to gold without a nuclear reactor. Nevertheless the methods and nomenclature developed by astrologers and alchemists are widely used today in astronomy and chemistry. Similarly the methods and nomenclature developed in eugenics have found their places in modern genetics.

Later Pearson and the Laboratory for National Eugenics used stylized symbols for males and females, only distantly resembling the original astronomical signs. A typical pedigree in this style is shown in Figure 5.

This nomenclature was used in medical and genetics journals up to the 1970s, usually as an alternative to the modern one. Sometimes the disputes between the proponents of these were rather bitter. Resta cites different possible reasons why Pearson-Galton symbols did not survive. We would suggest



I:1 André Bourbon; né: ignoré; âge au décès: ignoré.

I:2 Jeanne Trossier; né: ignoré; âge au décès: ignoré.

II:1 Alexis Vidal; né: 1777; âge au décès: 75; négociant, propriétaire.

II:2 Adélaïde Bourbon; né: 1775; âge au décès: 80.

II:3 Victor Chartron; né: ignoré; âge au décès: ignoré; négociant.

II:4 Laure Jaricot; né: ignoré; âge au décès: ignoré.

III:1 Pierre Joannon; né: 1806; âge au décès: 32; négociant, rentier.

III:2 Élise Vidal; né: 1814; âge au décès: 54.

III:3 Alexis Vidal; né: 1812; âge au décès: 73; chevalier de la Légion d'honneur, président du tribunal de commerce de Lyon, membre de la chambre de commerce de Lyon, président du conseil d'administration de la Caisse d'épargne de Lyon, administrateur des hôpitaux et hospices civils de Lyon, négociant.

III:4 Alexandre de Mortillet; né: 1794; âge au décès: 65; chevalier de la Légion d'honneur et de l'ordre de S^{t}-Ferdinand d'Espagne, capitaine de cavalerie, p^{taire} rentier.

III:5 Félicité Chartron; né: 1820; âge au décès: 53.

III:6 Alexandrine de Mortillet; né: 1843; âge au décès: 19; fiancée à Paul Vigière d'Anval.

IV:1 Paul Joannon; né: 1834; âge au décès: 48; avocat.

IV:2 Laure de Mortillet; né: 1840; âge au décès: 31.

Figure 2: A pedigree based on the data of Figure 1

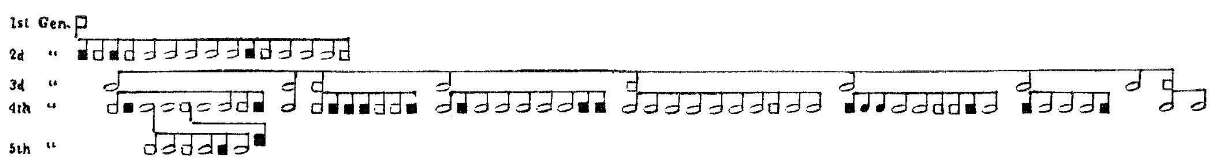


Figure 3: One of the first pedigrees, Earle (1845). From Resta, 1993

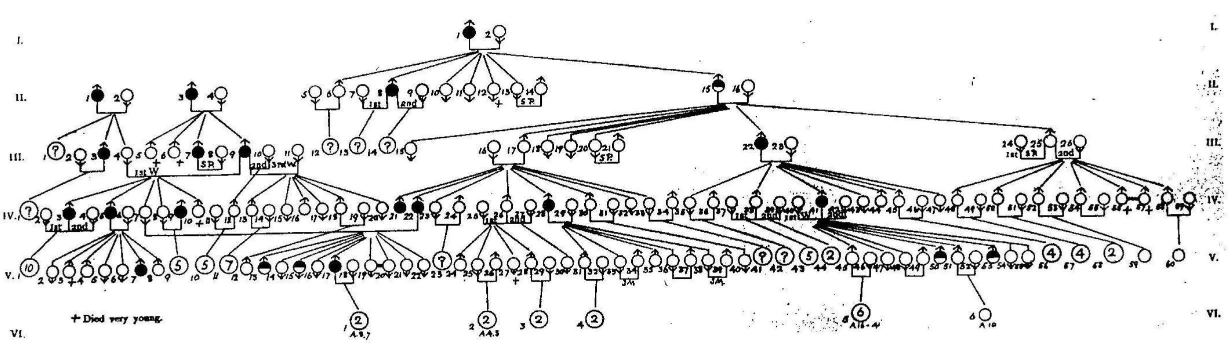


Figure 4: A pedigree using Mars and Venus symbols, Pearson (1912). From Resta, 1993

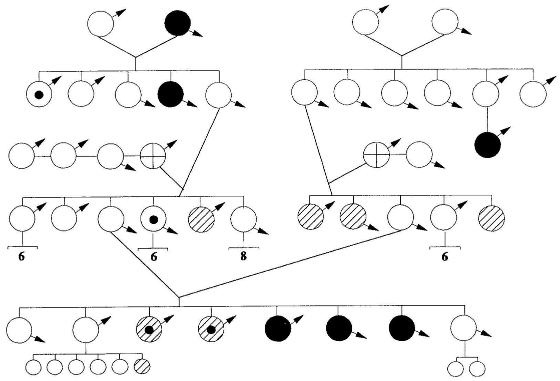


Figure 5: A pedigree using stylized Galton-Pearson Symbols (Mott, 1910). From Resta, 1993

that the problem was in the legibility; sometimes it is difficult to see the thin arrows used to differentiate between males and females on the diagrams, especially at small sizes. The modern method of using squares and circles leads to much better legibility. One of the lessons of classical typography is that the more legible solution usually wins in the long run (the run may be very long, however).

A more legible way to represent pedigrees can be found in the works of German authors. A rather forceful pedigree in the German *Sippschaftstafel* style is shown in Figure 6. It is anything but illegible. Use of circles and squares makes the task of distinguishing between males and females rather easy.

This style was developed by Henry Goddard and Charles Davenport, and approved by the powerful Eugenics Records Office (ERO) in the US. ERO popularized this style in numerous publications. It provided instruction, free blank forms and stamps with circles and squares to the families willing to furnish their pedigrees to ERO. A sample pedigree from an ERO pamphlet is shown in Figure 7. It looks almost like a modern pedigree, especially if we compare it to a hand drawn one (Figure 8).

Today pedigrees in Goddard-Davenport styles are ubiquitous. It is almost impossible to find a journal in genetics, hereditary diseases or related fields without at least several papers with pedigrees. Some typical pedigrees are shown in Figures 9 and 10. Note the interesting way to show haplotypes in Figure 10.

Modern pedigrees are legible and clear. They are also beautiful. The relatively short history of medical pedigrees shows, that the quest for clarity and legibility also causes beauty, almost as a side effect. This should not be surprising for students of typographical art: we know that aesthetics of a printed copy is always related to a clear representation of the author's thoughts.

3 Interfaces

Since our programs (Veytsman and Akhmadeeva, 2007a; Veytsman and Akhmadeeva, 2007c) are intended primarily for people with minimal TEXnical background, user-friendly interfaces are important for them. There are two main items to set up for a program: *what to print* and *how to print.* Accordingly there are two major interfaces: setting up the pedigree contents and setting up the pedigree layout and appearance.

We choose spreadsheets for the first task, setting up the contents of the pedigree. A user puts the information about proband and her or his relatives in a table, like the one shown in Figure 11. Such tables can be easily prepared with popular spreadsheet programs. One can argue whether a spreadsheet is an optimal input interface, but it has the advantage of being familiar to most users. Indeed, many geneticists already store the information in spreadsheets, so the use of our programs would be natural to them.

Another advantage of this interface is the fact that tables like the one in Figure 11 can be easily obtained from SQL databases. Thus our program can be integrated with larger database-driven projects.

For the second task, setting up the layout of the pedigree, the interface is much less easy. It involves setting up configuration files, which are snippets of Perl code, as shown in Figure 12. This was a design decision: we did not foresee our users changing the styles of their pedigrees. While this conclusion might be right for some (many?) situations, it was definitely not right for the application described in Section 1: the default style was not designed for a huge pedigree with more than three hundred persons, so we ought to change the configuration file. Nevertheless we still doubt that making changes in the pedigree layout too easy is necessarily a Good Thing. Probably a better solution would be to offer a user a set of preconfigured layouts.

4 The future

Our quest for better typesetting of pedigrees surprisingly showed that the preliminary design decisions we made (Veytsman and Akhmadeeva, 2007a; Veytsman and Akhmadeeva, 2007c) were sound. Of course, there are still many ways to improve the program suites.

When this work was reported at TUG 2009, Karl Berry suggested setting up a web site, where

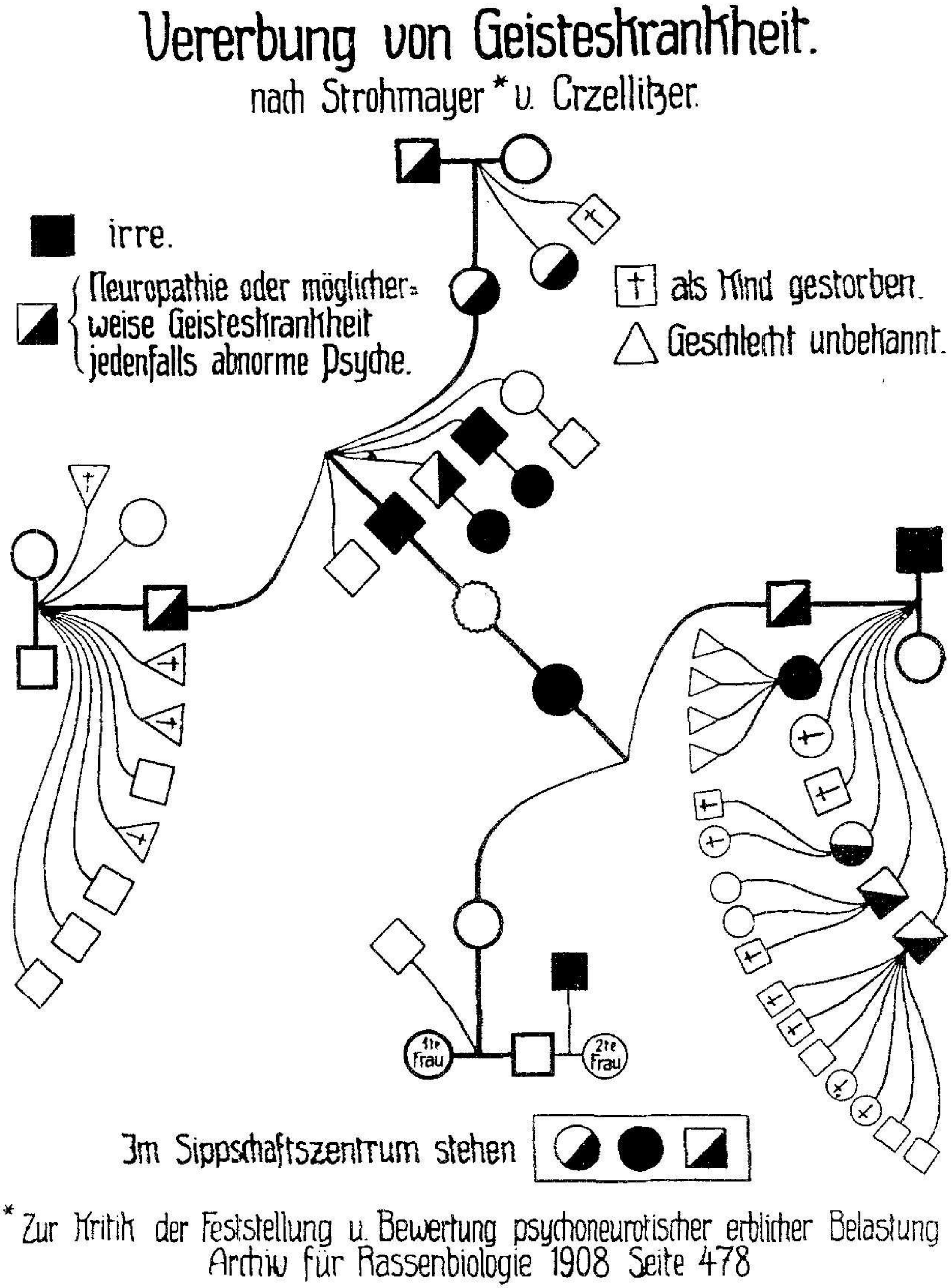


Figure 6: A pedigree in *Sippschaftstafel* style (Rüdin, 1910). From Resta, 1993

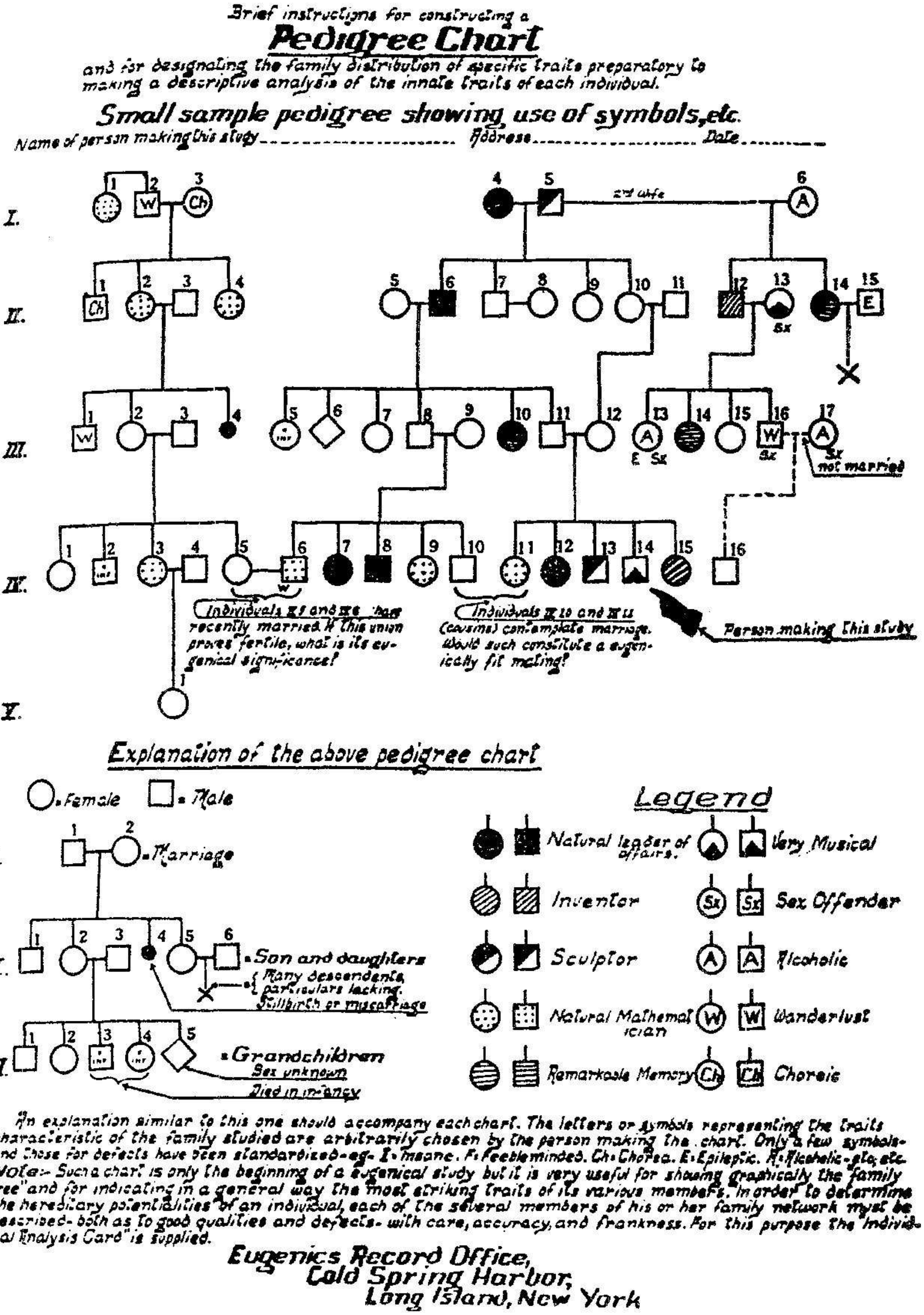


Figure 7: Sample pedigree from a Eugenics Records Office pamphlet, 1911. From Resta, 1993

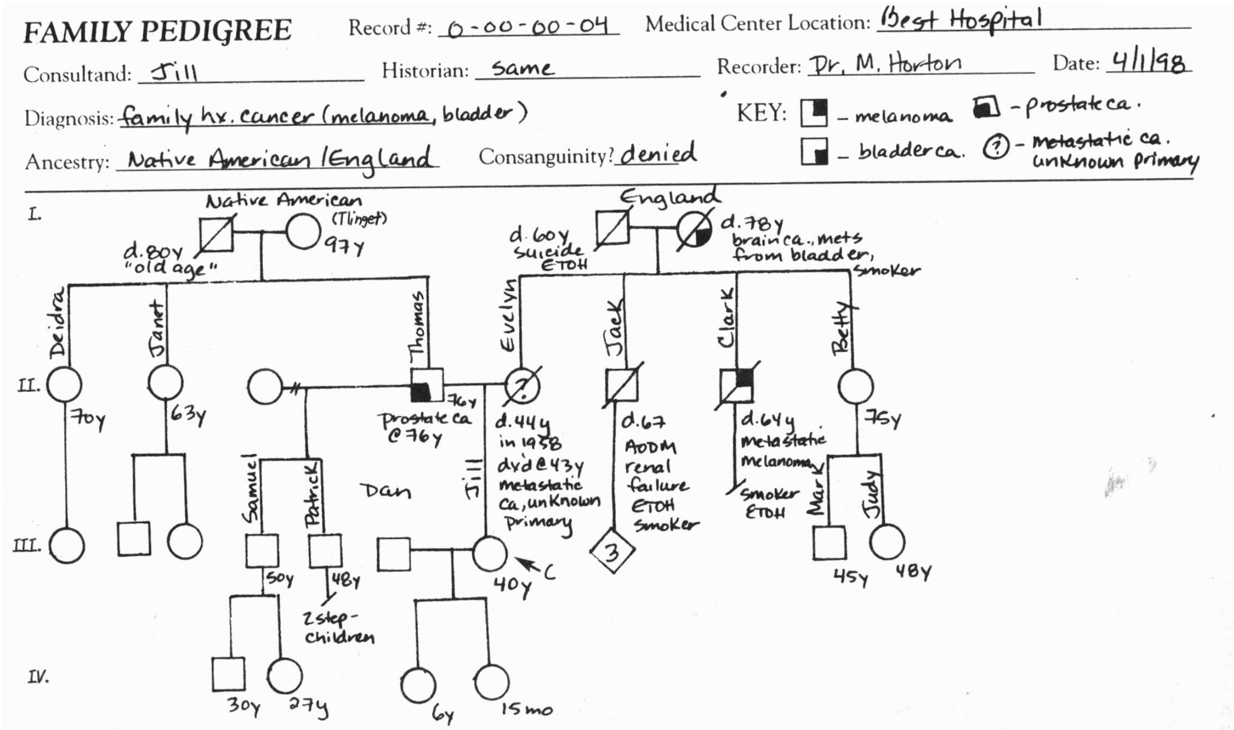


Figure 8: A modern hand-drawn pedigree. From Bennett, 1999

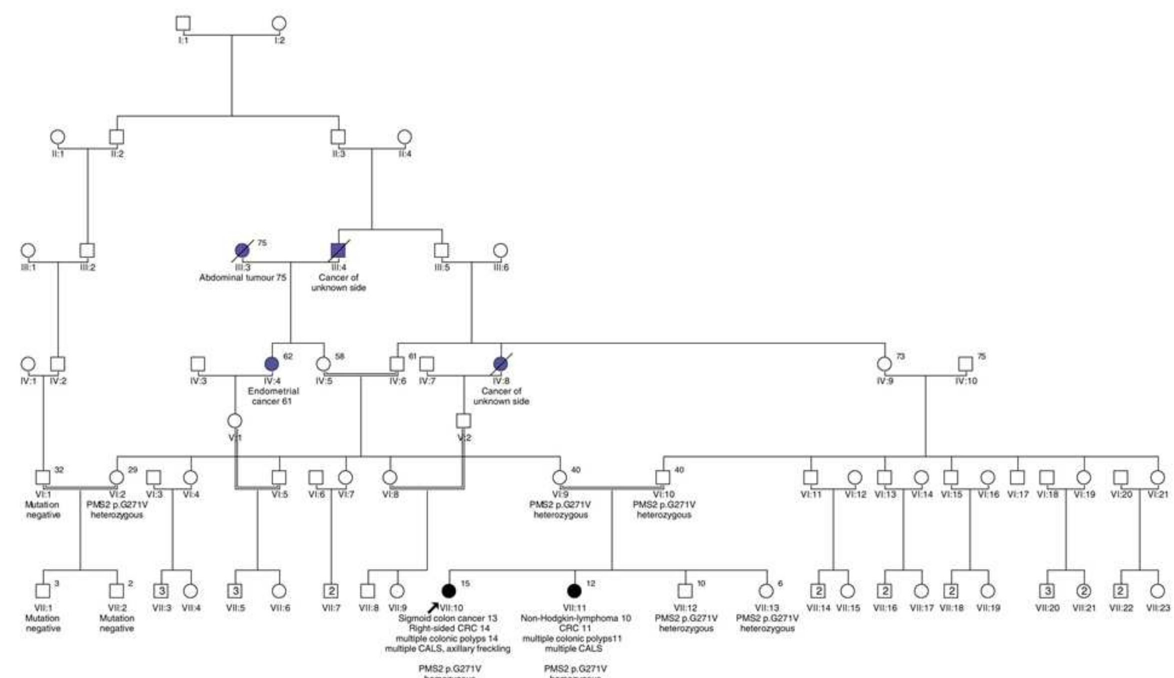


Figure 2 Pedigree of family 2. Tumours and age of onset are reported. Black symbols indicate CCS-related tumours (CRC, colorectal cancer). Blue symbols indicate other tumours. Numbers on right-top give the current age or age of death. The index patient is indicated by an arrow. In addition, signs of NF1 and mutational status are given.

Figure 9: A pedigree from Krüger et al., 2008

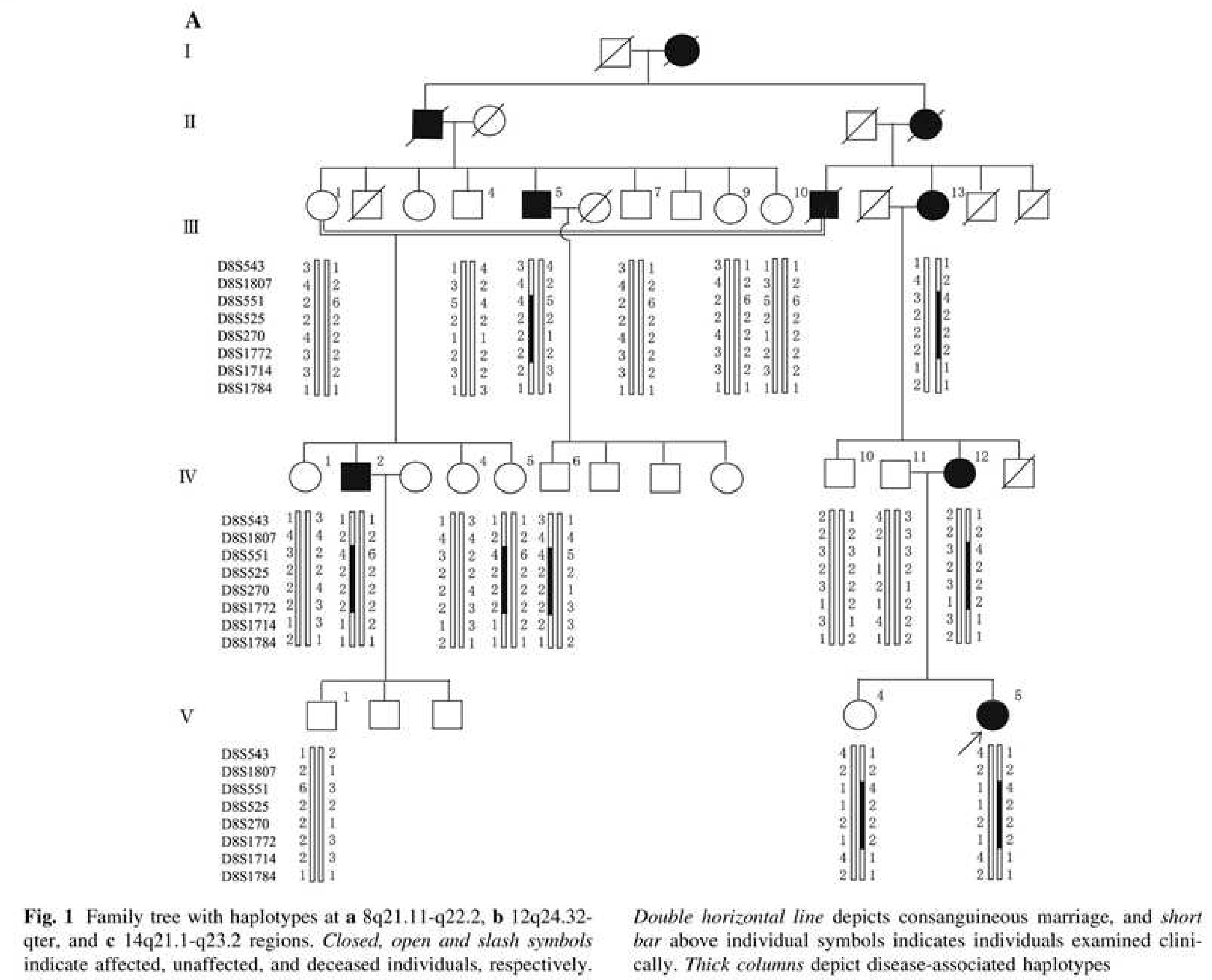


Figure 10: A pedigree from Nakashima et al., 2008

```
Id |Name                 |Sex   |DoB | DoD|Mother|Father|Proband|Comment
AV |Alexis Vidal         |male  |1777|1852|      |      |       |n\'egociant, propri\'etaire
AB |Ad\'ela\"\i{}de Bourbon|female|1775|1855|JT    |AnB   |       |
EV |\'Elise Vidal        |female|1814|1868|AB    |AV    |       |
PJ |Pierre Joannon       |male  |1806|1838|      |      |       |n\'egociant, rentier
PaJ|Paul Joannon         |male  |1834|1882|EV    |PJ    |       |avocat
...
```

Figure 11: An example of pedigree input

people could create simple typeset pedigrees without the trouble of installing the full TeX suite — and perhaps becoming interested enough in the results to install it anyway. This is an idea worth pursuing.

Karl Pearson noted in 1912, *A complete pedigree is often a work of great labour, and its finished form is frequently a work of art.* We hope our work helps to make pedigree drawing less laborious — while preserving the beauty of the result.

Acknowledgements

We appreciate the kind permission by Prof. Resta to use his illustrations for this paper.

We are grateful to Karl Berry for his tireless support and great suggestions.

One of the authors (LA) would like to acknowledge the travel support from the TeX Users Group, Russian Federation President's Board for Support

```
# Do we want to print a legend?
$printlegend = 1;

# Fields to include in the legend.
# Delete Name for privacy.
@fieldsforlegend = qw(Name DoB AgeAtDeath
                      Comment);

# Fields to put at the node.
# Delete Name for privacy.
our @fieldsforchart = qw();
```

Figure 12: A fragment of our configuration file

of Young Russian Scientists and Scientific Schools (grant No. MD-1195.2008.7), Russian Foundation for Basic Research (grant No. 09-04-08060-z) and Ministry of Education and Science of the Russian Federation (grant No. NK-30P/12).

References

Akhmadeeva, Leila. "Using a New Package for Drawing Pedigrees for Teaching Medical Genetics". *Eur. J. Hum. Gen.* **15**(Suppl. 1), 338, 2007.

Bennett, Robin L. *The Practical Guide to the Genetic Family History*. Wiley-Liss, Inc., New York; Chichester; Weinheim; Brisbane; Singapore; Toronto, 1999.

Coustillas, Françoise, and D. Girou. "[Example of Genealogy Tree with PSTricks]". `http://tug.org/PSTricks/main.cgi?file=Examples/Genealogy/genealogy`, 2004.

Krüger, Stefan, M. Kinzel, C. Walldorf, S. Gottschling, A. Bier, S. Tinschert, A. von Stackelberg, W. Henn, H. Görgens, S. Boue, K. Kölble, R. Büttner, and H. K. Schackert. "Homozygous PMS2 Germline Mutations in Two Families With Early-Onset Haematological Malignancy, Brain Tumours, HNPCC-Associated Tumours, and Signs of Neurofibromatosis Type 1". *Eur. J. Hum. Gen.* **16**(1), 62–72, 2008.

Nakashima, Mitsuko, M. Nakano, A. Hirano, T. Kishino, S. Kondoh, N. Miwa, N. Niikawa, and K.-i. Yoshiura. "Genome-wide linkage analysis and mutation analysis of hereditary congenital blepharoptosis in a Japanese family." *J. of Hum. Gen.* **53**(1), 34–41, 2008.

Resta, Robert G. "The Crane's Foot: The Rise of the Pedigree in The Human Genetics". *J. Genetic Couns.* **2**(4), 235–260, 1993.

Veytsman, Boris, and L. Akhmadeeva. "Drawing Medical Pedigree Trees with TEX and PSTricks". *PracTEX J.* (4), 2006. `http://www.tug.org/pracjourn/2006-4/veytsman`.

Veytsman, Boris, and L. Akhmadeeva. *Creating Medical Pedigrees with PSTricks and LATEX*, 2007a. `http://mirror.ctan.org/graphics/pstricks/contrib/pedigree/pst-pdgr`.

Veytsman, Boris, and L. Akhmadeeva. "Drawing Medical Pedigree Trees with TEX and PSTricks". *TUGboat* **28**(1), 100–109, 2007b. `http://www.tug.org/TUGboat/Articles/tb28-1/tb88veytsman-pedigree.pdf`.

Veytsman, Boris, and L. Akhmadeeva. *A Program For Automatic Pedigree Construction With pst-pdgr. User Manual and Algorithm Description*, 2007c. `http://mirror.ctan.org/graphics/pstricks/contrib/pedigree/pedigree-perl`.

Veytsman, Boris, and L. Akhmadeeva. "Medical Pedigrees with TEX and PSTricks: New Advances and Challenges". *TUGboat* **29**(3), 484, 2008. `http://www.tug.org/TUGboat/Articles/tb29-3/tb93abstracts.pdf`.

◇ Boris Veytsman
Computational Materials Science Center, MS 6A2
George Mason University
Fairfax, VA 22030
`borisv (at) lk dot net`

◇ Leila Akhmadeeva
Bashkir State Medical University
3 Lenina St., Ufa, 450000, Russia
`la (at) ufaneuro dot org`