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DNA-minisatellite mutations: recent investigations concerning distribution and impact on parentage testing

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Summary. At least 815 meioses were studied in the *Hin*fI polymorphisms of DNA minisatellite loci D1S7, D2S44, D7S21, D7S22, and D12S11 in order to collect data on respective mutation rates. At locus D7S21 (probe MS31) a striking difference between the paternal and maternal mutation rate was observed (1.5% versus 0.2%). This study also describes, how to deal biostatistically with paternal mutations in parentage testing. Possible implications of mutations are illustrated by the description of 2 cases. Case 1 reports an "exclusion" of mother and father with probe MS1. Case 2 describes 2 paternal "exclusions" with probes MS31 and G3. The statistical likelihood for a paternal "exclusion" with 2 of the 5 probes is 0.13%. By omitting probe MS1, this frequency can be reduced to 0.02%. Nevertheless, the second case clearly shows, that informative blood group markers cannot be replaced by DNA polymorphisms.

Key words: Single locus probes – Meioses – Mutation rates

Zusammenfassung. 815-2004 Meiosen wurden in den *Hin*fI-Polymorphismen der DNA-Loci D1S7, D2S44, D7S22 und D12S11 untersucht, um Daten über Mutationsfrequenzen zu gewinnen. Getrennt nach paternalen und maternalen Meiosen wurden die in Tabelle 1 dargestellten Mutationsraten beobachtet. Am DNA-Locus D7S21 (Sonde MS31) wurde ein signifikanter Unterschied zwischen paterneller und materneller Mutationsrate festgestellt (1,5% im Vergleich zu 0,2%). Die Arbeit beschreibt weiterhin, wie biostatistisch mit (paternellen) Mutationen im Vaterschaftsgutachten umgegangen werden muß. Die Bedeutung von Mutationen illustrieren 2 Falldarstellungen: Der 1. Fall beschreibt einen „Eltern-Kind-Ausschluß" mit Sonde MS1. Der 2. Fall berichtet von 2 paternellen „Ausschlußkonstellationen" mit den Sonden MS31 und G3.

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Schlüsselwörter: Single locus-Sonden – Meiosen – Mutationsraten

Introduction

In parentage testing aberrant inheritance of blood groups occurs unexpectedly and may result in false conclusions, especially in false exclusions of putative fathers. Blood group serologists have been aware of such pitfalls for many years because they have experienced highly unexpected parent/child combinations in all conventional blood group systems [1, 3–6, 10–13, 15, 16, 18–22, 24, 27–30, 33–36, 38–45, 48–50, 54, 56, 57, 59, 60, 62–64, 66].

Aberrant inheritances may be caused by:

"silent" alleles,
mutations due to base exchanges,
unequal cross-overs or
deletions.

Of these, silent alleles are the most common cause of false parent/child exclusions. The alleles Fy*0 and Fy*X [9, 31, 37] contribute most frequently to the "silent allele series". Both variants are usually grouped under the term Fy*0, which is reported to occur in Germans at a frequency between 1.6% and 3.0% [51, 53, 55, 61]. This shows that the number of exceptions from the expected mode of inheritance is quite high. Nevertheless, the Duffy blood groups are not only commonly used in parentage testing, they are also explicitly recommended [8]. In contrast, there have been many warnings against the use of DNA polymorphisms [46]. It has been pointed out, that DNA polymorphisms should only be used in addition to the entire battery of conventional polymorphisms [46]. One argument was the "unknown, however considerably high number" of mutations at VNTR loci. In response to this lack of logic, this paper aims at reporting paternal and maternal mutation rates observed

at 5 VNTR loci. This paper will also present the implications of the occurrence of a mutation in a paternity case. Studies of 2 extraordinary families with mutations will also be described.

Mutations and methods

All the persons tested (single individuals, multi-member families, and persons involved in paternity cases) were Caucasians.

In parentage cases, paternity was established by conventional hemogenetic tests ($W \geq 99.8\%$ at a given a priori of 0.5) while non-paternity was concluded on the basis of at least 2 exclusions. Techniques for DNA isolation, endonuclease digestion, electrophoresis and hybridisation have been described elsewhere [25]. The mobility of fragments was measured independently on autoradiographs by 2 staff members using a digitising tablet. Fragments differing in mobility by 0.5 mm could be resolved. The so-called "local method" was used, which means that the next neighbouring molecular weight markers were taken as references.

At least 815 meioses were examined in the *Hinf*I polymorphisms of loci D1S7, D7S21, D12S11, D7S22 and D2S44.

Definition of a mutation at a DNA locus

Germline length mutations at human DNA loci have been directly measured in human pedigrees [32, 52]. Mutations are sporadic. With the (here reported) exception of locus D7S21, they may occur with similar frequencies in both sexes. They can involve the gain or loss of numbers of repeat units, consistent with length changes arising primarily from unequal exchange at meioses [32, 65]. A further cause of length changes are point mutations at restriction sites producing either "new" sites or destroying "old" sites.

If in serologically established families one single restriction fragment of a child could not be exactly attributed to either parent by visual comparison in a side-by-side run we have declared this a mutation, regardless of whether the respective difference of size measurement was within the range of our standard deviation of 1.8% or not.

Results

I. Mutation rates

Table 1 shows the number of investigated meioses along with the respective mutation rates.

Since mutations involving changes of less than 100 bp cannot always be reliably resolved in electrophoresis systems, the true mutation rate, especially at locus D1S7 (repeat length: 9 bp), is presumably higher than the rate shown in Table 1.

II. Comparison of paternal and maternal mutation rates

Although the data show differences between maternal and paternal mutation rates, only the mutation rates observed at locus D7S21 revealed significant differences between paternal and maternal meioses. The Chi-square test revealed a significant difference between both sexes ($\hat{\chi}^2 = 11.3 > 9.550 = \chi^2_{0.001}$). This difference was also confirmed by means of Fisher's exact method. It is interesting that there is no significant difference between paternal and maternal mutation rates with locus D1S7 which has the highest overall number of mutations.

Table 1. Meioses and mutation rates observed at 5 VNTR loci

Locus	Maternal meioses			Paternal meioses		
	Total	Mutated	% Mutated	Total	Mutated	% Mutated
D1S7	1116	45	4.03	866	36	4.16
D7S21	1127	2	0.18	877	13	1.48
D12S11	1123	1	0.09	870	5	0.57
D7S22	1115	2	0.18	865	6	0.69
D2S44	471	1	0.21	344	0	0.00

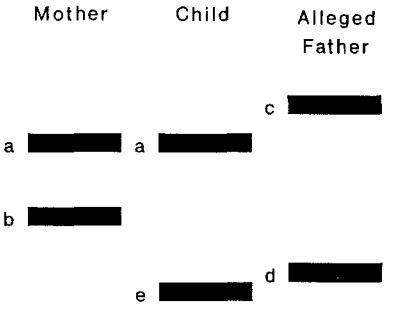

Fig. 1. Mutation band-pattern

Comparisons with other studies [7, 32, 52] show that the uneven distribution of mutations at locus D7S21 has not been observed before even though this observation was not unexpected. A female's complement of oocytes arise through approximately 24 postzygotic cell divisions whereas approximately 400 divisions separate the male zygote from mature sperm [58]. This explanation, however, does not imply that there may not also exist DNA loci having an excess of maternal "errors" [14].

III. Calculation of likelihoods

1. Theoretical considerations. Figure 1 illustrates a typical "exclusion" or "mutation" fragment pattern from a locus-specific DNA polymorphism. To calculate the likelihood of paternity, the possibility of a mutational event must be included in the genetic model [17]. It is assumed, that an allele x may change (it's fragment size) to an allele y, while being transmitted from parent to child; m_{xy} may denote the probability of such an event. Including this possibility, several explanations for the above band pattern are rendered possible under the assumption of paternity. One (unlikely) possibility is, that allele b is transmitted from the mother to the child and changes to allele e, while c is transmitted from the father to the child by changing into allele a. The probability of this event is $\frac{1}{2} m_{be} \cdot \frac{1}{2} m_{ca}$. This event is highly unlikely, because not only 2 mutations are required but also because mother and child obviously carry the allele a.

Table 2. Possible explanation of the fragment pattern

Maternal fragment → filial fragment	Paternal fragment → filial fragment	Transmission probability
$a \rightarrow a$	$c \rightarrow e$	$\frac{1}{2} \cdot \frac{1}{2} m_{ce}$
$a \rightarrow a$	$d \rightarrow e$	$\frac{1}{2} \cdot \frac{1}{2} m_{de}$

The likelihood for the fragment pattern under the assumption of paternity can therefore be calculated as

$$X = \underset{\text{mat. phenotype}}{2f(a)f(b)} \cdot \underset{\text{pat. phenotype}}{2f(c)f(d)} \cdot \underset{\text{transm. prob.}}{\frac{1}{2} \cdot \frac{1}{2}} (m_{ce} + m_{de}).$$

The likelihood under non-paternity can be calculated as

$$Y = 2f(a)f(b) \cdot 2f(c)f(d) \cdot [f(e)\,\tfrac{1}{2}(1 + m_{ba}) + f(a)\,\tfrac{1}{2}(m_{ae} + m_{be})]$$
$$\approx 2f(a)f(b) \cdot 2f(c)f(d) \cdot f(e) \cdot \tfrac{1}{2}.$$

Consequently, the likelihood ratio is

$$Y/X = \frac{2f(e)}{m_{ce} + m_{de}}.$$

If all possibilities requiring more than one "mutation" are considered negligible due to low probability, only 2 relevant explanations remain (Table 2).

The problem with this formula is that for various reasons the mutation rate of a specific allele cannot be estimated. However the rate is far smaller than the overall mutation rate summarized in Table 1. Additionally, one has to take into account, that the term "mutational event" encompasses different origins of the length variations. Small variations in the fragment size may occur more often than larger ones. Restriction site mutations are believed to be less frequent than length changes within the minisatellite [65].

In order to evaluate this type of fragment pattern in terms of likelihood ratios, one has to choose a less specific approach. A mutation rate, that can be estimated for a locus specific DNA polymorphism is the overall mutation rate μ, which may differ from the maternal mutation rate. More precisely, μ is the probability of the occurrence of a "mutated" fragment under paternity. At this level, only one fact is drawn from the fragment pattern: either the pattern is compatible with paternity or not. The frequencies of the involved "alleles" (= fragments) are not taken into account, and the resulting likelihoods are the same for all "mutation patterns" for a given enzyme/probe combination.

Under non-paternity the probability of a "mutation pattern" is $1 - r$, where r is the probability of an (wrong) inclusion. r can be estimated from empirical data [25].

The likelihood ratio which can then be calculated is

$$Y/X = \frac{1 - r}{\mu} \text{ [17].}$$

2. Application to paternity tests. This method was applied to data for the loci D1S7, D7S21, D12S11, D7S22, and D2S44 (probes MS1, MS31, MS43, G3, and YNH24, respectively).

The observed paternal mutation rates and "wrong inclusion" probabilities are summarized in Table 3.

Table 3. Estimation of μ and r, likelihood values

Locus	Probe	n	μ%	r%	Y/X	EM	W%
D1S7	MS1	866	4.16	2.13	23.53	11.37	4.08
D7S21	MS31	877	1.48	5.31	63.98	11.81	1.54
D12S11	MS43	870	0.57	6.74	163.61	12.21	0.61
D7S22	G3	865	0.69	2.42	141.42	12.15	0.70
D2S44	YNH24	344	0	7.51	*	*	*

* Calculation not possible until a paternal mutation is observed

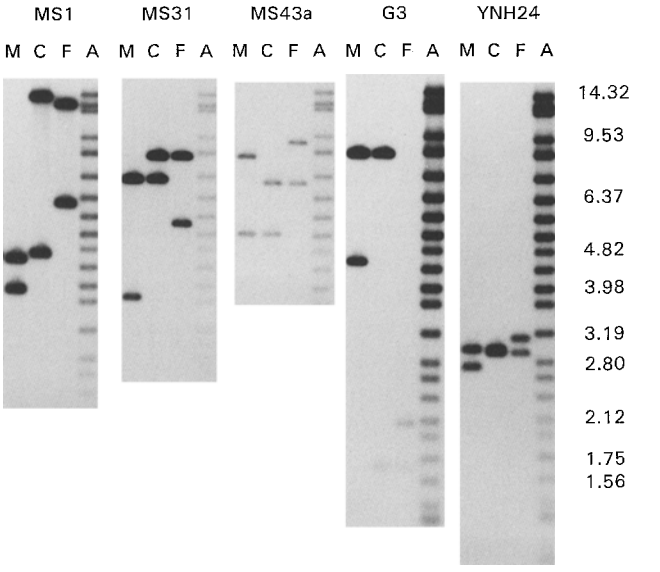

Fig. 2. Example of a double mutant offspring. Both parental fragments at locus D1S7 (MS1) are mismatched, while the offspring fragments (C) at loci D7S1, D12S11, D7S22, and D2S44 match correctly the mother (M) and the father (F). (Molecular weight marker is in *lane A*)

Locus D1S7 shows the highest mutation rate in both sexes, while, as has often been reported, this locus produces the smallest number of false inclusions (~2%) [25, 52].

Table 3 shows that a small mutation rate leads to an increase of evidence against paternity, once an "exclusion pattern" is observed.

IV. Family studies with unusual observations

Case 1: Figure 2 illustrates the occurrence of 2 parental mutations at locus D1S7 (probe MS1).

Both parental fragments at locus D1S7 (probe MS1) are mismatched, while the offspring fragments (C) at loci D7S21, D12S11, D7S22, and D2S44 match correctly the mother (M) and the father (F); molecular weight standards (A).

Case 2: Figure 3 illustrates the occurrence of 2 paternal mutations at loci D7S21 and D7S22 (probes MS31 and G3).

In this family 12 conventional blood group systems (ABO, MNSs, Rhesus, Duffy, Gc, Tf, Pi, acP, PGM_1,

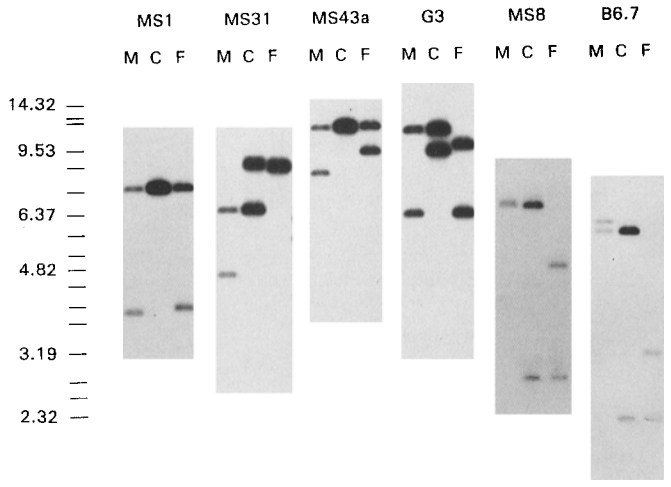

Fig. 3. Example of a double mutant offspring. Both paternal fragments with probes MS31 and G3 are mismatched, while the offspring fragments with probes MS1, MS8, MS43a, YNH24, and B6.7 match correctly the father. (M = mother, C = child, F = father, A = molecular weight marker)

GPT, EsD, and GLO) were initially tested. The "alleged" father could not be excluded from paternity (EM = 7.1643 ≙ W = 99.85%; PI: 685; A = 99.7%). The additional results obtained with 7 VNTR probes were as follows (sizes of restriction fragments given in kilobases = kb)

Locus	Probe	Child	Mother	Alleged father
D1S7	MS1	7.6/ –	7.6/4.0	7.6/4.1
D7S21	MS31	**8.6**/ 6.5	6.5/4.7	8.5/–
D7S22	G3	**9.8**/11.5	11.5/6.5	10.2/6.5
D12S11	MS43	11.1/11.0	11.0/7.9	11.1/9.2
D5S43	MS8	2.8/ 6.7	6.7/–	2.8/4.9
D2S44	YNH24	3.8/ 3.4	3.4/2.7	3.8/1.8
	B6.7	2.3/ 5.8	5.8/6.1	2.3/3.2

The paternal *Hinf*I fragments generated with probes MS31 and G3 showed slight mismatches, which we interpreted as mutations. The overall statistical evaluation (which includes the apparent "exclusions" with loci D7S21 and D7S22) of this case is as follows:

EM (blood groups) = 7.1643 ≙ W = 99.8%
EM (MS1) = 8.5821 ≙ W = 96%
EM (MS31) = 11.8060 ≙ W = 1.54%
EM (G3) = 12.1505 ≙ W = 0.70%
EM (MS43) = 8.8943 ≙ W = 92.5%
EM (MS8) = 8.9777 ≙ W = 91.3%
EM (YNH24) = 9.0645 ≙ W = 89.6%
EM (B6.7) = 8.7243 ≙ W = 94.97%
EM (total) = 5.3637 ≙ W = 99.998%

The occurrence of 2 mutant paternal fragments is said to be rare [2]. Taking the mutation rates for loci D7S21 and D7S22 into account, the probability that both genetic systems would produce false exclusions is

$$\frac{1}{\frac{1}{1.48\% \times 0.69\%}} = 0.010\% \text{ or approx. 1 in 10,000 cases with true fathers.}$$

It has been proposed in "DNA recommendations" that probe MS1 should not be used in paternity tests because of its high mutation rate. However, if this proposal were followed, a lot of information in the vast majority of non-exclusions would be lost (high probability values in inclusions, and smallest number of false inclusions).

It is of interest to estimate the probability of two paternal mutations (in one case).

The respective calculation for probes MS1, MS31, MS43a, and G3 would be as follows (probe YNH24 is not mentioned in this context, because we did not observe a paternal mutation up to now):

MS1	MS31	MS43a	G3	
0.0416	0.0148	0.9943	0.9931	0.0006079
0.0416	0.9852	0.0057	0.9931	0.0002320
0.0416	0.9852	0.9942	0.0069	0.0002812
0.9584	0.0148	0.0057	0.9931	0.0000803
0.9584	0.0148	0.9943	0.0069	0.0000973
0.9584	0.9852	0.0057	0.0069	0.0000371

The calculation would result in a total probability of 0.001336 or 0.13%.

By omitting probe MS1 from the programme one would reduce the possibility of such an event to a total probability of 0.02%. This study provides a further argument that it is unrealistic to expect that conventional blood group markers can be entirely replaced by DNA polymorphisms. As we and others have already demonstrated in recent publications, a large battery of blood group systems, protein/enzyme markers, the HLA-antigens and DNA polymorphisms may be required to solve problematic cases [23, 24, 26, 47]. Abandonment of a major part of established hemogenetic tools is counterproductive to scientific progress. "Improvement" of technology must not result in the impossibility to resolve difficult cases.

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References

1. Alper CA, Klemperer MR, Rosen F (1969) Inherited deficiency of the third component of human complement (C'3). J Clin Invest 48:553
2. Balazs I, Baird M, Clyne M, Meade E (1989) Human population genetic studies of five hypervariable DNA loci. Am J Hum Genet 44:182–190

3. Beckers TH, Loghem JJ van, Dunsford I (1955) A second example of the weak antigen A, occurring in the offspring of group 0 parents. Vox Sang 5:145
4. Bender K, Kasulke D, Mayerovà A, Hummel K, Weidinger S, Epplen JT, Wienker TF (1991) New mutation versus exclusion at the alpha-1-antitrypsin locus: a multifaceted approach in a problematical paternity case. Hum Hered 41:1–11
5. Bertrams J, Mauff G (1986) A silent allele of properdin factor B polymorphism (Bf*Q0) in five family members. In: Brinkmann B, Henningsen K (eds) Advances in forensic haemogenetics 1. Springer, Berlin Heidelberg, pp 93–96
6. Brinkmann B, Hoppe HH, Sachs H-W, Weber W, Heide KG (1974) Über das Vorkommen des stummen Allels P in 10 deutschen Familien. Z Rechtsmed 75:25–32
7. Brinkmann B, Rand S, Wiegand P (1991) Population and family data of RFLP's using selected single- and multi-locus systems. Int J Leg Med 104:81–86
8. Bundesgesundheitsamt (1990) Neufassung der Richtlinien des BGA für die Erstellung von Blutgruppengutachten. Bundesgesundheitsblatt 33(6):264–268
9. Chown B, Lewis M, Kaita H (1965) The Duffy blood group system in Caucasians: evidence for a new allele. Am J Hum Genet 17:384
10. Cook PJL, Robson EB, Buckton KE, Jacobs PA, Polani PE (1974) Segregation of genetic markers in families with chromosome polymorphisms and structural rearrangements involving chromosome 1. Ann Hum Genet 37:261
11. Crome W (1935) Über Blutgruppenfragen: Mutter M, Kind N. Dtsch Z Ges Gerichtl Med 24:267
12. Dodd BE, Lincoln PJ, Insley J (1983) An apparent exclusion of maternity disclosed by tests for Rh and PGM_1. 10. Internationaler Kongreß der Gesellschaft für Forensische Blutgruppenkunde, München, 11.–15.10., pp 131–134
13. Dykes DD, Polesky HF (1988) Incidence of the PLG*Q0 allele in human populations. In: Mayr WR (ed) Advances in forensic haemogenetics 2. Springer, Berlin Heidelberg, pp 261–266
14. Eggermann T, Nöthen M, Erdmann J, Eiben B, Ahlert D, Propping P, Schwanitz G (1991) Parental origin of the extra chromosome in trisomy 18 determined using short sequence repeat DNA polymorphisms. Abstract 4. Tagung der Gesellschaft für Humangenetik, p 269
15. Espinheira RM, Geada H, Mendonça M, Reys L (1988) "Silent" alleles in paternity testing. In: Mayr WR (ed) Advances in forensic haemogenetics 2. Springer, Berlin Heidelberg, pp 254–258
16. Fiedler H, Pettenkofer H (1968) Ein „neuer" Phänotyp im Isoenzymsystem der Phosphoglucomutasen des Menschen (PGM_10). Blut 18:33
17. Fimmers R, Henke L, Henke J, Baur MP (1992) How to deal with mutations in DNA testing? In: Rittner C, Schneider PM (eds) Advances in forensic haemogenetics 4. Springer, Berlin Heidelberg, pp 285–287
18. Francis BJ, Hatcher DE (1966) MN blood types: The S−s−U+ and the M_1 phenotypes. Vox Sang 11:213
19. Gianetti M, Stadler E, Rittner C, Lomas C, Tippett P (1983) A rare Rh haplotype producing C^w and c, and D and e in a German family. Vox Sang 44:319–321
20. Habibi B, Andre J, Fouillade MT, Lopez M, Salmon C (1976) An unusual Rh phenotype indicating heterogeneity of the C^w antigen. Vox Sang 31:103–108
21. Haselhorst G, Lauer A (1930) Über eine Blutgruppenkombination Mutter AB und Kind 0. Zeitschrift für Konstitutionslehre 15:205
22. Heiken A, Giles CM (1967) Evidence of mutation within the Rhesus blood group system. Nature 213:699
23. Henke J, Baur MP, Hoffmann K, Henke L (1991) Zur Anwendung aussagekräftiger Single Locus DNA-Polymorphismen in komplizierten defizienten Abstammungsbegutachtungen. Ärztl Lab 37:175–179
24. Henke J, Schweitzer H, Cleef S, Epplen JT, Baur MP (1988) Aberrant MN bloodgroup inheritance in a German family: a 'silent' allele? Forensic Sci Int 39:279–285
25. Henke L, Cleef S, Zakrzewska M, Henke J (1991) Population genetic data determined for five different single locus minisatellite probes. In: Berg T, Jeffreys AJ, Wolff R, Dolf G (eds) DNA fingerprinting: approaches and applications. Birkhäuser Verlag, Basel
26. Henke L, Paas H, Hoffmann K, Henke J (1990) Zum Einsatz von DNA-Polymorphismen in der Abstammungsbegutachtung. Z Rechtsmed 103:235–248
27. Henningsen K (1958) A family study involving a new rare Rh chromosome (d−− or −−−). VIIth Congress of the International Society of Blood Transfusion, Rome. Karger, Basel, p 667
28. Herbich J, Fisher RA, Hopkinson DA (1970) Atypical segregation of human red cell acid phosphatase phenotypes: evidence for a rare silent allele p°. Ann Hum Genet 34:145
29. Hoppe HH, Goedde HG, Agarwal DP, Benkmann HG, Hirth L, Janssen W (1978) A silent gene (C3−) producing partial deficiency of the third component of human complement. Hum Hered 28:141
30. Ishimori T, Hasekura H (1967) A Japanese with no detectable Rh blood group antigens due to silent Rh alleles or deleted chromosomes. Transfusion 7:84
31. Issitt PD (1985) Applied blood group serology, 3rd edn. Montgomery Scientific Publications, Miami
32. Jeffreys AJ, Royle NJ, Wilson V, Wong Z (1988) Spontaneous mutation rates to new length alleles at tandem repetitive hypervariable loci in human DNA. Nature 332:278–281
33. Jungwirth J (1967) Problematische Rhesusausschlüsse. Dtsch Z Ges Gerichtl Med 59:164
34. Kaita H, Lewis M, Chown B, Gard E (1959) A further example of the Kell blood group phenotype K−, k−, Kp(a−b−). Nature 183:1586
35. Krauland W, Smerling M (1970) Reinerbigkeitsausschlüsse SS/ss. Ärztl Lab 16:98
36. Levine P, Celano MJ, Falkowski F, Chambers J, Hunter OB, English CT (1964) A second example of −−−/−−− blood, or Rh_{null}. Nature 204:892
37. Lewis M, Kaita H, Chown B (1972) The Duffy blood group system in Caucasians. Vox Sang 23:523
38. Madsen G, Heistö H (1968) A Korean family showing inheritance of A and B on the same chromosome. Vox Sang 14:211
39. Matsunaga E (1962) An inert allele Hp° at the Hp locus. Jpn J Hum Genet 7:133
40. Mauff G, Rittner C (1982) Joint report on C3, Bf and C6 reference typings. IV. Int Workshop for the Genetics of Complement, Boston
41. Metaxas MN, Metaxas-Buehler M (1977) Genetik des MNSs-Blutgruppensystems. 7. Internationaler Kongreß der Gesellschaft für Forensische Blutgruppenkunde, Hamburg, pp 103–118
42. Polesky HF, Souhrada JM, Dykes DD (1983) The frequency of "null" genes calculated from trios in disputed parentage cases. 10. Internationaler Kongreß der Gesellschaft für Forensische Blutgruppenkunde, München, pp 161–166
43. Prokop O, Rackwitz A (1968) Beweis für die Existenz eines neuen Gc-Gens, aufgedeckt durch eine anscheinend inkompatible Mutter-Kind-Paarung. Dtsch Z Ges Gerichtl Med 62:261
44. Püschel K, Krüger A, Söder-Bräunlich R (1988) Further evidence of a silent Tf allele. In: Mayr WR (ed) Advances in forensic haemogenetics 2. Springer, Berlin Heidelberg, pp 259–260
45. Rasmuson M, Heiken A (1966) Frequency of occurrence of the human Rh complexes D(c)(e), d(c)(e), D−−, and −−−. Nature 212:1377–1379
46. Ritter H (1991) Die humangenetische Abstammungsbegutachtung. Familienrichterzeitung 6:646–649

47. Rittner C, Schneider PM, Rittner G (1992) Zum Beitrag des DNA-Gutachtens in Fällen mit verstorbenem Putativvater. Der Amtsvormund 65(2):105–114
48. Sachs HW, Reuter W, Tippett P, Gavin J (1978) A Rh gene complex producing both C^w and c antigen. Vox Sang 35:272–274
49. Schleyer F, Spielmann W, Oepen I (1973) Kombination von Rh Deletionstyp und stummem Fy-Gen. Beitr Gerichtl Med 30:389
50. Smerling M (1971) S^u in der weißen Bevölkerung. Bericht über Familienuntersuchungen. Beitr gerichtl Med 28:237
51. Smerling M (1976) Zur Serologie und Genetik des Duffy-Systems. Z Rechtsmed 78:121–135
52. Smith JC, Anwar R, Riley J, Jenner D, Markham AF, Jeffreys AJ (1990) Highly polymorphic minisatellite sequences: allele frequencies and mutation rates for five locus specific probes in a Caucasian population. J Forensic Sci Soc 30:19–32
53. Sorgo G, Piso C (1972) Das System Duffy: Genfrequenzen und Familienuntersuchungen. Blut 24:89–93
54. Speiser P, Pausch V (1977) GPT° in drei Generationen. Ärztl Lab 23:487–490
55. Spielmann W, Schilling L, Teixidor D (1968) Genfrequenzen und Vererbung im Duffy-System. Hum Genet 6:200–206
56. Tippett P (1977) Some recent observations in the Rh, Lutheran and Kell blood group systems. 7. Internationaler Kongreß der Gesellschaft für Forensische Blutgruppenkunde, Hamburg, pp 89–102
57. Trube-Becker E, Henke J (1981) Großmutter/Mutter/Kind-Inkompatibilität aufgrund des Rhesus-Genkomplexes (C)D(e). Z Morphol Anthropol 72(2):205–212
58. Vogel F, Rathenberg R (1975) Spontaneous mutation in man. Adv Hum Genet 5:223–318
59. Weber W (1988) Nachweis des „stummen" Gens PGP° am Phosphoglycolat-Phosphatase-Locus. In: Mayr WR (ed) Advances in forensic haemogenetics 2. Springer, Berlin Heidelberg, pp 250–253
60. Weissmann J, Oepen I, Hilgermann R (1979) Ein seltener Phänotyp: GPT 0. Ärztl Lab 25:229–231
61. Weissmann J, Swart J, Pribilla O (1982) Das Duffy-System: Genfrequenzen und Familienuntersuchungen in Schleswig-Holstein. Ärztl Lab 28:225–228
62. Wendt GG, Kirchberg G, Rube M, Ritter H (1971) Problematischer Mutter-Kind-Ausschluß mit PGM_1. Humangenetik 11:171
63. Wenk RE, Houtz TD, Brooks M, Bard K (1983) Unexpressed HLA haplotype and erroneous maternal exclusion. 10. Internationaler Kongreß der Gesellschaft für Forensische Blutgruppenkunde, München, pp 35–40
64. Wetterling G (1988) Discrepancy between gene and protein products within the PGM_1 system shown by improved resolution on immobiline gels. In: Mayr WR (ed) Advances in forensic haemogenetics 2. Springer, Berlin Heidelberg, pp 97–101
65. Wolff RK, Nakamura Y, White R (1988) Molecular characterization of a spontaneously generated new allele at a VNTR locus: no exchange of flanking DNA sequence. Genomics 3:347–351
66. Yokoyama M, Mermod LE, Stegmaier A (1967) Further examples of Jk(a−b−) blood in Hawaii. Vox Sang 12:15