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Application of Gm Typing in Cases of Disputed Paternity

What is the current status of employing human blood groups to exclude paternity? Dr. A. S. Wiener [*1*] believes that the problem of *qualification of experts* is still the main factor for forensic immunogenetics. In discussing exceptions to blood group inheritance and mutations, Dr. Wiener wrote that the problem of Bombay bloods, Rh null, M^g, etc. has had little effect—since the frequency is of the same order of magnitude as mutation which has always been with us.

Along the same line, Dr. Fred Allen [*2*] thinks that it may be wise in all cases to let the court know that you don't consider the blood grouping results as absolutely infallible because of the occurrence of rare exceptions to the rules. He points out that one should do as much testing as possible rather than limit it to ABO, Rh, and MN. One must, of course, indicate to the court the amount of experience that has been obtained with each system and the degree of reliance that one can place on it. In England and the Continent, most of the systems, including enzymes, are accepted for whatever evidentiary value they may contribute.

Statistics have been employed for estimating the nonpaternity rate by using blood group data on mother-husband-child trios. The maximum-likelihood method allows for the use of data on several blood group systems. The following assumptions have to be adopted in the computations even though they may not be absolutely correct [*3*]:

1. The women in the trio with the child is truly the mother of the child.
2. Unusual modes of gene transmission, unusual genes, and mutations are so rare they can be neglected.
3. There is no blood type misclassification.
4. The blood group systems are mutually independent.

Our purpose in this study was to reappraise the usefulness of the Gm markers of human IgG immunoglobulins as a basis for exclusion in cases of disputed paternity [*4–39*]. We determined the serum Gm types in 50 cases by using antisera for the Gm antigens Gm(a)

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Gm(b°), Gm(f), and Gm(g). In most of these cases, the blood groups had also been established.

Materials and Methods

The Gm factors are genetically determined antigens on human IgG (γG) immunoglobulin heavy chains. IgG is only one of 5 different molecular classes of immunoglobulin. By now, more than 20 factors have been described in the Gm system. Table 1, from Giblett [*40*], *Genetic Markers in Human Blood*, lists the original names of the antigen systems we used, the new World Health Organization (WHO) names assigned to them, and notes the credit of discovery.

It has been firmly established that the Gm factors are inherited as autosomal dominant traits. The character is thus expressed no matter whether a subject is heterozygous or homozygous for that factor. Gm typing is performed by an agglutination-inhibition method involving 3 components. Component 1 is an Rh-positive indicator cell which has been coated with IgG—ordinarily from a serum containing incomplete anti-Rh antibodies. Component 2 is the specific anti-Gm antibody, usually from an immunized human or animal. We have used sera from rabbits and baboons. These test components are adjusted so that strong agglutination will occur but the reaction is not in antibody excess. Upon mixing the third component (unknown serum) with Component 2, the presence of a specific Gm antigen in that unknown serum will neutralize the antibody of Component 2, thereby inhibiting agglutination of the indicator cell. This is a positive test.

Absence of the specific antigen in the unknown, of course, permits the antibody to agglutinate the indicator cell. A model for these reactions (Fig. 1) describes Giblett's concept of how the test system works.

The relationships between the Gm factors and the different subclasses of heavy chain IgG is still being argued. Accepted, however, is the fact that groups of Gm factors are

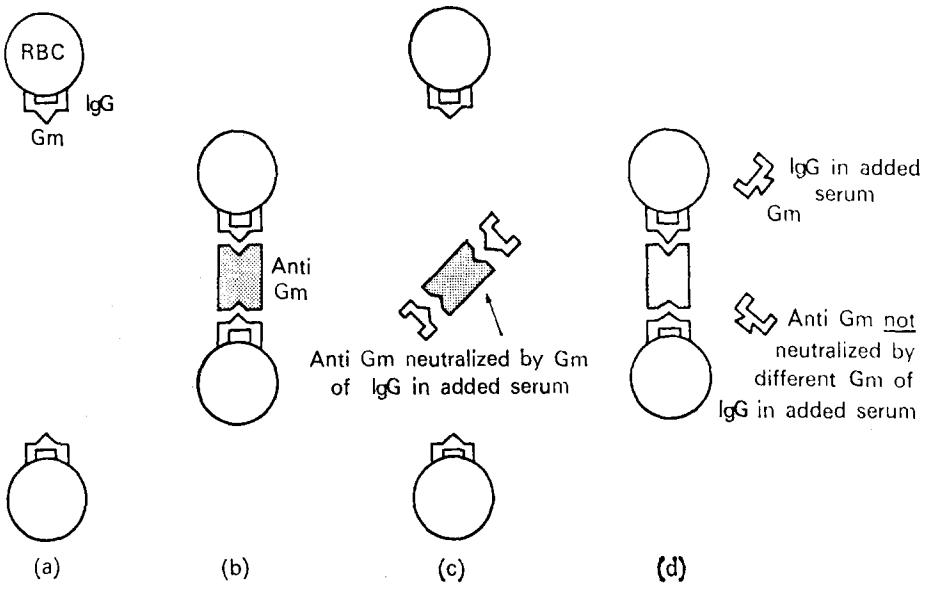

FIG. 1—*Genetic markers in human blood as described by Giblett.*

IgG	Caucasoid	Negroid	Mongoloid
αG1	a	a	a a a
	z f	z	f z z
αG3	g b	b	b g b

Tested only with anti-Gm(a), -Gm(b°), - Gm(f), and -Gm(z)

FIG. 2—*Racial distribution of Gm phenogroups arranged by heavy chain (IgG) subclass.*

genetically transmitted as single units probably as a group of closely linked loci. These groups of Gm factors are called *gene complexes* or *phenogroups*, and different phenogroups are characteristic of different racial groups. Thus, in addition to the stable autosomal dominant mode of inheritance, a second useful feature of the Gm system results from these racial differences and accounts for their ability to show the source of each gene in progeny from parents of different racial mixtures. Figure 2 indicates the major phenogroups for each race arranged in vertical sets of Gm factors. The two major phenogroups shown for caucasians are isoallelic to each other. Normal subjects may, therefore, be homozygous for either allele or heterozygous for the pair. Negroids have a single major phenogroup and although the *same* markers are found in caucasoids, the combinations differ; that is, Gm a,b negroid versus Gm a,g or f,b caucasoid. The frequency among negroids of Dakar for Gm (azb) for example, is 98 percent; while the most common caucasoid gene complex, Gm (azg), has a frequency of only about 60 percent in Europe and America. There are also characteristic phenogroups among mongoloids producing even clearer segregation than occurs in caucasian populations.

From the foregoing, we believe it is evident that the rules for the inheritance of Gm factors are similar to those for the blood groups.

Rule 1 states "A child cannot have a Gm factor unless that factor is present in one parent." Rule 2: "A child must have any Gm factor for which either parent is homozygous. Rule 3: "Gm phenogroups are transmitted as a unit."

Results

Figure 3 shows the pedigree of a Gm exclusion based upon Rule 1, and Fig. 4 an exclusion based upon Rule 3. Table 2 presents our results. Fifty cases were tested for Gm factors, and five (10 percent) alleged fathers were excluded. Thirty-three of these 50 cases were also tested for blood groups, and four (12 percent) alleged fathers, none among the five excluded by Gm tests, were shown incapable of being the biologic fathers of these children.

TABLE 1—*Subclasses of IgG (from Giblett* [40]).

Present Name	Previous Nomenclatures[a] (1) (2) (3)	Proportion of Total IgG in Serum
IgG_1	We γ2b C	0.70
IgG_2	Ne γ2a	0.18
IgG_3	Vi γ2c Z	0.08
IgG_4	Ge γ2d	0.03

[a] (1) Grey and Kunkel, 1964; (2) Terry and Fahey, 1964; (3) Ballieux et al, 1964.

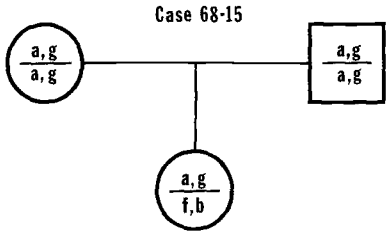

FIG. 3—*Paternity exclusion by Rule 1.*

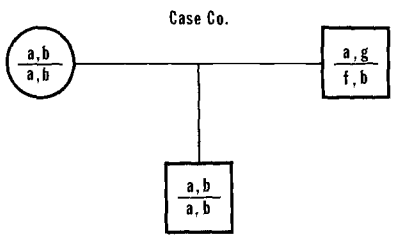

FIG. 4—*Paternity exclusion by Rule 3.*

TABLE 2—*Use of Gm types and blood groups in 50 cases of disputed paternity.*

Method	Families Tested	Gm Types	Paternity Excluded By Blood Groups	Percent
Gm Types	50	5[a]		10
Blood Groups and Gm Types	33		4	12
TOTAL	50		9	18

[a] Four of these also tested by blood groups.

Discussion

The practical use of Gm typing poses certain problems and emphasizes a number of advantages. Among the problems: It is necessary to understand and observe general technics for testing serum proteins. As in *any* serologic system, carefully selected controls, both positive and negative, should be included in each typing experiment. Under certain conditions if the serum IgG levels are low or absent, erroneous conclusions may result. Most important are the age of a child and whether one may be dealing with congenital or acquired immune deficiencies. Serum electrophoresis and immunodiffusion tests can easily establish the immunoglobulin levels. Normally low IgG levels in young children can still be accurately tested if appropriate weaker controls are included in these panels. It must also be remembered that maternal, rather than endogenous IgG is high during the first 15 weeks of life. The procedure is thus best delayed until a child is at least six months of age.

On the advantage side: The method is reliable and reproducible. It will detect about one-third[4] of falsely accused men. Since the inheritance of the Gm factors is independent of blood group systems, all or most of these additional exclusions are additive. Gm typing is particularly useful when samples have to be transported long distances or stored for long intervals and then retested. Under these circumstances, serum is far more easily handled than blood.

Summary

The use of Gm typing provided about twice as many genetic exclusions in a group of 50 cases of disputed paternity as could be excluded by blood groups alone. Serum genetic markers such as Gm have a valid and useful place in the solution of forensic problems.

[4] The exact value is elusive because of different degrees of racial admixture in the American population.

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