

The M quadruplets:

I. Probability of uniovular origin judged from qualitative traits

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The M girl quadruplets were born in Lansing, Michigan, on May 19, 1930. Objective evidence relating to the number of zygotes or fertilized eggs from which they may have arisen has been published by Clarke (1932), Pryor (1936), MacArthur and MacArthur (1937), and Gardner and Newman (1943). These authors were convinced that the girls were monozygotic in origin. I shall here review the old and new evidence relating to zygoty and shall then employ data on simple or discontinuous hereditary traits in an attempt to assess the probability that the girls are monozygotic.

While dizygotic (DZ) twins and larger numbers of genetically different birth mates can usually be shown to have some simple hereditary difference, no equally simple and conclusive evidence can be obtained to confirm a monozygotic (MZ) relationship. Except when tissue grafts can be shown to grow permanently, or when a common chorionic membrane has been demonstrated, the diagnosis of genetic identity must rest on subjective evaluation or on calculated probabilities. The currently available methods of computing probability lack empirical validation, but their potential usefulness in twins seems to be great. Extension of the methods to higher orders of plural birth is desirable because single sets of triplets, quadruplets or quintuplets are often the subject of extensive research efforts, calling for particular attention to the zygoty diagnosis. The present report illustrates problems that arise in the application to quadruplets of methods of calculation devised for twins. The paper to follow, concerning quantitative differences in this set of quadruplets, will illustrate an additional extension of the twin type of calculations, and will suggest one approach to the problem of genotypic differences in variability, so difficult to attack in human genetics.

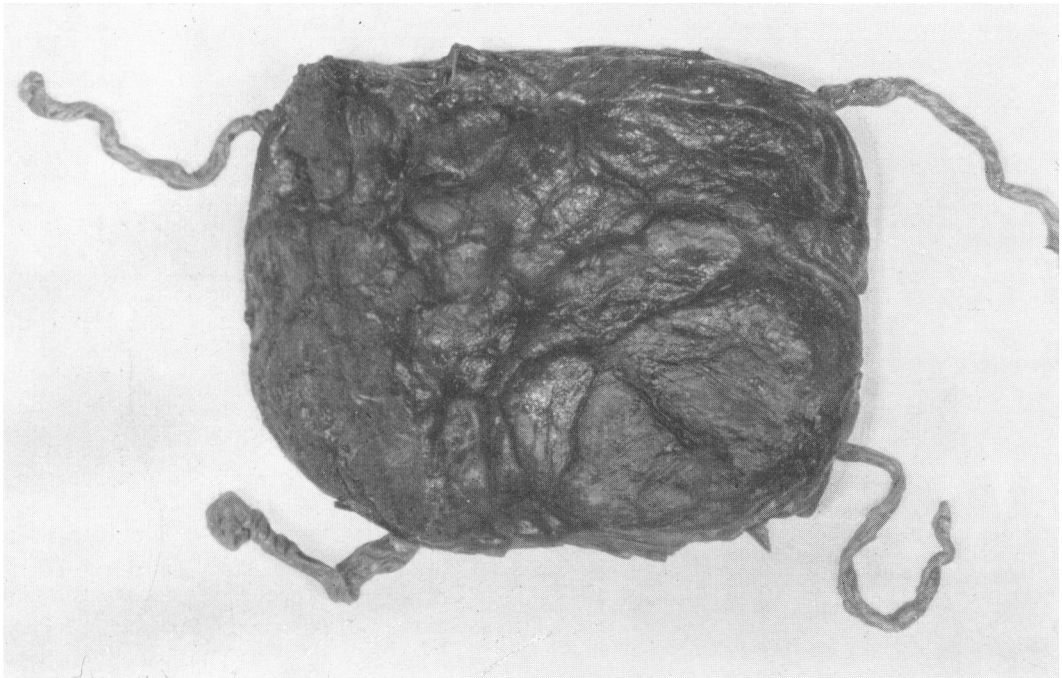


Fig. 1. Maternal aspect of the placenta

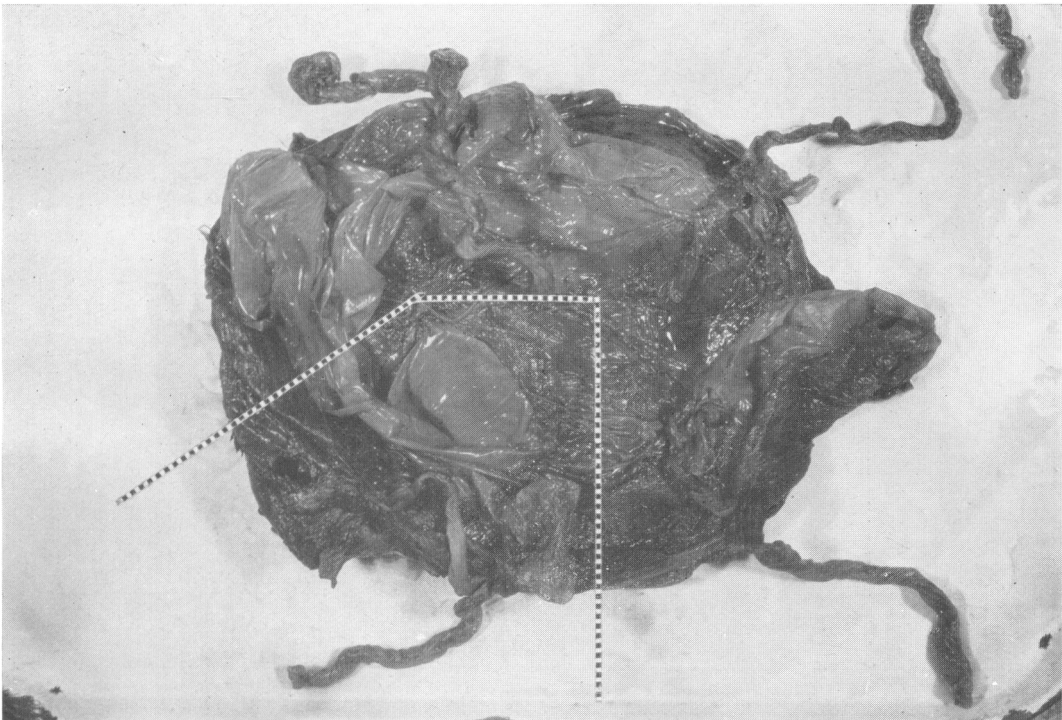


Fig. 2. Foetal aspect of the placenta. Broken line indicates area diagrammed in fig. 3

Observations relating to zygosity

PLACENTA AND FETAL MEMBRANES

Clarke (1932) stated that the physician who attended the delivery described the placenta as monochorial. Recent attempts to locate the placenta have been unsuccessful. However, it was originally photographed from both aspects by Dr. Russell J. Himmelberger, who kindly consented to use of the pictures (Figures 1 and 2). Figure 2 shows a flap of thick membrane across the lower right corner, isolating

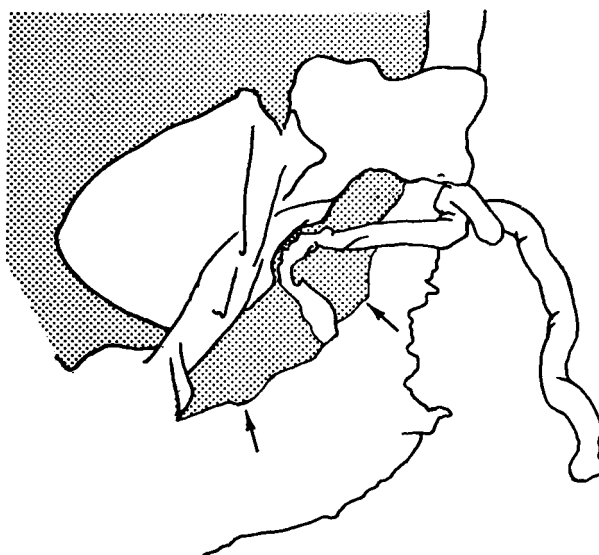


Fig. 3. Diagram of portion of placenta to show septum or detached strip of chorion between one cord and the other three. Shaded area is interpreted as the floor of the amniotic sac or sacs

one cord. It is possible, however, that this apparent septum is merely a strip of chorion displaced from the margin of the placenta, and that the cord emerges through a rent as indicated in the drawing (Figure 3). The possibility can be ruled out that Figure 2 represents a second set of quadruplets, three girls and a boy, born in 1953 in the same hospital, because the twists and knots of the four cords correspond exactly to those in the picture of the maternal surface (Figure 1), which was published by Pryor in 1936.

The photographs support the belief that at least three of the girls shared one chorionic sac, and are not incompatible with the obstetrician's report that all four were within one chorion. Even if there were two chorionic sacs, a common zygotic origin would be possible.

SIGNIFICANCE OF CONCORDANCE IN SEX

If one egg is fertilized by one sperm, subsequent division of the embryo will produce genetically identical individuals, necessarily of the same sex. When two eggs are separately fertilized the probability is one-half that the zygotes will be of the same sex and one-half that they will be of different sex. Two subsequent divisions of these opposite-sex zygotes will result in quadruplets in either a 3 : 1 sex distribution or a 2 : 2 distribution, depending on whether one embryo divides twice or both embryos divide once. When three zygotes are formed initially, the probability is only one-fourth that both the second and third will have the same sex as the first. The subsequent single division of one of the early embryos required to produce quadruplets may again yield either a 3 : 1 or a 2 : 2 ratio of the sexes. Finally, if quadruplets originate from four separate eggs, the sex distribution will be random, with a probability of only one-eighth that they will all be of one sex.

The above reasoning may suggest that any given set of same-sex quadruplets is more likely to have originated from one than from two eggs, and much more likely from one than from 3 or 4 eggs, but this is not necessarily true. If four-egg quadruplet sets proved to be eight times as frequent as one-egg sets, the same-sex fraction of the former would be as numerous as the total of one-egg sets. *The relative numbers of MZ and other types of quadruplets are therefore of primary importance* in any estimate of probability of zygosity, and this will be discussed in the section on probability calculations. For the present, one can say only that sex of the M quadruplets is consistent with a monozygotic origin.

BLOOD ANTIGENS AND PTC TASTE REACTION

Serological tests were not employed in previous studies of these quadruplets. The present finding of similar reactions in eight blood group systems therefore affords

Table 1 - Blood Factors of the M Family

	ABO	Rh					MN	S	s	Fy ^a	K	JK ^a	Le ^a	P
		D	C	E	c	e								
Mother	O	+	+	O	O	+	M	+	+	+	O	+	O	O
Father	A	+	+	+	+	+	M	+	+	+	O	+	+	+
A	O	+	+	+	+	+	M	+	+	+	O	+	O	O
B	O	+	+	+	+	+	M	+	+	+	O	+	O	O
C	O	+	+	+	+	+	M	+	+	+	O	+	O	O
D	O	+	+	+	+	+	M	+	+	+	O	+	O	O

an impressive independent confirmation of the conclusions reached by the other investigators. The results of the tests are shown in Table 1. These tests were kindly done by Dr. P. Levine at the Ortho Research Laboratories, Raritan, N. J. Independent confirmation was obtained by Dr. Paul Schmidt in the Division of Biologics

Standards, National Institutes of Health, for ABO, MN, Duffy, Kell, and the first four Rh factors.

MacArthur and MacArthur (1937) studied taste reactions of the family with PTC paper, and found the girls and both their parents to be non-tasters. This result was confirmed in the present study with serial dilutions of PTC as prescribed by Harris and Kalmus (1950), except that waxed paper cups were substituted for glass tumblers. Neither parent could taste even the strongest concentration (1300 mg/L). One of the quadruplets, D, could reliably distinguish the third concentration from water, and the other three girls could distinguish the second concentration (650 mg/L). These thresholds are all well within the usual non-taster range. Since both parents are evidently homozygous non-tasters, all their offspring must be, also, and the test does not help to decide the zygosity of the quadruplets.

DERMATOGLYPHICS

In the original study by Clarke, palm and sole prints were obtained when the quadruplets were 8 months old. These were not adequate for detailed analysis, but Clarke was able to say that for all the girls, the left hand of each was more like the left hand of her sisters than it was like her own right hand. MacArthur and MacArthur

Table 2 - Ridge Counts of Finger Prints

	Left fingers					Total	Total	Right fingers				
	5	4	3	2	1			1	2	3	4	5
A	0-8	0-14	0-10	4-0	0-12	48	51	12-0	9-5	10-0	9-0	11-0
B	0-9	0-11	0-11	0-3	0-10	44	58	11-0	13-0	11-0	16-0	7-0
C	0-6	0-15	0-9	2-0	0-15	47	51	16-0	6-0	11-0	11-0	7-0
D	0-10	0-3	0-3	0-4	0-9	29	32	11-0	0-3	5-0	7-0	6-0

published good finger, palm and sole prints taken of the girls at age 6 years. Their counts of the fingerprints, subsequently confirmed by Gardner and Newman (1943a), are reproduced in Table 2. They concluded that "when these quadruplets are considered and compared as if they were six pairs of twins, they were found to differ only slightly more than do the average of seventy pairs of identical twins, and decidedly less than the average of as many fraternal twins".

The dermatoglyphics of the M quadruplets will be discussed at length in the paper on quantitative differences.

PIGMENTATION AND OTHER TRAITS

Early photographs and reports indicated a very close physical resemblance among the four girls. While this resemblance has diminished somewhat in adulthood, it

was still impressive when they were eighteen years of age (Figure 4). The best early description is again that of MacArthur and MacArthur, which we will quote at length.

“The four girls are practically quadruplicates in a great number of characters: they all have dark hazel eyes quite precisely matched both in color and patterns, the same long dark brown lashes, very fair complexion, and straight fair hair. The



Fig. 4. The M quadruplets at age 18

hair now resembles the father's, the mother's being dark and curly. The ears are remarkably similar and have the lobe free as in the mother, not attached as in the father. Other noticeable features are the breadth of the nose at the root, the similarity of the teeth, the lateral extent of the mouth and jaw, and the habitual slight parting of the rather thin lips. A first impression is that one might learn to distinguish

them by the somewhat rounder faces of A and D, and by the still marked (but apparently diminishing) differences in sizes...”.

As it happened, the differences in stature subsequently increased. However, even the increased differences observed by Gardner and Newman (1943) when the girls were 10 years old permitted these authors to say that the greatest difference was no greater than the average between one-egg twin pairs. At that age their heights were 133, 129, 132 and 126 cm. and their weights were 54, 51, 53 and 49.5 lbs. The close parallel between height and weight preserves a degree of similarity in body build greater than would be judged from either measure taken alone.

Cephalic indices given by Gardner and Newman were 70.6 for A, C and D and 73.9 for B.

All the girls were found by Pryor (1936) to have closely similar sequences of ossification of the bones of the wrist and hand. The sequences were the same in A as in B and also the same in C as in D. The differences between these pairs involved the two multangular bones and the navicular, which ossify at almost the same time. X-rays taken at age 21.8 months were made available to Dr. Nancy Bayley of this institute by Dr. L. W. Sontag of the Fels Research Institute. These show that maturation was in the same sequence as height and weight, that is, A was the most mature, while C, B and D followed in that order. Dr. Bayley estimated their developmental ages as 15, 13, 12 and under 11 months.

Finally, Pryor (1936, 1939) pointed out that all the girls had an extra epiphysis at the base of the second metacarpal bone. This variation is regarded as very rare by Pryor, but Caffey (1956) has found it in many normal children. Pryor reported finding the anomaly in both of a pair of siblings, so that concordance in this trait is not particularly strong evidence of genetic identity. This observation will be weighed more carefully in the following section.

Probability calculations

The foregoing evidence appears to establish genetic identity of the M quadruplets beyond any serious doubt, but in view of the rarity of identical quadruplets, further analysis seems warranted.

In recent years methods have been developed for attaching a probability figure to the diagnosis of monozygosity in twins (Essen-Möller, 1941; Smith and Penrose, 1955; Clark and Schull, 1955). To my knowledge, the attempt has not been made to apply such a method to higher orders of plural birth.

With respect to simple hereditary traits, the methods used for twins can be applied almost directly to quadruplets. For twins, the relative frequency of MZ and DZ types provides an initial relative probability, to be modified by the probabilities derived from hereditary traits. The method of Smith and Penrose, essentially the same as that of Essen-Möller, then begins by estimating the proportion of fraternal twins that are expected to be alike among those in which either has the trait concerned. The relative chance of drawing a concordant set from identical or fraternal

twins is given by the relative frequency of concordant identical or of concordant fraternal twins, respectively. With respect to simple hereditary traits, identical twins will all be alike, and the relative frequency of concordant identical twins may be taken as unity. The final estimate desired is the absolute probability, with respect to the trait, that the twins in question are dizygotic. This is the frequency of concordant fraternal twins (cD) among all concordant twins (cM + cD):

$$P_D = \frac{cD}{cM + cD} \quad (1)$$

The probability with respect to a trait is meaningless until combined with the initial relative probability.

Any useful probability estimate must be based on a number of traits combined, and for this purpose the figure required for either type of twins is the frequency of concordance with respect to *all* the traits concerned. This frequency is obtained as the product of the initial relative probability and the separate probabilities of concordance for individual traits, Π cD for Dz pairs and Π cM (usually 1) for MZ pairs:

$$P_D = \frac{\Pi cD}{\Pi cM + \Pi cD} \quad (2)$$

Zygoty diagnosis in twins faces only two alternatives. In the case of quadruplets, one, two, three, or four eggs must be considered, and the relative frequencies of these types of quadruplet are not known. They may be estimated, for the present problem, either from a theoretical model of the genesis of multiple embryos, or from the scant frequency data available in the literature. As it happens, these two approaches support each other well.

RELATIVE FREQUENCY OF QUADRUPLLET TYPES, THEORETICAL

Nichols (1952) found 114 sets of quadruplets in records of U. S. births from 1915 to 1948; 45 were of one sex, 43 had a 3 : 1 sex distribution, and 26 had a 2 : 2 sex distribution. The Chi-square test can be used in this problem to compare the goodness of fit of different models to Nichols' observations.

Newman and Gardner (1942) suggested that the four possible numbers of eggs occurred among quadruplets with equal frequency, but that when two eggs produce quadruplets it is always by two divisions of one egg, yielding three products of one egg and a single product of the other. In mixed-sex, two-egg quadruplet sets, therefore, there would always be three of one sex and one of the other. On these assumptions the probability of observing sex-concordance types in the numbers given by Nichols would be between five and ten per cent (Chi-square 5.13 with two degrees of freedom). The Newman-Gardner supposition that dizygotic sets are always of the 3 : 1 kind has already been violated by one case report (Sarkar, 1943), and if

this restriction is removed from Gardner and Newman's hypothesis, the probability of Nichols' data increases to between 20 and 30 per cent.

Another simple model with possible variations assumes that higher order plural births result from random occurrence and repetition of the two twinning mechanisms, both extra ovulation and division of zygotes (Allen and Firschein, 1957; Bulmer, 1958). This hypothesis requires that all zygotes be equally susceptible to division, including those resulting from previous divisions. In the form described by Allen and Firschein, the model leads consistently to an overestimate of the total of plural births; in the form described by Bulmer, it leads to an underestimate for quadruplets.

Allen and Firschein obtained the following formula, in which a is the relative frequency of one-egg twins, b the relative frequency of two-egg twins:

$$\text{Quadruplets} = 6a^3 + 6a^2b + 3ab^2 + b^3. \quad (3)$$

The successive terms represent the frequencies of one-egg to four-egg quadruplets, in that order. Since the frequency of DZ twins varies considerably with maternal age while that of MZ twins is almost constant, the relative values of a and b should be obtained for a maternal age group corresponding to that of the mother in question.

Mrs. M was 31 at the birth of the quadruplets, and this was her first pregnancy. According to Italian data published by McArthur (1953), the expected frequency of DZ twin confinements at this maternal age is 9.5 per thousand, that of MZ twin confinements, 3.7. These figures yield relative values of 2.57 and 1, which numbers may be used for b and a , respectively, in formula (3). This substitution leads to relative frequencies of 6, 15.4, 19.8 and 17.0 for the four zygosity types or, as proportions, .103, .265, .340 and .292. From these proportions and the theoretical probabilities of sex-concordance in each type, the probability of Nichols' observations is .70 (Chi-square .715).

The model described by Bulmer predicts the following proportions of zygosity types:

$$\text{Quadruplets} = a^3 + 3a^2b + \frac{3}{2}ab^2 + \frac{1}{6}b^3 \quad (4)$$

According to this formula, the class frequencies are .05, .36, .46, and .13, and the probability of Nichols' observations is a little less than 70 per cent (Chi-square .86). Allen and Firschein's model thus fits these quadruplet observations a little better than does Bulmer's. But the theoretical approach gives little reason for choosing between them.¹

¹ A method of estimating zygosity type frequencies directly from plural birth statistics will be explained in a future paper.

RELATIVE FREQUENCY OF QUADRUPLLET TYPES, EMPIRICAL

If the 114 quadruplet births reported by Nichols had all been classified as to ovularity, we should now have a very good estimate of the relative frequencies of the four zygotity types. I have found in the literature only 17 sets of presumably Caucasian race that can be classified with even slight confidence (Table 3). At least nine of these were studied by the classical anthropological methods, which could be expected to yield a decision for any set and to be unbiased to this extent. The other eight represent a selection from about 20 reports of those sets that happened to have a decisive combination of common fetal envelopes and sex differences, augmented in a few instances by strong resemblances or by blood group observations. The last eight cases are likely, therefore, to be somewhat biased in favor of lower orders of zygotity and in favor of discordant sex. The series cannot be regarded as a representative sample of quadruplets, but it seems to be the closest approach to such a sample now available.

The frequencies appearing in the table for two, three and four-egg quadruplets provide the best empirical estimates for these types. The two one-egg sets are of little value, because one of them is the set whose zygotity is here in question. However,

Table 3 - Reported Sets of Quadruplets for Which a Useful Diagnosis of Zygotity is Available. Method of diagnosis: R = resemblance or similarity method; S = sex; B = blood antigens; M = foetal membranes (two or more in a common chorion)

Definitive reference	Name or Location	Birth	Sex	Method of diagnosis	Number of zygotes			
					1	2	3	4
MacArthur and MacArthur 1937	Lansing	1930	♂+♂	R	X			
Gardner and Newman 1940a	Perricone	1929	♂+♂+♂+♂	R				X
Gardner and Newman 1940b	Keys	1915	♂+♂+♂+♂	R			X	
Schlaginhaufin	Gehri	1880±	♂+♂+♂+♂	R, S				X
Gardner and Newman 1942	Badgett	1939	♂+♂+♂+♂	R		X		
Gardner and Newman 1943	Kaspar	1936	♂+♂+♂+♂	R, S		X		
Sarkar 1943	Derner	1927	♂+♂+♂+♂	R, B		X		
Gardner and Newman 1944	Schense	1931	♂+♂+♂+♂	R, S				X
Walker 1947	Zarief	1944	♂+♂+♂+♂	R, S				X
Miettinen 1952	Jouppila	1951±	♂+♂+♂+♂	R, B, S			X	
Lancaster 1944	Brown	1941	♂+♂+♂+♂	M, S		X		
Lartigue and Prudent 1944	Bannalec	1943	♂+♂+♂+♂	M, R, S			X	
Ullery 1945	Philadelphia	1944	♂+♂+♂+♂	M, S		X		
Hartman et al 1949	Latrobe	1948	♂+♂+♂+♂	M, S		X		
Blechnann et al. 1950	La Celle Saint-Cloud	1948	♂+♂+♂+♂	R, B, S			X	
Walsh 1952	Bellingen	1950	♂+♂+♂+♂	B, S				X
Scarle 1953	Westminster	1950	♂+♂+♂+♂	M	X			
					2	6	4	5

the frequency of MZ sets can be obtained indirectly from the relative numbers of the other three classes, together with the sex-concordance data of Nichols. In Nichols' 114 sets 45, or 39.5 per cent, are unisexual. This unisexual group presumably includes, in addition to the unknown monozygotic sets, fractions of the other zygosity types with frequencies that can be estimated from Table 3. The proportion of MZ sets required to give the total the correct composition with regard to sex concordance can be obtained algebraically. If X is the number of MZ sets expected to occur in a population with other types of quadruplets at the frequencies given in table 3,

$$\frac{1}{2} \times 6 + \frac{1}{4} \times 4 + \frac{1}{8} \times 5 + X = .395 (15 + X),$$

$$X = 2.15.$$

When the numbers 2.15, 6, 4 and 5 are converted to proportions they become .125, .350, .233 and .292. Of course, these proportions fit Nichols' data almost exactly because they are based upon them. The main difference between the proportions predicted by Allen and Firschein's model and the empirical proportions found here is a reversal of the relative frequencies of the two- and three-egg types. The ratio of two-egg to one-egg types is close to 3.0 by either approach, 2.57 theoretically and 2.8 empirically. As will appear in the following paragraph, possible errors in the estimated frequencies of three- and four-egg types will not affect the conclusions in the present problem. For present calculations, the four types will be assumed to have relative frequencies of 1, 3, 3, 3.

PROBABILITIES BASED ON UNIT HEREDITARY TRAITS

With respect to hereditary traits for which the population is polymorphic, three-egg and four-egg quadruplets are very unlikely to be concordant in more than a few. The probability of concordance in sex is 1.0 for monozygotic quadruplets, 0.5 for dizygotics, 0.25 for trizygotics and 0.125 for tetrazygotics. The same probabilities apply to any trait for which one parent is known to be homozygous, the other heterozygous, when these genotypes can be distinguished. From the table of blood groups (Table 1) it will be seen that this is the case in the M family with respect to the ABO blood groups, P, Le^a, and Rh (mother, DCe/-Ce; father, probably DCe/-cE). In the case of the MNS system, both parents are heterozygous for Ss as are the girls. The probability of heterozygous children from heterozygous parents is again .5, so that in the MNS types, too, the probabilities of concordance are 1, .5, .25, and .125.

For the first six traits, therefore, the compound probabilities of concordance are 1⁶, .5⁶, .25⁶ and .125⁶, or 1, .0156, .00,024 and .00,000,38 for the four zygosity types (see Table 4). Clearly, the vast majority of quadruplets would have to be trizygotic or tetrazygotic in order for these two types to have a significant probability in this set of quadruplets; from the preceding section it is clear that neither type is more than a minority. The DZ group still has a significant possibility when the above

figures are weighted by the ratio of DZ to MZ quadruplets. If this ratio is approximately 3, the relative frequency of dizygotic quadruplets concordant for all six of these traits is $3 \times .0156$ or $.047$.

A small further reduction in the probability of dizygosity can be obtained from the Duffy (Fy^a) and Kidd (Jk^a) blood types. In both of these cases, a majority of positive-reacting persons are heterozygous, and if parents are both heterozygous, one fourth of their offspring are expected to be recessive. From the tables and methods of Smith and Penrose (1955), the relative chance of concordance in DZ twins (cD) is found to be $.88$ in the case of the Duffy factor and $.91$ in the case of the Kidd factor. The relative frequency of dizygotic quadruplets concordant for these two factors in addition to the six discussed above, if all are assumed to be independent, is $3 \times .0156 \times .88 \times .91 = .0375$. The probability, P_D , that the M quadruplets are dizygotic rather than monozygotic is then $.0375/(1 + .0375)$, or $.036$.

OTHER SIMPLE TRAITS

A four per cent probability of error in twin diagnosis would be tolerable if definite, but in these calculations doubt is raised by the inaccurate assumption of independence of the traits, the possibility of selective mortality of some of the possible combinations, and other unknowns. A further fourfold reduction in the probability of a two-egg origin of the M girls would seem sufficient to compensate these uncertainties. This is possible if use is made of discontinuous hereditary traits for which a Mendelian mechanism is not delineated. Genetic considerations permit the fixing of reasonable and conservative probabilities for concordance in some of these characters, and two examples will be given.

The M quadruplets all have blond hair, now as when they were described by the MacArthurs. Their mother's hair has always been dark brown; their father's hair was blond, but a little darker than the girls' hair. Whatever doubts may be raised about the inheritance of hair color, ordinary blondness is certainly not dominant over brunette (Burks 1938). In order to have blond adult offspring, the mother is probably heterozygous for some genes controlling hair pigmentation, and the probability of blond or even medium-dark hair in offspring appears to be no greater than $.5$. This figure therefore is a conservative estimate of the relative chance of dizygosity on the basis of hair color.

An extra epiphysis at the base of the first metacarpal bone is not common, though its Mendelian basis is unknown. It is unlikely that a given pair of parents should have enough of the necessary genes, or create a sufficiently unusual environment, to produce the trait in more than half of their offspring. Here again a probability of $.5$ that any one child should have the trait seems to be quite conservative. If the trait did not depend entirely on heredity, the probability of concordance in MZ twins would be less than 1, but that for DZ twins would be reduced proportionately and the relative chance for the DZ hypothesis would still be $.5$.

When the expectations of concordance in the skeletal anomaly and in hair color are combined with those of the foregoing sub-section, as shown in Table 4, the probability that the M quadruplets are dizygotic falls below the one percent level. The

Table 4 - Relative Chances of Concordance for Different Hypotheses of Quadruplet Origin, Given Phenotypes as in the M Girls

Trait	Number of zygotes or eggs			
	1	2	3	4
Sex	1	.5	.25	.125
Blood antigens				
ABO	1	.5	.25	.125
Rh	1	.5	.25	.125
P	1	.5	.25	.125
Le ^a	1	.5	.25	.125
Ss	1	.5	.25	.125
Initial odds	1	3	3	3
Product (relative frequencies)	1	.047	.00,07	.00,001,1
Blood antigens				
Fy ^a	1	.88		
Jk ^a	1	.91		
Hair color	1	.5		
Wrist anomaly	1	.5		
Product (relative frequencies)	1	.0093		

assignment of probabilities for similarity of ear lobe, iris pattern and hair form would be more difficult, but together these traits would be very likely to reduce the probability of dizygosity to a half or a third of one per cent.

Summary

The M quadruplets have been regarded as monozygotic by all investigators who have studied them carefully. Previous authors have based their diagnosis on the description of the placenta, on early physical resemblances, and on qualitative features.

The addition of blood group tests to the criteria now tends to confirm the earlier conclusion. From an extension of methods devised for use in twins, it appears that the probability that these quadruplets originated from more than one zygote is less

than one per cent. However, some quantitative differences, especially in finger prints, require a more elaborate analysis, and such an analysis will be presented and discussed in a second article.

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RIASSUNTO

I Quadrigemini M sono stati considerati monozigotici da tutti quelli che li hanno studiati attentamente. Autori precedenti hanno basato la loro diagnosi sulla descrizione della placenta, sulla precoce somiglianza fisica e sui tratti qualitativi.

L'esame dei gruppi sanguigni, aggiunto a questi criteri, tende ora a confermare la precedente conclusione. Estendendo a questo caso l'applicazione dei metodi adottati per i gemelli, appare che la probabilità che questi quadrigemini derivino da più di uno zigote è minore all'1%. Tuttavia è necessaria una analisi più elaborata per quanto riguarda alcune differenze quantitative, soprattutto per le impronte digitali e tale analisi verrà presentata e discussa in un secondo articolo.

RÉSUMÉ

Les Quadruplés M ont été considérés monozygotiques par tous ceux qui les ont étudiés attentivement. Les auteurs précédents ont fait leur diagnose sur la base de la description de la placenta, sur la précoce ressemblance physique et sur les traits qualitatifs.

L'examen des groupes sanguins, ajouté à ces critères, confirme maintenant la conclusion précédente. L'application d'un ensemble de mé-

thodes gémellaires démontre que la probabilité que ces quadruplés tiennent leur origine de plus qu'un seul zygote est moindre de 1%. Une analyse plus élaborée est cependant nécessaire pour ce qui concerne certaines différences quantitatives, surtout pour les empreintes digitales et cette analyse sera présentée et discutée dans une deuxième étude.

ZUSAMMENFASSUNG

Die M Vierlinge waren bei alle die sie aufmerksam untersuchten wie EZ betrachtet. Bisher, haben andere Verfasser die Diagnose auf die Beschreibung der Plazenta, auf die physische Ähnlichkeit und auf die qualitativen Merkmale begründet.

Dieser Schluss ist auch durch die heutige Blutgruppen Untersuchung bestätigt. Zwillings-

methoden schauen dass es eine Wahrscheinlichkeit minder als 1% gibt, dass die Vierlinge nicht EZ sind. Doch ist es nötig eine breitere Analyse über einige quantitativen Unterschiede (besonders über die Fingerdrücke) zu machen und so eine Analyse wird in einem zweiten Artikel festgestellt und diskutiert.