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IS THERE A LACK OF O (ABO BLOOD SYSTEM) NEWBORNS?

To the Editor: The relative lack of homozygotes for the HLA [1–3] and the Rh [4, 5] systems seems to explain the maintenance of these polymorphisms. Does this occur for the ABO system? The most conspicuous deviation for the ABO system is the lack of *AB* individuals, found mainly in newborn infants [6, 7]; this has been explained by the mistyping of A_2B as *B* group [6, 8]; however, the lack of *AB* has been recently found in *Rh*(+) but not in *Rh*(−) infants, which makes the hypothesis of mistyping insufficient as the sole explanatory factor [9]. It is possible to demonstrate, by simulation, that in the conventional analysis of Hardy-Weinberg equilibrium (H-WE) the lack of *O* individuals leads to a lack of *AB* ones, this latter being commonly larger than the former in the χ^2 test for H-WE [10].

A recent paper by Schaap et al. [11] shows strong evidence for the lack of O newborns. Unfortunately, they compared the phenotypic distribution of mothers with that of their infants by a simple χ^2 test without allowing for the

covariance between both generations. This method increased the type II statistical error and did not allow them to uncover the lack of recessive homozygotes.

To demonstrate that mothers do not differ from their infants, it is necessary to continue the analysis; otherwise, if assortative mating occurs or fathers belong to a different population, the method of combination of classes should be biased.

Tests to compare phenotypic and gene frequencies between mothers and their offspring that allow for the covariance have been developed in relation to Rh [5]; they have the structure of a z test for proportions. These z tests for the difference in *A*, *B*, and *O* groups between mothers and infants of the Schaap et al. study are: 1.42 ($P < .08$), 1.64 ($P < .051$), and 2.24 ($P < .0125$), respectively, a highly significant result. The AB group was not tested because of its small frequency and dependence on the other groups. The z test for the difference in the *O* gene frequency is 2.50 ($P < .007$). Therefore, there are a significant reduction of *O* and an excess of $A + B$ infants in relation to their mothers.

Even though the sample is not in H-WE, it is important to study this equilibrium in the whole mother-infant matrix to see the directions of deviations; this is shown in table 1, where expected numbers have been calculated according to the maximum likelihood method applied to the matrix [12]. Mother-infant pairs can be named according to the respective phenotypes, as, for example, *AB-A* pairs are *A* infants born to *AB* mothers.

The total χ^2_{11} in the matrix is 12.94 ($.4 > P > .3$); this nonsignificant figure is due to the large type II statistical error the χ^2 for H-WE has. Iterations find those gene frequencies that minimize the differences between observed and expected values. Since the matrix is symmetrical, *A-O* must equal *O-A* pairs, *B-O* must equal *O-B* pairs, and so on. Table 1 shows, as Schaap et al. found, a lack of B-AB pairs ($\chi^2_1 = 3.21$, $.1 > P > .05$); it also reveals the origin of the lack of O infants: fewer *A-O* than *O-A* pairs (χ^2_1 for equality of both = 4.65, $P < .05$) and fewer *B-O* than *O-B* pairs ($\chi^2_1 = .72$, $.5 > P > .4$). They deviate from H-WE in the same direction as expected according to this suggestion.

The fact that there are more *O-A* and *O-B* pairs than expected may be interpreted as anisophenic (preference to mate a different phenotype) mating, but the above-mentioned asymmetry and the fact that the four diagonal elements have more observed than expected values contradict this interpretation. The lack of *A-O* and *B-O* pairs and the excess of *O-A* and *O-B* pairs is in contradiction to what is known about ABO feto-maternal incompatibility. The conclusion is that homozygous *O* mothers are more prone to deliver a heterozygous *AO* and *BO* (non-O) infant than expected, while heterozygous non-*O* mothers appear less prone to deliver an *O* infant than expected. This situation is similar to that found in the Rh system. Table 2 presents this similarity. *Rh*(+)-*Rh*(−) must equal *Rh*(−)-*Rh*(+) pairs, as well as non-*O*-*O* must equal *O*-non-*O* pairs. It is well known that heterozygotes for both systems are rejected by homozygous recessive mothers rather late in pregnancy; on the other hand, homozygotes for the Rh system seem to be lost early in development [4, 5] and preferentially by heterozygous mothers in the case of Rh(−) conceptions [5].

TABLE 1

MOTHER-INFANT PAIRS FOR THE ABO BLOOD GROUPS (SCHAAP ET AL. DATA [11])

	MOTHER													
	AB			A			B			O			TOTAL	
INFANT	Ob.*	Ex.*	χ^2	Ob.	Ex.	χ^2	Ob.	Ex.	χ^2	Ob.	Ex.	χ^2	Ob.	Ex.
AB	15	9.7	2.8	18	18.7	0	9	16.1	3.1	0	0	0	42	44.5
A	18	18.7	0	123	119.5	0.1	9	12.5	1.0	53	43.9	1.9	203	194.6
B	16	16.1	0	12	12.5	0	54	49.1	0.5	28	25.3	0.3	110	101.0
O	0	0	0	33	43.9	2.7	22	25.3	0.4	90	88.9	0	145	158.1
Total	49	44.5	0.5	186	194.6	0.4	94	101.0	0.5	171	158.1	1.1	500	...

* Ob. = observed; Ex. = expected.

TABLE 2

COMPARISON OF Rh AND ABO BLOOD SYSTEMS

	Rh SYSTEM VALENZUELA AND HARB [5] INFANT				ABO SYSTEM SCHAAP ET AL. [11] INFANT		
MOTHER	Rh(+)	Rh(−)	Total	MOTHER	Non-O	O	Total
Rh(+)	5,721	449	6,170	Non-O	274	55	329
Rh(−)	544	260	804	O	81	90	171
Total	6,265	709	6,974	Total	355	145	500

The Schaap et al. data agree well with these predictions: they found more abortions in *O* mothers whose last infant was a non-*O* individual and fewer abortions in non-*O* mothers whose last infant was an *O* individual.

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