

## PLACENTAL PHOSPHOGLUCOMUTASE POLYMORPHISM IN PORTO ALEGRE, BRAZIL

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### ABSTRACT

Placental phosphoglucomutase (*PGM1*, *PGM2* and *PGM3* loci) was investigated in a sample of 442 newborns (54% Whites and 46% Blacks) from Porto Alegre, Rio Grande do Sul, Brazil. The gene frequencies found were: Whites:  $PGM1^*2 = 0.24$ ;  $PGM2^*1 = 1.00$ ;  $PGM3^*2 = 0.32$ ; Blacks:  $PGM1^*2 = 0.22$ ;  $PGM2^*1 = 1.00$  and  $PGM3^*2 = 0.45$ . A heterozygous individual for a possible null allele at the *PGM1* locus was found among the Blacks. No significant relationships were found in the joint distributions of *PGM1* and *PGM3*, nor was any association detected between *PGM1* or *PGM3* distributions and fetal or placental development.

### INTRODUCTION

Phosphoglucomutase isozymes are controlled in all human tissues by three different loci, *PGM1*, *PGM2* and *PGM3*. The components determined by *PGM1* and *PGM2* can be easily demonstrated in hemolysates but those of *PGM3*, although present, are not so easily detectable in red blood cells. At the *PGM1* and *PGM3* loci there are two commonly occurring alleles; *PGM1* polymorphism was first described by Spencer *et al.* (1964) and *PGM3* polymorphism by Hopkinson and Harris (1968).

Although *PGM1* polymorphism has been investigated in Porto Alegre (Silva *et al.*, 1981) and other Brazilian populations (Azevedo, 1969, Conti, 1985, Azevedo *et al.*, 1987, and Conceição *et al.*, 1987), data on *PGM3* polymorphism are available only for a trihybrid population from Salvador, Bahia (Azevedo *et al.*, 1983).

The phosphoglucomutase isozymes determined by each of the three loci are fully developed in placental tissue, where the different types correspond to the fetal genotype. Since phosphoglucomutase catalyzes the reversible conversion of glucose-1-phosphate to glucose-6-phosphate and is an important enzyme in carbohydrate metabolism, it may play an important role during fetal life.

The present paper reports the PGM phenotype distribution in placental tissue from a Southern Brazilian population and investigates some association between PGM phenotypes and fetal or placental development.

## MATERIAL AND METHODS

Placental samples were obtained from 442 newborns (54% Whites and 46% Blacks) at the Santa Casa de Misericórdia Hospital, Porto Alegre, Rio Grande do Sul, Brazil, and stored at  $-20^{\circ}\text{C}$  until use. For the extract a small piece of tissue was washed in saline to remove excess blood, minced and homogenized in an equal volume of distilled water (g:v). The homogenates were centrifuged at 2000 rpm for 20 minutes and the supernatants were mixed with 2% 2-mercaptoethanol (3:1) and used for electrophoresis. Horizontal starch gel electrophoresis was carried out according to Spencer *et al.* (1964) with the buffer dilutions suggested by Blake and Omoto (1975) and gels were stained by the method of Hopkinson and Harris (1968).

## RESULTS AND DISCUSSION

The phenotype distributions of *PGMI* are shown in Table I. There were no differences in PGM1 distributions between Blacks and Whites. The gene frequencies ( $PGMI^*2 = 0.22$  for Blacks and  $0.24$  for Whites) were very similar to those previously reported for red blood cells from the same population (Silva *et al.*, 1981). The occurrence of a possible  $PGMI^*0$  allele in the Black group was particularly interesting: one child was classified as type 1-1, while his mother was classified as 2-2. An additional test on the cord blood cells of the propositus confirmed the 1-1 phenotype found in the placenta. Both child and mother were then tested for other genetic markers such as ABO, Rh, ceruloplasmin, albumin, transferrin, haptoglobin, esterase D, glyoxalase and acid phosphatase. No other exclusion was found. All babies whose samples had been collected on the same day as the propositus were retested, and so were their mothers; the results were identical to those obtained the first time. Although no quantitative analysis was possible, since the family could not be located, the assumption is that a  $PGMI^*0$  allele is segregating in this family, the mother being  $PGMI^*2/PGMI^*0$  and her son  $PGMI^*1/PGMI^*0$ . No other mother/son exclusion at this locus was found. The frequency of the  $PGMI^*0$  allele in this population was then estimated at 0.002, but this may be an underestimate since we have no information

about paternal *PGM1* phenotypes. Null alleles at the *PGM1* locus have already been described (Fiedler and Pettenkofer, 1968, 1969, Wendt *et al.*, 1971, Brinkmann *et al.*, 1972, 1973, Ueno *et al.*, 1976; Herzog and Libich, 1982; Ferrell *et al.*, 1984; Ward *et al.*, 1985), and most of them were detected through mother/son incompatibility.

The *PGM3* distributions (Table I) differed between Blacks and Whites ( $\chi^2 = 13.1$ ; 2d.f;  $P < 0.01$ ), the *PGM3\*2* frequency being higher in Blacks. The *PGM3\*2* frequency in Whites (0.32) was higher than those reported for White European populations (for a review, see Tills *et al.*, 1983). This may be possibly due to racial admixture, since Franco *et al.* (1982) detected 8% of Black admixture in Whites from Porto Alegre. The *PGM3\*2* value found here for the Black group (0.45) is lower than that observed in Nigeria (0.66; Hopkinson and Harris, 1968) but similar to that of the only other study on a Brazilian population, a trihybrid sample from Salvador (0.46; Azevedo *et al.*, 1983).

Table I - *PGM1* and *PGM3* phenotype distributions.

Phenotype	Whites		Blacks		Total	
	No.	%	No.	%		
<i>PGM1</i>	1-1	134	56	120	59	254
	2-1	93	39	78	39	171
	2-2	11	5	5	2	16
	1-0	0	0	1	<1	1
	Total	238		204		442
<i>PGM3</i>	1-1	119	50	69	34	188
	2-1	84	35	86	42	170
	2-2	35	15	49	24	84
	Total	238		204		442

Gene frequencies: *PGM1\*2*: Whites = 0.24; Blacks = 0.22.

*PGM3\*2*: Whites = 0.32; Blacks = 0.45.

No variation was found at the *PGM2* locus, all samples showing the 1-1 phenotype.

Association tests considering the joint distributions of *PGM1* and *PGM3* according to Spiess (1977) showed no significant departures from those expected by chance.

The distributions of *PGM1* and *PGM3* in relation to intrauterine development are given in Table II. On the basis of birth weight and gestational age, intrauterine development was classified as small for gestational age (S), appropriate for gestational age (A) and large for gestational age (L), according to Battaglia and Lubchenco (1967) and Ségre (1984). Since there were no differences between Blacks and Whites in *PGM1* distribution, this analysis was done considering the distributions of the two racial groups as a whole. There was no significant deviation from the expected values in *PGM1* and *PGM3* distribution in relation to intrauterine development.

Table II - Distribution of *PGM1* and *PGM3* types in relation to intrauterine fetal development.

Phenotype		Intrauterine development <sup>1</sup>					
		S		A		L	
		No.	%	No.	%	No.	%
<i>PGM1</i>							
Whites	1-1	14	7	162	79	29	14
and	2-1	14	10	112	78	18	12
Blacks	2-2	0	0	10	79	4	21
<i>PGM3</i>							
Whites	1-1	7	7	75	77	16	16
	2-1	1	1	62	89	7	10
	2-2	3	9	26	79	4	12
Blacks	1-1	7	12	44	77	6	11
	2-1	8	12	47	70	13	18
	2-2	2	6	31	81	5	13

<sup>1</sup> Classification according to Battaglia and Lubchenco (1967) and Ségre (1984): S - small for gestational age; A - appropriate for gestational age, and L - large for gestational age.

The relationships among mean placental weight and *PGM1* or *PGM3* phenotypes are shown in Table III. For this analysis only the newborns classified as appropriate for gestational age were considered, since Trindade *et al.* (1979) verified significant differences in placental weight in relation to gestational age in newborns of low or high birth weight, but not in newborns of adequate birth weight for gestational age. No significant differences were found in placental weight among *PGM1* or *PGM3* phenotypes.

Table III - Distribution of *PGM1* and *PGM3* types in relation to mean placenta weight (g.).

Phenotypes		Whites		Blacks	
		No.	$\bar{x} \pm s.d.$	No.	$\bar{x} \pm s.d.$
<i>PGM1</i>	1-1	91	590 $\pm$ 96	70	580 $\pm$ 102
	2-1	63	591 $\pm$ 107	48	575 $\pm$ 134
	2-2	7	611 $\pm$ 161	3	530 $\pm$ 36
<i>PGM3</i>	1-1	74	598 $\pm$ 106	44	584 $\pm$ 117
	2-1	61	587 $\pm$ 95	47	575 $\pm$ 110
	2-2	26	595 $\pm$ 106	31	568 $\pm$ 119

Therefore the present data suggest that there is no association between PGM phenotypes and fetal or placental growth, or if such association exists, it is not detectable in a sample of this size.

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### RESUMO

A fosfoglucomutase placentar (locos *PGM1*, *PGM2* e *PGM3*) foi investigada em uma amostra de 442 recém-nascidos (54% Brancos e 46% Negros) da população de Porto Alegre. As frequências gênicas observadas foram: Brancos: *PGM1*\*2 = 0.24, *PGM2*\*1 = 1.00 e *PGM3*\*2 = 0.32; Negros: *PGM1*\*2 = 0.22, *PGM2*\*1 = 1.00 e *PGM3*\*2 = 0.45. Detectou-se entre os negros um indivíduo heterozigoto para um possível alelo nulo no loco *PGM1*. Não foi verificada associação nas distribuições conjuntas entre os locos *PGM1* e *PGM3*, bem como, não se encontrou efeito dos fenótipos de *PGM1* e *PGM3* no desenvolvimento do feto ou da placenta.

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