Humangenetik 4, 81—83 (1967)

Glucose-6-phosphate Dehydrogenase Deficiency in Spain

G. Flatz and Ria Düren
Universitäts-Kinderklinik Bonn (Direktor: Prof. Dr. H. Hungerland)

Received February 6, 1967

Qui de fetge va que no passi pel favar!
Who suffers from the liver should not pass through a fava field!

Examination of 2520 male subjects in Spain by the Dye Reduction Test revealed five cases of Glucose-6-phosphate dehydrogenase deficiency, all originating from the east coast of Spain and the Balearic Islands. In these areas the enzyme deficiency seems to occur focally at low frequencies near 1%.

The long standing knowledge of a relation between jaundice and fava beans which is evident from the quoted Menorcan proverb, suggests an appreciable incidence of erythrocytic glucose-6-phosphate dehydrogenase deficiency (G-6-PDD) in the population of the Balearic islands and, by implication, in other parts of Spain. The same expectation may be derived from the high frequency of G-6-PDD in other parts of the Mediterranean area. Surprisingly, only a few cases of favism or G-6-PDD have been reported from Spain. Population surveys are limited. In 1953, Surinyach, Marcolongo, Alcobe and Llebaria made a survey of favism based on clinical data and case histories (the cause of favism not being known at that time). They concluded that the constitution predisposing to favism occurred frequently on the Balearic Islands (particularly on Menorca), on the east coast, in the south and west of Spain (Estremadura). Rotella, Miserachs, Coll-Sampol and Surinyach (1961) reported a case of favism with massive hemolysis and renal failure in a Menorcan patient. G-6-PD activity was apparently not tested. The first case of proved G-6-PDD from Spain seems to have been reported by Rico-Irles, Navarro, Mora-Lara and Pelaez (1963) who made a survey of hospital patients in southern Spain. Later the same group of authors (Mora-Lara, Rico-Irles, Navarro, Gomez and Pelaez, 1964) reported two further families with G-6-PDD from Granada and Valencia. In Barcelona, Guasch (1965) examined 400 healthy persons for G-6-PDD with negative results.

In order to determine incidence and distribution of G-6-PDD in Spain we examined 2520 male subjects (unselected with respect to favism or other hemolytic episodes) and several families and individuals with a history of favism or hemoglobinuria. The Dye Reduction Test (Motulsky and Campbell-Kraut, 1960) was used to identify G-6-PDD. With our method discoloration is complete in 20 to 40 min in normal males. In males with "Mediterranean type" G-6-PDD discoloration is not complete before 2 hrs.

The results (summarized in Table 1) reveal a very low incidence of G-6-PDD in the population of Spain. In the general survey of 2520 probands only 5 with

G-6-PDD were found. All five cases originate in the province of Valencia or on the Balearic Islands. No G-6-PDD was detected in the groups from western and southern Spain; in particular, the enzyme deficiency was absent from 192 samples of two villages with a population of "Mauric" (North African) origin. In the groups from western Spain (Estremadura) and from Valencia there were seven samples with slightly prolonged discoloration (50 to 65 min). Although this

Table 1. *The Geographic Distribution of Glucose-6-Phosphate Dehydrogenase Deficiency in Spain*

Area	Province or location	Number examined	Number G-6-PD deficient
Central and North		170	—
West (Estremadura)	Cáceres	342	—
South	Câdiz	309	—
	Málaga	424	—
East Coast	Murcia	221	—
	Ebro Delta	96	—
	Valencia	504	1[1]
Balearic Islands	Mallorca	242	3[2]
	Menorca	212	1[3]
Total		2520	5

[1] Found among 104 samples from the district of Sueca.
[2] Found among 132 samples from the district of Sineu.
[3] Found among 114 samples from the district of Ciudadela.

finding doesnot carry much weight in view of the limitation to a single screening test the occurrence of a "mild type" of G-6-PDD cannot be excluded. In the area of Valencia and on the Balearic Islands the "regular type" of severe G-6-PDD seems to occur focally with a frequency near 1%.

In 6 families (3 from the province of Valencia, 1 from Mallorca and 2 from Menorca) where a history of favism (discoloration of urine and jaundice after ingestion of fava beans) was given, G-6-PDD was detected in one or more members. In Menorca a number of persons with a less certain history of favism (usually vague symptoms, e.g. head-ache or abdominal pain after ingestion of fava beans or walking through a fava field) were examined. None of them was G-6-PD deficient although they had figured as cases of favism in previous surveys.

There is considerable evidence for a parallel distribution of G-6-PDD and falciparum malaria in other parts of the Mediterranean area (review: MOTULSKY, 1964). In Spain malaria was frequent in Estremadura, Andalusia, along the eastern littoral and on the Balearic Islands. The low frequency of G-6-PDD in our survey precludes a valid comparison of distribution data. If foci with a somewhat higher frequency of G-6-PDD are detected a comparison with the former distribution of malaria (well documented by the governmental Servicio Antipaludico) may be possible. In view of the congruence of the global distribution of G-6-PDD and β-thalassemia it is interesting to note that the reported cases of β-thalassemia major originate almost entirely on the Mediterranean coast and on the Balearic Islands (CRUZ-HERNANDEZ and VELASQUEZ, 1962).

We are highly indebted to Dr. J. Bosch-Marin for facilitating the collection of blood samples. Further acknowledgements will be made in a detailed report which will be presented as doctoral thesis to the Medical Faculty of the University of Bonn by Miss R. Düren.

Literature

Cruz-Hernandez, M., y B. E. Velasquez: La talasemia en España. Medicamenta (Madr.) **378**, 199—206 (1962).

Guasch, J.: Personal communication 1965.

Mora-Lara, R., J. Rico-Irles, A. Navarro, J. Gomez y J. Pelaez: Favismo y deficit de glucosa-6-fosfato dehidrogenasa. Med. clin. (Barcelona) **42**, 421—427 (1964).

Motulsky, A. G.: Hereditary red cell traits and malaria. Amer. J. trop. Med. Hyg. **13**, 147—158 (1964).

— and J. M. Campbell-Kraut: Population genetics of glucose-6-phosphate dehydrogenase deficiency of the red cell. In: Proc., Conf. on genetic polymorphism and geographic variations in disease. B. Blumberg, ed., p. 159—180. New York: Grune and Stratton 1960.

Rico-Irles, J., A. Navarro, R. Mora-Lara y J. Pelaez: Favismo y deficit de glucosa-6-fosfato dehidrogenasa. Med. clin. (Barcelona) **41**, 359—363 (1963).

Rotellar, E., M. Miserachs, J. Coll-Sampol et R. Surinyach: Insuffisances rénales aigues par hémolyse de la totalité des hématies des malades. Presse méd. **69**, 1429—1435 (1961).

Surinyach, R., F. Marcolongo, S. Alcobe y C. A. Llebaria: Favismo y hemolisis alimentaria. 4 Congresso international de higiene y medicinas mediterraneas, Barcelona 1956.

Privatdozent Dr. G. Flatz
Universitäts-Kinderklinik
5300 Bonn, Adenauerallee 119