

Laboratory of Biology
Faculty of Science
University of Valladolid
(Prof. J. Planas)

The values of haptoglobins and their relation to the genetic type in a group of donors *

by

Planas, J., Viñas, J.**, Castro, S. De, Arribas, J. M. and Martín-Mateo, M. C.

(Received for publication on november 12th, 1964)

Haptoglobins, serum glucoproteins included among the alpha-2 globulins, are found in the serum of the adult human individual in proportions which oscillate between fairly wide limits.

At the moment of birth it is only possible to determine the presence of this protein fraction in 10 % of newborn babies, and only from the fourth month does it become evident in all individuals (7).

From this period on, the variations which depart remarkably from an average value, whether in one direction or the other, have a physiopathological cause, so that the haptoglobin level has a clinical interest (6, 7).

Different authors (2, 3, 4, 6, 8, 11) give normal values, approximating to 100 mg Hp per 100 cc of serum. Similarly, most of the authors find sexual differences, the values being higher in the males.

According to NYMAN (7, 8), there is a certain relation between the level of haptoglobin and the genetic type of

the individuals, with the result that the type Hp 1-1 is that which presents the highest average level and the type Hp 2-2 the lowest. This relation has also been observed by other authors, all of whom utilized a rather small number of individuals (1, 2, 13,).

In the present work, a study has been made of a group of blood donors consisting of 1.143 individuals, in order to determine the average value and distribution, as also to establish precisely, in a numerous group, the relation between the genetic type and the level of haptoglobin.

Material and methods

We have analysed the sera proceeding from 1.143 blood donors enrolled in the Knickerbocker blood bank of Barce-

* Work carried out with a subsidy from the Promotion of University Research, of the Ministry of National Education.

** Knickerbocker Laboratories (Barcelona).

lona. This group includes individuals of both sexes and is clearly heterogeneous with regard to ages.

The evaluation of the haptoglobin content has been carried out following the activation method of JAYLE (5), based on the peroxidase activity of the haptoglobin-hemoglobin complex, using ethylic hydroperoxide as substrate.

The identification of the genetic types of haptoglobins has been carried out with electrophoresis in starch gel, following the technique described in a previous publication (10).

Results

In table I is indicated the average value and the type variations obtained in the group studied, and also the average values corresponding to men and women. In the same table are included the average levels found in the references, corresponding to normal individuals.

Figure 1 expresses the overall distribution of the haptoglobin values in the

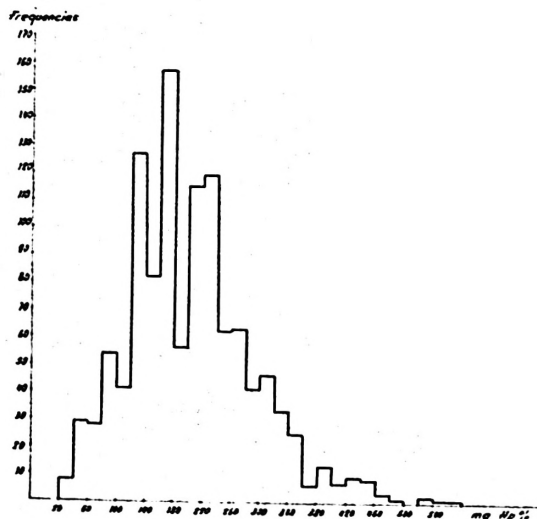


FIG. 1. Distribution of the haptoglobin values in a group of 1143 donors.

group of donors, without distinction of sex.

In table II are shown the average values corresponding to the haptoglobin levels, taking into account the genetic type to which they belong.

TABLE I

Content of serum haptoglobin in different groups of normal individuals. The average values are expressed in mg Hp per 100 c.c. of serum and are followed by their standard deviations.

Author References	Overall average values		Males		Females	
	N.º	mg Hp %	N.º	mg Hp %	N.º	mg Hp %
Present work	1143	216 ± 83	917	223 ± 88	219	188 ± 79
Castro and col. (3)	98	115 ± 27	58	123 ± 30	40	106 ± 29
Hever (4)	176	110 ± 36	119	111 ± 36	57	106 ± 36
Nyman (8)				147 ± 56		122 ± 39
Nyman (9)	150	109 ± 40				
Jayle and Dormann (6)	1000	98 ± 40				
Schumacher and Schlumber- ger (11)					22	117 ± 37
Barros and Godinho (2)			87	121 ± 44		

TABLE II

Average values of haptoglobins in the three phenotypes. All the values are expressed in mg Hp per 100 c.c. of serum.

Author References	Hp 1-1		Hp 2-1		Hp 2-2	
	N.º	mg Hp%	N.º	mg Hp%	N.º	mg Hp%
Present work	188	255 ± 78	602	214 ± 91	353	215 ± 96
Nyman (8)	59	177 ± 39	130	140 ± 48	86	107 ± 44
Barros and Godinho (2)	22	152 ± 30	36	129 ± 41	29	87 ± 35
Smith and Owen (13)		135 ± 44		133 ± 48		94 ± 49
Allison (1)		156 ± 34		156 ± 34		130 ± 26

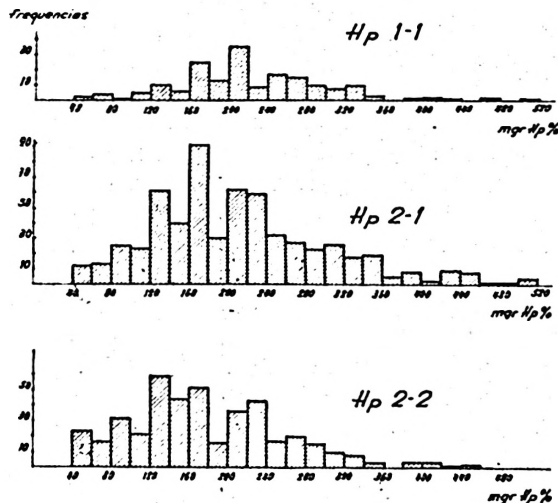


FIG. 2. Relation existing between the level of haptoglobins and the corresponding genetic type

In figure 2 may be observed, in the histograms, the different distribution of the haptoglobin values when they are grouped in accordance with the haptoglobinic phenotype.

Discussion

The results obtained in this group of blood donors allow to appreciate (table I) how the average value departs noticeably from the values quoted previously. The

discrepancy which exists is founded principally on two facts: a) the remarkable increase in the average value in relation to those observed in normal subjects; and b) the increase in dispersion. It would seem, therefore, that the rise in the average value is accompanied by a parallel increase in dispersion.

This remarkable increase is especially significant when it is compared with the value found in a previous publication (3) in a group of normal individuals who were not blood donors, the same technique being used for the purpose.

The professional character of the majority of the donors analysed may be the reason for such a difference, though we do not know what causes the rise in the level of haptoglobin in the serum as a result of repeated bloodletting in individuals with a hemoglobin value never lower than 125 gr. Hb per 100 cc. of blood.

We should point out, on the contrary, that Nyman (9) has obtained a value of 109 ± 40 mg Hp % for a group of 150 donors, in which the increase indicated by us is not observed.

The overall increase in the haptoglobin level, as also that of the dispersion of the values found, does not, at first sight, affect the sexual and phenotypic difference quoted by other authors

(tables I and II). In this way, we can also observe that the males have an average value (223 ± 88 mg Hp %) higher than that of the females (188 ± 79 mg Hp %); nevertheless, the differences is not statistically significant ($\epsilon = 0.3 < 1.96$). The sexual differences can be explained by a hormonal effect, for it has been proved that the androgens raise the level of haptoglobins, while the estrogens diminish it (11).

From the works of NYMAN (8, 9) we can know the relation between the level and the genetic types of haptoglobins, later analysed by other authors (1, 2, 13). In the group we have studied, this relation seems equally evident on comparing the distributions expressed in figure 2, and in the same sense as that observed in the bibliography: type Hp 1-1 presents the highest level and type Hp 2-2 presents the lowest. However, the average values found for each type in table II differ very little and there is no statistical significance to be found in the differences.

In our values we have not found any difference between the levels corresponding to type Hp 2-1 and those corresponding to type Hp 2-2. This has also been the case with ALLISON (1) and with SMITH and OWEN between the types Hp 1-1 and Hp 2-1.

It is interesting to compare the statistical significance of the data of the bibliography (tabla II). In the values indicated by NYMAN (8) and by BARROS and GODINHO (2), the application of the reduced deviation test (12), utilized with our data, also fails to provide a significant figure for a probability of 96 %.

The dispersion of the haptoglobin values found in this group of donors is rather high, as can be observed in figure 1. The distribution is asymmetric and the modal value is of order of 160 mg Hp %. The widespread of the values is the reason why no significance has been

found in the sexual differences and in those corresponding to the phenotypes.

The level of haptoglobin tends to increase with age (7).

It should be pointed out that the values of BARROS and GODINHO (2) shown in table I correspond to a homogeneous group consisting of soldiers of between 20 and 25 years old, giving an average value of 121 ± 44 mg Hp per 100 cc of serum.

Summary

A study has been made of the level of haptoglobins in a group of blood donors composed of 1143 individuals of both sexes. The content of haptoglobins has been determined by the iodometric technique of JAYLE.

The average values obtained are indicated, both for the overall group and for the two sexes separately. It has been found a considerable increase in these values, in respect to those obtained from groups of normal individuals who are not donors.

Sexual differences have been observed in the level of haptoglobin in the same sense as that found in references, but this is not statistically significant.

The relation between the genetic type and the level of haptoglobin has also been observed in this group, but the differences are also less pronounced.

* * *

We should like to express our sincere thanks to D. Juan González, of the Knickerbocker Laboratories (Barcelona), for his efficient work in collecting and sending the sera.

References

- (1) ALLISON, A. C. : *Proc. Roy. Soc. Med.*, **51**, 641, 1958. Referred by Jayle and Dormann, 6.
- (2) BARROS, F. and GODINHO, F. : *J. Soc. Cien. Med.*, **124**, 1, 1960.

- (3) CASTRO, S. DE, ARIBAS, J. M. and J. PLANAS : *Med. Clin.*, **22**, 261, 1964.
- (4) HEVER, O. : *Orvosi Hetilap.*, **24**, 1117, 1962.
- (5) JAYLE, M. F. : *Bull. Soc. Chim. Biol.*, **33**, 876, 1951.
- (6) JAYLE, M. F. et DORMANN, E. : «Les Haptoglobines». Masson et Cie., Paris, pp. 58, 1962.
- (7) JAYLE, M. F. and MORETTI, J. : *Prog. in Hematol.*, **3**, 342, 1962.
- (8) NYMAN, M. : *Scand. J. Clin. Invest.*, **39**, suppl. 1959. Referred by Jayle and Moretti, 7.
- (9) NYMAN, M. : *Protides Biol. Fluids*, 5th Colloq., Bruges, 1957, pp. 111, 1958.
- (10) PLANAS, J. : *Genét. Ibér.*, **15**, 103, 1963.
- (11) SCHUMACHER, G. und H. D. SCHLUMBERGER : *Klin. Wschr.*, **40**, 67, 1962.
- (12) SCHWARTS, D. : «Méthodes statistiques à l'usage des Médecins et des Biologistes». Ed. Médicales Flammarion, Paris, 1963.
- (13) SMITH, H. and J. A. OWEN : *Biochem. J.*, **78**, 723, 1961.

