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Disagreements between Observed and Expected Data in Erythrocyte Acid Phosphatase Polymorphism

Reference Laboratories for Enzyme Polymorphisms

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Summary. All caucasian data available on acid phosphatase polymorphism were examined for whether there exist significant differences between observed and expected data. There was found a decrease in the frequency of observed C-types in favour of the CB-group. The differences between observed and expected data are statistically significant. The phenomenon is still unexplained, but it is possibly due to errors in diagnosis.

Zusammenfassung. Alle Daten über den Polymorphismus der sauren Erythrocytenphosphatase, die aus europäischen Populationen zur Verfügung standen, wurden daraufhin überprüft, ob signifikante Unterschiede zwischen beobachteten und erwarteten Zahlen bestehen. Eine Abnahme der Häufigkeit beobachteter C-Typen war begleitet von einer Zunahme beobachteter CB-Typen. Die Unterschiede zwischen beobachteten und erwarteten Werten sind statistisch signifikant. Das Phänomen ist bisher ungeklärt, aber möglicherweise ist es durch Irrtümer in der Diagnose zu erklären.

Key words: Erythrocyte acid phosphatase — Polymorphism, acid phosphatase — Gene model, acid phosphatase.

In a previous report (Brinkmann *et al.*, 1971), dealing with gene frequencies of several enzyme polymorphisms, an unexpected high chi square in the red cell acid phosphatase polymorphism has been observed. On the purpose ro elucidate these obscurities the following studies have been performed.

Materials. All caucasian data, that were available about this polymorphism have been collected. The statistical methods that were used are referred in the next chapter.

Results and Discussion. All european populations, that have been investigated for acid phosphatase gene frequencies (exept for our's; see Table 3) are given in Table 1. The expected numbers, which are noted, have been calculated on the base of the corresponding gene frequencies in each group. An information analysis (2 J-test, Sachs, 1968) about all data of this table showed, that the distribution in the different population groups was homogeneous enough to allow a summarizing of all results. With these data chi square calculations were performed (Table 2). The same procedure was made with our relatively large population sample (Table 3).

Table 1. *Red cell acid phosphatase phenotypes of different caucasian populations. Observed and expected data*

References	n	AA		BB		AB		AC		BC		CC	
		obs.	exp.	obs.	exp.	obs.	exp.	obs.	exp.	obs.	exp.	obs.	exp.
Lamm (1968)	470	61	54.8	178	170.4	178	193.3	21	18.1	32	31.9	0	1.5
Hopkinson *et al.* (1963)	139	14	16.9	48	50.7	64	58.6	5	4.6	8	7.9	0	0.3
Hopkinson *et al.* (1964)	367	41	47.6	123	132.1	175	158.5	9	10.6	19	17.6	0	0.6
Giblett and Scott (1965)	193	33	30.0	61	57.5	76	83.2	10	9.0	13	12.5	0	0.7
Lai (1966)	260	33	28.2	107	109.8	103	104.7	4	5.6	13	10.8	0	0.3
Goedde *et al.* (1970)	681	102	100.9	213	212.9	293	292.9	28	29.5	43	42.7	2	2.1
Koops (1970)	302	46	40.8	99	95.7	116	125.0	14	15.4	26	23.6	1	1.5
Radam and Strauch (1966)	1188	145	155.9	387	394.9	516	496.4	55	52.5	80	83.5	5	4.4
Fiedler (1967)	405	53	46.0	155	150.0	153	166.0	15	15.0	29	27.0	0	1.0
Reimann and Schulze (1968)	681	99	91.1	237	230.2	273	289.6	27	26.3	45	41.8	0	2.0
Reimann and Willner (1968)	409	61	54.3	141	136.8	160	172.3	16	17.1	31	27.2	0	1.3
Pulverer *et al.* (1969)	500	51	54.5	179	186.0	211	201.3	17	19.8	41	36.6	1	1.8
Renninger (1970)	586	67	71.0	202	204.7	247	241.0	27	24.9	41	42.3	2	2.2
Pulverer *et al.*(1969)	1800	199	196.0	663	661.0	707	719.9	80	76.0	149	139.3	2	7.0
Goedde *et al.* (1966)	171	13	12.4	91	89.2	64	66.5	2	2.9	1	2.0	0	0.01
Richter (1967)	343	37	43.8	116	123.7	161	147.1	10	10.4	19	17.4	0	0.6
Wille *et al.* (1967)	300	21	28.8	117	124.1	134	119.6	10	8.7	18	18.0	0	0.7
Fuhrmann and Lichte (1966)	401	51	43.3	166	159.2	150	165.6	11	10.8	23	21.3	0	0.8
Krüger *et al.* (1968)	528	66	54.9	220	206.9	185	211.6	21	18.2	36	35.7	0	1.54
Pflugshaupt *et al.* (1970)	1365	147	161.5	486	502.9	604	570.1	41	46.0	82	81.2	5	3.3
Speiser and Pausch (1968)	410	46	54.0	128	135.0	185	171.0	22	19.0	29	29.0	0	2.0
Herzog and Bohatová (1969)	307	49	40.9	116	129.5	107	102.6	10	12.8	25	20.2	0	1.0
Nguyen van Cong and Moullec (1967)	487	47	50.3	198	198.6	203	199.9	16	12.6	23	24.9	0	0.8
Modiano *et al.* (1967)	417	36	28.5	183	180.7	132	143.5	14	17.5	51	44.1	1	2.7
Modiano *et al.* (1967)	365	24	26.3	149	150.0	127	125.7	21	17.7	43	42.3	1	2.9
Total	13075	1542	1532.7	4763	4792.5	5324	5325.9	506	501.0	920	880.8	20	43.0

A study of Tables 2 and 3 demonstrates, that high chi squares, indicating real discrepancies between observed and expected data, are present in two each corresponding groups only. These are involving the groups of phenotypes "C" and "CB". These differences however are levelled sufficiently when the deficient numbers of observed phenotypes "C" are filled up by an interchange with the exceeding numbers of observed types "CB". It is furthermore apparent from a study of Tables 2 and 3 that an addition of all chi squares results in a levelling of existing differences because of the high number of degrees of freedom.

Table 2. *Comparisons of observed and expected data of all summarized available caucasian red cell acid phosphatase types*

Acid phosphatase phenotypes	n			χ^2
	observed	expected		
AA	1542	1532.7		0.0564
BB	4763	4792.5		0.1816
AB	5324	5325.9		0.0007
AC	506	501.0		0.0499
BC	920	880.8		1.7446
CC	20	43.0		12.3023
Total	13075	13075.9	$\Sigma\chi^2$	$=14.3355$
			p (d.f. 5)	$=0.0136$

Table 3. *Comparisons of observed and expected data of red cell acid phosphatase types in a northern German population (Brinkmann et al. 1971)*

Acid phosphatase phenotypes	n			χ^2
	observed	expected		
AA	877	881.9		0.0272
BB	2364	2389.4		0.2700
AB	2922	2903.2		0.1217
AC	314	323.1		0.2563
BC	564	531.8		1.9497
CC	18	29.9		4.5459
Total	7059	7059.3	$\Sigma\chi^2$	$=7.1709$
			p (d.f. 5)	$=0.21$

Trends and distribution in both samples were found to be similar enough to allow an addition for a further test: In the order to test, whether the Hardy-Weinberg-equilibrium is present for the gene p^c an artificial gene model has been set up: Genes p^a and p^b artificially were considered to be identical, therefore added and named "p^x". Gene frequencies of "p^x" and "p^c" were estimated from the whole sample and chi square evaluation performed (Table 4). Differ-

ences between observed and expected data are significant. They are due to a clear excess of "observed" heterozygous types and to a corresponding deficit in the homozygous group "C".

The finding that differences between observed and expected data are significant and that they are due to displacements between two groups only, leads to the only possible explanation that a lot of EAP types, that were genotypically P^c/P^c, have been diagnosed wrong as "CB" types. Since the two types "C" and "CB" are only differing in the relative intensities of their corresponding isozymes – the type CB having roughly equal staining intensities in both isozymes and the type C having a slow very intense isozyme and a fast one which is rather faint–and since these differences are clear enough to avoid errors, it appears to be possible that there exists another series of EAP types, that are genotypically P^c/P^c and that are diagnosed to be P^c/P^b.

Table 4. *Comparison of acid phosphatase distribution according to an artificial gene model*[a]

Acid phosphatase types		*n*		Gene frequencies	
original notation	artificial notation	observed	expected		
AA + AB + BB	XX	17792	17825	p^x	= 0.9409
AC + BC	XC	2304	2239	p^c	= 0.0591
CC	CC	38	70		
Total		20134	20134	χ^{2b}	= 10.442
				p (d.f. 2)	= 0.005

[a] The model consists of 2 alleles only: the artificial gene p^x consists of the added genen p^a and p^b and the allele gene is the normal p^c. Three "types" exist: XX, XC and CC. Gene frequencies were estimated from summarized caucasian data (Tables 2 and 3).

[b] Chi square evaluation by the χ^2–$2 \times K$ contingency table (Freund, 1962).

From recent studies (Fisher and Harris, 1971) it appeared that the two isozymes, that are controlled by one allele, are conformational isomers which are evidently in equilibrium to each other. It is yet unknown whether there exist any factors (including conformational factors) that regulate or modulate the equilibrium constant and if so, whether they are genetically controlled too.

The phenomenon discussed above is under extensive studies now. By that time it has to be warned that there can exist a source of errors if one has to pass an opinion on a paternity proceeding.

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