## **Human Sociogenetics**

## Carlos Y Valenzuela\*

Programa de Genética Humana, ICBM, Facultad de Medicina, Universidad de Chile. Independencia 1027, Casilla 70061, Santiago, Chile.

#### ABSTRACT

In three cities of Chile (Santiago, Valparaiso, Valdivia) the A allele and phenotype (ABO blood group) are more frequent in the higher socioeconomic strata (SES) and the O allele and phenotype are in the lower ones. This constitutes a structured sociogenetic cline (SGC). The B allele and phenotypes (B+AB) present a rather erratic or contradictory distribution among SES. This SGC was also found in England. The standard interpretation of the origin and maintenance of this SGC in Chile is founded on socio-ethno-historic-cultural and drift factors followed by socioeconomic assortative mating that has occurred since the origin of Chileans by the admixture of Europeans and Amerindians. This interpretation is insufficient to explain the coincidence of the cline in England and Chile, and for some findings in Chile. 1) The A and Rh(-) frequencies of the highest SES in Chile are significantly higher than those found in Europeans. 2) The B gene and phenotypes (with AB) behave differently and in contradiction to the socio-ethno-cultural-historical process. 3) There is a significant interaction of the SGC with gender in Chile and England. There is not at present a putative relationship between ABO and psycho-social factors that could account for this sociogenetic interaction. This SGC seems to be present in societies with a hierarchical organization in relation to power, prestige, ownership, income and life style, and when sampling includes the most extreme SES. It has not been found in two samples from Ireland and in a sample from Chile taken from a public hospital, probably because those variables and conditions were not ascertained.

Key terms: ABO, Chile, England, Rh, socioeconomic strata, sociogenetics.

#### INTRODUCTION

#### Definitions and antecedents

By sociogenetics we mean the study of genetic factors that condition or determine the social structure of populations. Thus, sociogenetics studies the interactions between the social and genetic structures of populations (Valenzuela and Harb, 1977; Valenzuela, 1984a, 1988, 1998; Valenzuela et al., 1987). Sociogenetics was used, circa 1917-1940 (mostly by the Russian psychologist Lev Vygotsky), for studies on the bio-socio-ontogenesis of psycho-social phenomena. Vygotsky studied the maturation of biological mental factors of cognition and speech with socio-cultural experience (www.sonic. net/~cr2/sociohis. htm). If the socio-cultural matrix interacts dialectically with neuro-psychic factors, mostly genetically determined, to construct, in individuals and societies (interindividuals interactions) their neuro-psychic ontogeny, we see that both kinds of studies have the same goal. Vygotsky did not know about neuro-psycho-genetics, and in his time Mendelian genetics was just developing in the Soviet Union (and soon to be forbidden by the Stalin regime). Though Vygotsky was a convinced materialistic-dialectic citizen, he and his ideas were persecuted.

Luria's research was conducted in two important expeditions to Uzbekistan in 1931-1932. The expedition was designed by Vygotsky and Luria to investigate the principles of socio-historical psychology by comparing the psychological processes of groups of people who had been differentially affected by the collectivization of agriculture. An important participant in the project was Kurt Koffka, the famous Gestalt psychologist. The political system reprimanded Vygotsky and Luria for their cross-cultural research in Uzbekistan. Findings of cultural psychological differences were condemned as racist and antithetical to the government's egalitarian ideology, which insisted on the equal capability of all people. Vygotsky and Luria were forbidden from publishing their findings and from continuing their cultural historical research. Luria was forced to leave the Institute of Psychology at Moscow State University, and he subsequently undertook a new program of clinical investigations of aphasia in the Psychoneurological Academy in Kharkov (Vygotsky & Luria, 1930/1993, pp. 13-16; Van der Veer & Valsiner, 1991, pp. 253-255) (see: www.sonic. net/~cr2/sociohis.htm).

Recently, sociogenetics has appeared as the study of differential action of alleles on the social behavior of worms (Ardiel and Rankin, 2009) and genetic associations among human friendships (Fowler et al., 2011).

#### The Chilean Sociogenetic Cline (SGC) is an accepted population structure

Any researcher into human population genetics or anthropology in Chile knows, from direct observation, that the Chilean population is dramatically socio-ethno-phenotypicculturally stratified. As the Chilean population originated mostly from Chilean Amerindians and Caucasians, studies have tried to determine the proportion of the Amerindian admixture in socio-ethno-economic strata (Alvial and Henckel, 1963; Pinto-Cisternas et al., 1971; Workman, 1973; Valenzuela and Harb, 1977). Most Amerindians did not have the A and B alleles (ancient nomenclature for genetic systems to agree with quoted articles) of the ABO blood group nor the d or Rh (-) allele, when Europeans arrived in Chile (Matson et al., 1969, Etcheberry, 1997). Most or all of Amerindians were O, Rh(+) individuals. Spaniards have, and it is assumed had when they came to Chile, frequencies of A, B and Rh (-) alleles

Received: December 29, 2010. In revised form: May 31, 2011.Accepted: August 9, 2011.

<sup>\*</sup> Corresponding author: Carlos Y Valenzuela. Programa de Genética Humana, ICBM, Facultad de Medicina, Universidad de Chile. Independencia 1027, Casilla 700061, Independencia, Chile. Fax (56-2) 7373158; Phone (56-2) 9786302; e-mail: cvalenzuela@med.uchile.cl

near 0.29, 0.07 and 0.041, respectively (Campillo, 1976). So, the two systems lend themselves to the study of the Chilean socio-ethno-genetic stratification. In Chile, high socioeconomic strata (SES) had higher A, B and Rh(-) frequencies than low SES (Pinto-Cisternas et al., 1971; Valenzuela and Harb, 1977; Valenzuela, 1984a, 1988; Cohn et al., 1985; Valenzuela et al., 1987). Workman (1973) determined, with haptoglobins, ABO, MN, and Rh systems, 36% of Amerindian admixture in middle-low and low socioeconomic strata. He thought it extremely interesting to study the other strata.

### THE "STANDARD INTERPRETATION" OF THE SGC

The Chilean SGC was established with the arrival of Europeans (Spaniards) and has remained until now. The standard interpretation includes ethno-socio-genetic-cultural-population dynamics by which the SGC was installed and maintained. The nucleus of this interpretation includes three processes. I) The admixture of Europeans (mostly Spaniards) and Amerindians (human populations separated more than 1000 generations ago) who met near 16 generations ago; II) The distribution of Europeans, mostly in intellectual occupations or occupations with more power, prestige and income, while Amerindians and Mestizos were employed in manual occupations or occupations with less power and prestige and lower incomes. III) Positive (isophenic) socioeconomic assortative mating (Valenzuela, 1998, see below). Thus, Spaniards (or better Caucasoid Europeans) conserved intellectual occupations, land ownership, the military hierarchy, ecclesiastical positions, and the direction of the Chilean colony, and left manual occupations to Amerindians or to "Mestizos" (persons of mixed European-Amerindian mixed descent) to the present.

The first Spaniards arrived in 1541 and included around 200 individuals, all male with one exception. By 1580 Spaniards there were around 1000 men and 50 women, with an approximate Amerindian population of half a million (Thayer-Ojeda, 1919). The mixture of Spanish men and Amerindian women was obligatory and a rapidly increasing Mestizo population was established. The Mestizos had (and have) an interesting genetic composition: 1) Their autosome ancestry is 50% Caucasian and 50% Amerindian; 2) Mitochondrial inheritance is 100% Amerindian; 3) Chromosome Y is 100% Caucasian; 4) Chromosome X is 66.7% Amerindian and 33.3% Caucasian. Anthropometric, skin color, extended CED (Rh system) serotypes with 8 haplotypes and several other blood marker studies agree with the SGC demonstrated mainly with the ABO and Rh(-) alleles. They also agree with the asymmetric sexual composition (Valenzuela, 1975, 1983, 1997; Valenzuela et al., 1978, 1980; Zemelman et al., 2002). The SGC and the asymmetry of mating is well documented at present with molecular genetic markers in Chile (Acuña et al., 2002; Cifuentes et al., 2004) and in other Latin American populations (Rodas et al., 2003; Martínez et al., 2007).

The next waves of Spanish or European colonizers found a large Mestizo population and mated with Mestizo women, thus generating a cline in the Mestizo population with ½, ¼, 1/8 Amerindian ancestry. Spanish women arrived to Chile either married with Spanish men or mated in Chile with Spanish men, or with Mestizo men with a low proportion of Amerindian admixture (Am-Ad). By the mid-17<sup>th</sup> century more Spanish women began to arrive and a population of "Criollos" (individuals born in Chile whose ancestors were all Spaniards) was also installed. Thus, a clear socio-ethno-genetic cline was established. Spaniards or Criollos conserved the highest socioeconomic strata; then Mestizos with more Caucasian than Am-Ad; Mestizos with equal Caucasian and Am-Ad; Mestizos with more Amerindian than Caucasian admixture; and finally Amerindians. In the standard interpretation, the maintenance of this SGC occurred and occurs mainly by two factors: I) Isophenic (election of similar phenotype for mating) assortative mating by SES and ethnicity conserved the difference in the allele frequencies in at least Amerindians, Mestizo, and Europeans (Valenzuela and Harb, 1977, Valenzuela, 1998); II) Preferential new European immigration to high strata and preferential Amerindian internal "immigration" (or incorporation) to low strata (Valenzuela, 1983, 1998). The predictions of the standard interpretation are precise. I) in the highest strata the allele frequencies of A, B and Rh(-) should increase, at most, until the European frequencies; II) in the lowest strata these frequencies should reach the Amerindian frequencies, zero for the three; III) among all the strata the sociogenetic cline should be observed. The third condition is well documented as has been shown. But I) and II) are to be demonstrated. Unfortunately, racism was introduced into Chilean culture by Spaniards from the very beginning. To be "Indian" has to the present been considered negative; and the word "Indian" is still used as an offense This is a negative cultural factor that has contributed to maintaining the cline.

# Insufficiency of the standard interpretation to account for some SGC traits

By the late 60's and early 70's, the standard interpretation was considered insufficient to account for several traits of the SGC. An important condition is the maintenance of this SGC with highly separated classes for more than 450 years. Pinto-Cisternas et al. (1971) used the place of residence to estimate the socio-economic stratum and proportion of European ancestry. They sampled students living in Valparaiso (the second most populated city of Chile) according to places of residence. This sampling procedure is unbiased for the purpose of assigning a socioeconomic stratum to individuals, because the only trait that is important is place of residence, previously classified by the socioeconomic stratum. They found higher A frequency (fA) in higher SES and higher O frequency (fO, fB is the gene B frequency) in lower SES. They did not find a significant heterogeneous association by the  $\chi^2$  test with ABO phenotypes. However, the present study (with maximum likelihood estimates assuming Hardy-Weinberg equilibrium) of fA, fB and fO shows significant associations with strata (rA = -0.638; r0=0.632; rB=-0.023; P<0.069 for fA and fO, and P = 0.952 for fB, see APPENDIX 1), when using the socioeconomic classification alone. However, P was <0.025 for fA and fO when using socioeconomic and ancestry criteria together (not shown). The fB did not present association with strata and had an erratic behavior. This could not be due to the small number of B individuals because gene frequencies are estimated from the whole sample of the stratum, and the smallest stratum had 40 individuals (80 sampled genes). This erratic behavior of fB could not be produced by cultural, historical or sampling processes, because the expected behavior of B should be equal to that of the A allele (both were not present in Amerindians). It shows rather a systematically contradictory behavior with A. As well, the highest SES had A and O frequencies equal

to Spanish frequencies (in contradiction to the necessary mixture of colonizing men with Amerindian women), and these frequencies did not reached 0.0 and 1.0 (the expected frequencies in Amerindians), respectively in the lowest strata as expected from cultural and historical processes (see the standard interpretation). The difficulties of the standard model could be accounted for by a pattern of immigrations of Caucasians, mostly to the higher strata, and Amerindians to the lower ones (as mentioned); but, even accepting this pattern, it is still difficult to account for the condition of stability of ABO composition among strata over 450 years.

There have been 16 generations (near 25-30 years per generation) since the arrival of Europeans. We do not have estimates of inter-marriages among different SES (outbreeding). If the frequency of inter-strata marriages is 15%, the largest difference in gene frequencies should be reduced (in 16 generations) to 7.4% of the original difference. Thus, it was not expected to find a cline for the ABO or Rh systems in the Chilean population because it is highly probable that inter-strata couples occur with frequencies equal to or over 15%. Nobody discriminates, falls in love or marries according to blood groups. Thus other phenotypes should be the basis for mating selection, and the choice made exclusively within the ethno-socio-cultural-economic stratum should produce not a cline but two classes: Mestizo (or Amerindian-Europeans) and Criollos (or Europeans), because the original Amerindians, with whom the primary admixture was made, soon disappeared. The other Amerindians, who did not admix were incorporated slowly into the Chilean people as colonization advanced southward. Anthropometric traits or skin color may be used for this selection, but they are not related, as far as we know, with ABO or Rh phenotypes, thus they cannot produce the permanent asymmetric association between ABO or Rh phenotypes and SES. Behavioral and psychosocial traits have been reported to be associated with genetic markers in animals and humans (other than ABO, see Ardiel and Rankin, 2009, Fowler et al. 2011) but their analysis is out of the scope of this article. By that time we discovered, in a public maternity attending the lowest strata, an extraordinary similarity of the ABO frequencies between mothers and their newborns, even making the correction for mother-infant genetic dependence (Harb and Valenzuela, 1976).

Thus, we decided to study the frequencies of ABO alleles and phenotypes in two maternity wards in Santiago attending individuals from very different SES. We used the powerful ITO matrix method of genetic kinship (Li, 1976) applied to mothernewborn pairs. It allows estimating phenotype, genotype and gene frequencies of mothers, newborns and fathers. For example, the phenotype frequencies of newborns to O (genotype OO) mothers directly shows the gene frequencies of the fathers (a population Mendelian backcross). We chose mother-newborn pairs because this is an unbiased sample of all the population attended by a health service in that period. Another important advantage of the method is that with mother-newborn pairs we know the phenotypes, some genotypes and gene frequencies of at least two generations. Since, the parents of the mothers belong very probably to the same socioeconomic stratum; we know the tendency of genetic frequencies through three generations (90 years) in the same SES. The aim of this study was mainly: 1) to measure the difference of gene frequencies between both strata as an estimate of the sociogenetic cline, and 2) to measure the strength of assortative mating within each stratum by comparing the gene frequencies among mothers and fathers. We chose the maternity ward of the Hospital San José (HSJ), a public hospital attending persons from the lowest socioeconomic stratum and the maternity ward of Clínica Alemana (CAL), a private clinic attending persons from the middle and high SES (Valenzuela and Harb, 1977). A summary of results is presented in APPENDIX 2. There was a high degree of similarity of ABO phenotype frequencies between mothers and their newborns. The  $\chi^2_3$  tests for heterogeneity resulted non significant, even after multiplying them by 4 to correct for the genetic correlation between mothers and their newborn (1/2). The similarity was found in CAL although the clinic attends persons from several SES (middle to high) and persons coming from low SES (charity service). The difference in phenotype and gene frequencies between CAL and HSJ was highly significant and indicates they are two distinct gene pools. For example, the difference in fA (or p) is around 0.06, and since p in HSJ is 0.16, this implies a fraction equal to 37.5% of HSJ p. This does not happen with q or fB, with a difference 0.008 in 0.063, which is 12.7% of HSJ q. The fO (fO is the frequency of the O allele that is currently named r, the context indicates the difference with "r" the Pearson's correlation coefficient) depends completely on the other two frequencies. Again, as in Valparaiso, the strange behavior of the B allele indicated that a non-cultural-historical process occurred in ABO in relation to SES. It is remarkable that among the fathers' gene frequencies (estimated from newborns to OO mothers), fB was higher in HSJ than in CAL. This contradicts the situation expected by the standard interpretation. The behavior of fB cannot be due to randomness (the number of genes used to estimate gene frequencies is over 550) nor to bias in data collection since the entire population attended during this period was typed. It has often been said that samples from health services are greatly biased and do not represent to the total population. Besides mother-newborn pairs (unbiased sample of the total population), we also studied blood receptors and donors at CAL and HSJ, respectively to test for these biases. No bias could be detected in either service; genetic frequencies were similar to those of mother-newborn pairs. The difference in the A gene frequencies cannot be maintained for 16 generations with inter-stratum mating as low as 15% (the expected difference in gene frequencies should be 7.4% not 37.5%). The following analyses of published data seek to explain this situation. Is the SGC found in Chile for the ABO and Rh system produced and maintained exclusively by cultural factors or is it produced by sociogenetic conditions associated with the ABO or Rh systems?

#### THE SGC IS A TRUE PROCESS OCCURRING IN CHILE

#### Cross-linking socioeconomic and genetic classifications

Private and public health services are correlated with SES, but they include several strata. It was necessary to determine a correlation with a precise socioeconomic classification and blood groups. Data from Pinto-Cisternas et al. (1971) and from Valenzuela and Harb (1977) showed the SGC clearly and indicated that this could not be produced by cultural or historical processes alone, at least for the contradictory behavior of the B allele and groups (included AB). Place of residence includes several SES and this heterogeneity blurs socio-genetic relationships. We chose the classification of Orlando Sepúlveda based on occupations clustered according to power, prestige, life style, income, education level, place of residence and other less important variables. Unfortunately, it has not been published in international or national journals and was taken from a post-graduate thesis (Rona, 1972) and an internal publication of the University of Chile (Sepulveda, 1960). It classifies individuals into 13 strata that could be clustered into 5 or 3 new coalescent groups. From our perspective, the underlying paradigm of a socioeconomic classification is not relevant provided that it is based mainly on power (number of persons in charge), prestige (the social occupation), life style, ownership, income, and less importantly education (formal schooling). Any classification fitted our purposes if overlapping categories were minimal and extreme strata were well represented. From our naïve position, we accepted the socioeconomic classification independent of the sociological paradigm it is drawn from and made a link with blood group (genetic markers) phenotypes. The rationale of the procedure is a double blind scientific attitude and design. Geneticists accept without criticism the sociologists' ideology and classifications (socioeconomic strata), and sociologists accept without criticisms the geneticists' ideology and classifications (blood typing). The expected null hypothesis is that no correlation between the two kinds of categories should be found. Persons in a socioeconomic stratum cannot behave socio-culturally according to their blood groups unless there is a psycho-social function that relates the two kinds of traits. As well, blood types are randomly distributed among socioeconomic strata unless there is a genetic property of ABO that changes the probability of belonging to a particular SES. The possible association due to isophenic assortative mating is under control, because the expected phenotype and gene frequencies are estimated given the fixed ancestral (Caucasoid and Amerindian) gene frequencies and the rationale of population genetics. For example, if all the Amerindians were 0, fA were 0.0 and if Spaniards had fA = 0.3, the expected Mestizo fA after half and half admixture would be 0.15 (if the sample of Spaniards were representative of all the Spaniards in Spain).

In 1979 we undertook the study to link SES with the ABO and Rh system in blood donors in Santiago, Chile (Acuña et al. 1980). A sociological disciple of Prof. O Sepúlveda, J. Valenzuela, undertook the study of the correlation among socioeconomic classifications used in Chile and abroad. He worked with the Sepúlveda's classification, the Graffar classification (Valenzuela et al., 1976) and the occupational classification used in England (Office of Population Censuses and Surveys, 1970, used by Beardmore et al., 1983, in England and by Kelleher et al., 1990, in Ireland). He found a high correlation among them (0.85, personal communication). However, using the same information from Sepulveda's sample (a random sub-sample of 600 individuals) and the classification, he provided an accurate estimate of the proportion of the SES for the population of Santiago, Chile. With this information and ours on ABO and Rh systems from blood donors, classified according to the Sepulveda's classification, the SGC of the population of Santiago, Chile (Acuña et al., 1980; Valenzuela, 1984a, 1988; Valenzuela et al., 1987) could be estimated. It is presented in Table 1 and APPENDIX 1 (together with data from Valparaiso). With the sample of 600 cases, for estimating the proportion in each

stratum, and of 1,542 cases for estimating gene frequencies, using the same socioeconomic classification, estimates provide a good approximation of the SGC in the population of Santiago, Chile around 1960-1980. Thus, we sampled 1,542 blood donors to blood banks of private and public health services in Santiago. It is important to note that individuals (after giving informed consent) are first classified according to the socioeconomic stratum by Sepulveda's questionnaire, which included questions on power, income, ownership, education and occupation. After applying the questionnaire, information on blood groups typed by trained persons from the blood bank and by us (if necessary), was added to the record. Only one individual per family (blood donors very often come in families) was randomly chosen for the study. Classifying first by socioeconomic stratum and taking only one individual per family reduced greatly biases due to clinical ascertainment from blood banks. The situation is similar to the study of Pinto-Cisternas et al. (1971) in Valparaiso where the source of individuals is not relevant, because the variable to enter into the study was the socioeconomic stratum to which the individual belonged. Moreover, this was not a random sample of blood donors, because the extreme strata could be absent; we directed sampling to find the extreme strata. APPENDIX 1 presents some results of the study with blood donors in Santiago. We found a high negative correlation between fA and SES, keeping in mind that strata are numbered from the highest 1 to the lowest 13 [r(A-SES) = -0.777, P=0.0018]; a high positive correlation between fO and strata [r(O-SES) = 0.839, P=0.00034]; a positive but not significant correlation between fB and strata [r(B-SES) = 0.444,P=0.128]; and a positive, non-significant correlation between the B+AB frequency and strata [r(AB-SES) = 0.451, P = 0.122]. Among gene frequencies, fB correlated negatively with fA [r(A-B) = -0.844; P=0.00029) and significantly positive with fO [r(O-B) = 0.723; P=0.0053]. The same behavior occurs with f(B+AB, phenotypes), which correlates negatively with fA and

#### TABLE 1

Sociogenetic cline of the population of Santiago, Chile, with estimates of O and Rh(-)or d frequencies and Amerindian genetic admixture (from Valenzuela, 1984a and Valenzuela et al., 1987)

Classification in 5 strata								
Stratum	Population %	Frequ	encies	Am Admixture %				
		0	d					
Ι	4.7	0.6236	0.5000	- 19.4				
II	15.0	0.7099	0.3320	15.5				
III	8.0	0.7177	0.3138	20.5				
IV	41.0	0.7839	0.2367	37.5				
V	31.3	0.7846	0.2469	37.3				
Classification in 3 strata								
Ι	4.7	0.6236	0.5000	- 19.4				
II (II+III)	23.0	0.7126	0.3255	17.2				
III (IV+V)	72.3	0.7842	0.2411	37.4				

Sample sizes, methods for estimation of gene frequencies, percentage of Amerindian admixture, and frequencies for each SES are in the cited articles

positively with fO. This indicates that fB and f(B+AB) behave with the opposite fA frequency, but the same as that of fO. This contradictory behavior of the B allele and phenotypes (B+AB) with the A allele and phenotype refutes conclusively that cultural, historical or drift factors are the exclusive origin and factor maintaining the SGC. As mentioned above, because the B and A alleles were not present in Amerindians, they must behave equally under the standard interpretation. Moreover, f(B+AB) should behave the same as fA, not only because both genes were not in Amerindians but because the genotype AB includes the A gene [the expectancy of f(AB) is 2x(fA)x(fB)]. Thus, the AB phenotype, which should show the same tendency as the A phenotype under the culturalhistorical-drift hypothesis, behaves in contradiction to this expected behavior. Moreover, fAB correlates positively with fO, although this correlation should be highly negative [r(A-AB) =-0.306, P=0.309; r(O-AB) = 0.285, P=0.346]. Thus, the B allele shows "dominance" over the A and O alleles in relation to the distribution among SES (considering strata as phenotypes). The contradictory behavior of the B allele and B+AB phenotype with the A allele and with the expected behavior under the standard interpretation cannot be due to either random variations (more than 3,000 independent genes) or to the bias of ascertainment of the service (because the individuals were classified first by their socioeconomic stratum and came from several blood banks in Santiago).

Table 1 shows a conclusive confirmation of the SGC: an impressive negative percentage of Am-Ad in stratum I. This is due to the fact that this stratum had higher frequencies of Rh(-), A and B genes than the Spanish sample used to estimate the ancestral gene frequencies. Under the standard interpretation A, B and Rh(-) gene frequencies of Chileans cannot be higher than the respective European frequencies. This is a second conclusive refutation of the cultural-historical-drift factors hypothesis as unique factors of the SGC. These negative percentages of Am-Ad in stratum I indicate that genetic factors are involved in the concentration of A and Rh(-) in this stratum, and in decreasing the expected B frequency. The lowest strata did not show the near zero frequency of A, B and Rh(-) expected under the Standard Interpretation.

#### Difficulties arising from misconceptions about connection between racism and biotic determination of socioeconomic structures

The reader might ask why, if these studies began in the early 70s, so much time passed (10 years or more) before publishing the complete SGC (Valenzuela, 1984a, 1988; Valenzuela et al., 1987). We had the same problem as Vygotsky, our articles, accepted scientifically, were rejected by some editorial boards because they were thought to contribute to racism. The debate on human races was so ideologically laden that race was taken out from debates and replaced by "ethnic group". It was considered dangerous for politicians or editors to include any reference to races or biotic determination of sociopsychic characters in speeches or journals. Although genetic factors that determine the social structure have nothing to do with racial conflicts and are contradictory with racism (genes determine some phenotypes independently of ethnic groups), it became more and more difficult to publish these studies (Prof. Beardmore told me he had the same problem in England). Our article (Valenzuela et al., 1987) with data collected in 1979 (Acuña et al, 1980) prepared to contribute to the discussion of the Beardmore and Karimi-Booshehri (1983) article was published in 1987 and a further discussion of the subject was, at last, published in 1988 (Valenzuela, 1988). It is a paradox that similar research works of Vygotsky and ours were persecuted in the Soviet Union and in the capitalist world, respectively.

#### Extending the study to larger samples and genetic markers

We and other researchers have made several studies with genetic markers and Chilean populations whose SES were known. We then tested our hypothesis of the SGC. We extended the sample of mother-newborn pairs from CAL (to 6,974 mother-newborn pairs) and HSJ (to 1,379 mothernewborn pairs). We also studied a sample from the Regional Hospital of Temuco (a public health service for the low and middle-low SES that attends a population with a high prevalence of Amerindians) and classified individuals according to Chilean, European and Amerindian surnames. The SGC was found to be in complete agreement with the European and Amerindian proportion of surnames in the three hospitals (Valenzuela, 1984a). The proportion of Am-Ad of SES mostly from middle-low and low strata was consistent, as an average, with the SGC in studies with alleles of haptoglobin (Hp), esterase D (EsD), phosphoglucomutase 1 (PGM-1), Xg blood group, Gm and Km immunoglobulin allotypes and the other haplotypes of the CDE (present nomenclature of Rh) locus (Valenzuela et al., 1980, 1983; Valenzuela, 1984a, Arcos-Burgos et al., 1997). However, the variance of the admixture estimates was enormous (Acuña, 1982). This heterogeneity of the percentage of Am-Ad calculated with different genetic markers indicates that evolutionary processes operated, such as selection (diseases) and drift. Thus the percentage of Am-Ad should be estimated by several markers including "neutral" molecular markers. Recently, the SGC was described with molecular genetic markers and their frequencies agree with previous average estimates of Am-Ad and the SGC (Acuña et al., 2002; Cifuentes et al., 2004). If ABO and Rh are related (as they really are) to SES, they yield biased estimates of ethnic admixture. Table 2 presents an extended study with 25,501 mother-newborn pairs from the University Hospital, which attends the middle-low and low SES. Results agreed with previous ones. Again, the frequency of B yields lower estimates of Am-Ad. Bias of ascertainment or due to random sampling are not possible in these mother-newborn samples (more than 85,000 independent genes were ascertained).

A study performed in Valdivia (Chile), which applied Sepúlveda's socioeconomic classification among blood donors of private and public blood banks, found the same SGC as found in Santiago (Cohn et al., 1985). Table 3 presents data from our databank (Valenzuela et al., 1987; Valenzuela, 1988) and Cohn et al., 1985. This synthesis was presented previously, but with a few changes (Valenzuela, 1988). The concordance of the two samples is evident. For the population of Valdivia, with a larger Amerindian component, a larger Am-Ad can be expected. Both samples have a small number of individuals from the highest SES. Persons from highest strata go rarely to blood banks as blood donors. Although these are small numbers (36 and 6), the agreement in gene frequencies and Am-Ad is remarkable and significant. Again the B allele does not agree with what would be expected under the standard interpretation. The Am-Ad for fB was 100% in Santiago and -25.52% in Valdivia. This erratic behavior of fB indicates the participation of genes in the SGC. The following sections summarize the demonstration that the relationships between ABO and SES are true genetic associations that are not due to cultural, historical factors or produced by drift. They deal with some contradictory data from literature.

# THE ABO-SES ASSOCIATION IS A TRUE GENETIC-SOCIAL ASSOCIATION

#### The ABO-socioeconomic association is found not only in Chile

Beardmore and Karimi-Booshehri (1983) performed a study in blood banks in England and found the same SGC. They studied blood donors from SW England and Yorkshire and divide them into Native (born in that locality) and Migrant (4 independent samples). The authors used the same English socioeconomic classification for which a correlation of 0.85 with Sepúlveda's classification was found. They knew our results (Valenzuela and Harb, 1977) and considered it as a product of Spanish-Am-Ad alone (we showed this was not the case). Table 4 presents a summary of the distribution found in the studied cities in England. The A allele and phenotype were more frequent in the highest socioeconomic stratum and the O allele and phenotype in the lowest; the B allele and phenotype were rather erratically distributed among strata. The AB phenotype frequency increases as the socioeconomic stratum decreases (similar to the O phenotype, with the

#### TABLE 2

Gene frequency and percentage of Amerindian admixture (Am-Ad). Samples from the University Clinical Hospital (UCH, middle-low and low SES), Hospital San José (HSJ, middle-low and low SES) and Clínica Alemana (CAL, middle and high SES) (Valenzuela, 1988)

Parameter	UCH	HSJ	CAL
Ν	25,501*	1,251*	6,974*
p (fA)	0.1722	0.1666	0.2253
SE p	0.00146	0.00651	0.00316
% Am-Ad p	39.87	41.83	21.33
q (fB)	0.0582	0.0579	0.0622
SE q	0.00087	0.00390	0.00172
% Am-Ad	13.13	13.58	7.16
r (fO)	0.7696	0.7755	0.7125
SE r	0.00162	0.00724	0.00341
% Am-Ad	34.83	34.45	18.66
d fRh(-)	0.2546	0.2135	0.3395
SE d	0.00303	0.01381	0.00563
% Am-Ad	37.37	47.46	16.44

SE = Standard Error; \* mother-newborn pairs.

STRATA	Ι		]	II	Ι	II
SAMPLES	(S)	(V)	(S)	(V)	(S)	(V)
Ν	36	6	259	278	1247	368
Parameter						
p (fA)	0.3764	0.2992	0.2200	0.1648	0.1626	0.1234
SE (p)	0.0651	0.1453	0.0194	0.0165	0.0077	0.0125
% Am-Ad	-31.42	- 4.47	23.18	42.45	43.23	56.69
q (fB)	0.0000	0.0890	0.0579	0.0442	0.0556	0.0474
SE (q)	0.0000	0.0841	0.0104	0.0088	0.0047	0.0079
% Am-Ad	100.00	-25.52	13.58	34.03	17.01	29.25
r (fO)	0.6236	0.6118	0.7221	0.7910	0.7818	0.8292
SE (r)	0.0651	0.1543	0.0209	0.0180	0.0086	0.0143
% Am-Ad	- 6.48	- 9.82 21.39	40.88	38.27	51.68	
d Rh(-)	0.5000	0.4082	0.3229	0.2162	0.2420	0.1880
SE (d)	0.0719	0.1826	0.0294	0.0293	0.0137	0.0256
% Am-Ad	-23.06	- 0.47	20.53	46.79	40.44	53.73

 TABLE 3

 Gene frequencies (ABO and Rh systems) and percentage of Amerindian admixture, samples from Santiago (S) (Valenzuela et al., 1987) and Valdivia (V) (Cohn et al., 1985)

Nomenclature as in Table 2.

exception of stratum IV). This is in contradiction with the A frequency that shows the inverse distribution (with the exception of stratum IV) and with the erratic behavior of the B frequency. The correlation between the A and AB frequencies is r(A-AB) = -0.84 (P=0.074), a significant figure considering the expected r(A-AB) equal to 0.39. This erratic and contradictory behavior of the B allele and phenotypes indicates a genetic component in the SGC not explained by bias of ascertainment or sampling random variation (more than 18,000 independent genes). It is improbable that the disagreement was due to some blood bank strategy to obtain more blood of a particular type. How could AB individuals from 4 different samples in two cities concur with blood banks in frequencies that correlated inversely to the A frequencies? As well, the SGC was found equally in the four independent groups (Native and Migrant from two localities). The SGC was more extreme in Native than in Migrants. Finding the same correlation between ABO phenotypes and SES, and the same contradictory behavior of B and AB phenotypes in England (in four independent subsamples) and in Chile (in four independent cities) is strong evidence of genetic factors acting on the SGC. The ethnic origin of England people is different from that of Chileans,

excepting for their common Indo-European component (Celtic and Germanic origin of Spaniards). The ancient peoples of the United Kingdom (Ancient Britons and Picts) received first a Celtic immigration from the continent (Britons, Gaels). After them, several population of Germanic origin came to the British Isles: Jutes, Danes, Vikings, Angles, Saxons and Frisians. The Romans also invaded most of England. In the 10<sup>th</sup> century, Normans, a Danish (or Norwegian)-Viking people established in Normandy, France; they assimilated the French culture and mixed with Frankish and Gallo-Roman people living there. From Normandy they invaded England (11th century) and incorporated into the UK, mostly to the English population and the government (Norman-French-Plantagenet Dynasty) and high SES. Celtic people remained mostly in Wales (Gaels), Scotland (Gaels and Scots) and Ireland (Gaels), while in England the Anglo-Saxon-Norman composition was prevalent. Vikings (non Normans), Jutes and Frisians incorporated in smaller proportions and are widespread in the UK; Danes (also included in the State) could have a larger presence. Since Celts, Romans, Angles, Saxons, Danes, Jutes, Frisians, Vikings and Normans are all from Indo-European origins with similar ABO and Rh frequencies, it is difficult to explain the enormous differences of these frequencies among the SES of the present English people. Celts had lower frequencies of A than the other Indo-European groups but their contribution to the English population was smaller (http://www.bloodbook. com/world-abo.html; http://www.blood.co.uk/aboutblood/blood-around-the-world/). If Normans had a higher frequency of A (as present Norwegians have, see reference above) and installed a system of power over the other groups, the conditions to generate a sociogenetic cline are possible. However, there have been nearly 30 generations since the 9th century to the present, and any cline should be greatly diluted. The extent to which the Anglo-Saxon cultural, ethnic and genealogical component subsisted, integrated or prevailed over the Celtic, Norman and other Germanic cultural, ethnic and genealogical components is a fascinating subject to be studied now by adding molecular genetic analyses.

We had newspaper information from Japan of a similar SGC; we could not find scientific evidence for SGC in current international reference systems. An extensive literature on ABO blood groups and social position or personality traits could be found in Japan (http://www010.upp.so-net.ne.jp/abofan/data-e.htm). Since the study in England did not find a significant non random association between Rh and SES, hereafter we shall not analyze this system.

#### The SGC interacts with sex

Some studies showed higher frequency of the A blood group and a lower one of the O group in men than in women, of the same populations (Fisher and Fraser-Roberts, 1943; Valenzuela et al., 1980, Beardmore and Karimi-Booshehri, 1984; Valenzuela, 1988, this study). This difference is maintained in samples from blood donors, along with the SES, in the English study (Beardmore and Karimi-Booshehri, 1984) and among samples of medical students (high SES), a random sample of children participating in a longitudinal

 TABLE 4

 ABO gene frequencies with their standard error (SE) per socioeconomic stratum in England (From Beardmore and Karimi-Booshehri, 1983) and the B and AB groups per strata.

Socioeconomic Stratum

ABO	Ι	II	III	IV	V	Total
p (fA)	0.3725	0.2946	0.2566	0.2683	0.2479	0.2690
SE	0.0176	0.0083	0.0060	0.0079	0.0067	0.0035
q (fB)	0.0453	0.0613	0.0567	0.0649	0.0640	0.0604
SE	0.0067	0.0040	0.0030	0.0041	0.0036	0.0017
r (fO)	0.5822	0.6441	0.6867	0.6668	0.6881	0.6706
SE	0.0179	0.0087	0.0063	0.0083	0.0072	0.0037
B type%	6.35	9.22	7.87	9.43	8.70	8.55
AB type%	2.46	2.63	3.15	3.11	3.71	3.15
$\chi^2_1$ (H-W)	2.0	7.3	0.9	1.1	3.1	0.4

SE = Standard Error;  $\chi^2_1$  H-W =  $\chi^2_1$  for Hardy-Weinberg equilibrium; f = gene frequency.

study (low SES), blood donors and blood receptors in Chile (Valenzuela and Harb, 1977; Valenzuela et al., 1980; Valenzuela, 1988). Alternatively a cytogenetic process named consociated chromosome segregation (the Y chromosome may be associated preferentially to one chromosome 9, where the ABO system is coded, see Valenzuela et al., 1980) and a strong association of ABO, Rh and other genetic systems with the sex ratio at birth (Valenzuela et al., 1980, Valenzuela, 2010) can partially explain this association in Chile, but not in England. Thus the interaction of the SGC with gender is additional evidence for the true relationship between genetic factors and SES. Women may work in occupations associated with less power, prestige and income than men, as it seems it really is.

# Refutations of cultural-historic-drift factors as the unique origin of the SGC

While the standard interpretation of the European-Amerindian admixture and socioeconomic assortative mating can account for the nucleus of the SGC, it cannot account for data showing the direct participation of genetic influence on the cline. We summarize five situations, facts or processes that indicate that genetic factors are involved in the genesis and maintenance of the SGC and refute cultural-historicdrift factors as the only cause of this cline. 1) The SGC is clearly present in Chile and England. The highest SES from the Chilean samples from Santiago (Valenzuela et al., 1987) and Valdivia (Cohn et al., 1985) have ABO frequencies almost equal to the English frequencies found in four large samples from two locations (Beardmore and Karimi-Booshehri, 1984) belonging to the highest stratum, and quite different from the other SES of Chile (see Valenzuela, 1988). 2) The erratic or contradictory behavior of the B allele either alone or in genotypes BB, BO and AB, with the expected behavior deduced from the behavior of A and O alleles. Particularly, the AB phenotype should be distributed equally as the A phenotype, but we observe in Chile (Santiago, Temuco and Valdivia) and in England (four samples from two locations) that the AB distribution is contradictory to the A distribution. The erratic or contradictory behavior of the B group among SES; the B gene behaves as dominant over the A and O alleles. 3) In Chile, the highest SES presented significant higher frequencies of A, B and Rh(-) genes than those found in Spaniards. This is impossible under the standard interpretation of the production of the SGC by culturalhistoric-drift factors alone. 4) There is a significant (SGC)-sex interactions in England and in Chile. Women present a less evident cline than men. 5) The observed distribution of ABO genes and alleles among SES does not fit properly with the expected distribution from the standard interpretation that cannot account either for its invariant maintenance for more than 450 years, with minimal inter-strata mating. The first four situations were presented more than twenty years ago (Valenzuela, 1988); they remained ignored, perhaps, because it was published in a journal considered ideologically biased (the journal of sociobiologists). It is interesting to note (as we have already mentioned) that most scientific references, as for example those given in the Japanese quotation (http:// www010.upp.so-net.ne.jp/abofan/data-e.htm) are published in journals that are not indexed in current international reference systems.

#### DISCUSSION

#### Three important contexts for SGC research

There are three scientific problems related to the SGC under research. I) The existence of the SGC that is well documented through this article. It is also evidenced that this SGC is not due exclusively to historical, cultural or drift processes. II) The maintenance of the SGC since the arrival of Europeans to Chile and their mixture with Amerindians. The fact that Europeans had important frequencies of A, B and Rh(-) alleles, while Amerindians lacked these indicates that at the origin and in the first century the cline had to be maintained. The studies with mother-newborn pairs show that the cline has been maintained at least for the last century. Considering these two facts and the condition that gene frequencies in both kinds of evidence agree with the nucleus of the standard interpretation, we conclude that the cline was maintained for these 450 years. III) The causal mechanism of the non-random association between ABO and Rh alleles and socioeconomic strata. Only hypotheses could be proposed in this point. These hypotheses are the standard ones that formal genetics indicate for any gene-phenotype association. I) Pleiotropic effect: the A, B, O and Rh alleles are directly involved in the neuropsycho-socio-cultural functions that condition the probability to belong to a particular socio-economic stratum. Hard work is necessary at this point. Are ABO sub-groups involved in the SGC? Are AA homozygotes or AO heterozygotes cumulated in the high SES? II) Linkage association: A, B, O and Rh alleles are linked in linkage disequilibrium with the responsible genes of association. This hypothesis is improbable, because the SGC was found in more than 10 independent populations from Chile, England and very probably in Japan; thus crossover could minimize any linkage association. III) Gene interaction: A, B, O and Rh alleles interact with other genes to produce the association. The pleiotropic effect has been examined in relation to intelligence and psychological traits. We studied interactions between academic performance and intelligence and genetic markers. Significant intelligence-ABO blood group interactions were found but did not show the expected relationship to account for the SGC (Valenzuela et al., 1998). A previous study found that A2 (A subgroup) individuals have a higher IQ than the others (Gibson et al., 1973). Several articles have found significant weak correlation between ABO and psychological or psychiatric conditions; they are controversial and are not going to be dealt with here (see quotation: http://www010.upp.so-net.ne.jp/abofan/data-e.htm). The personality traits involved in the genesis and maintenance of the SGC are not known. We propose that they are related to power, ownership, life style, prestige and entrepreneurial abilities. However, a great deal of work in basic psychology is necessary to provide conceptual and operational definitions for such psychological traits. ABO substances appeared early in evolution. They are found from bacteria to humans. That is why the hypothesis on linkage disequilibrium between ABO and genes that condition the SGC does not have factual support. There are thousands scientific articles relating ABO blood groups with diseases; only one indicates a relationship with SES (Suadicani et al., 2000). In Chile we have contributed to the study of ABO, Rh, MNSs and typhoid fever; we did not find significant associations between ABO and this disease in the middle-low and low SES (Herrera et al., 1992).

#### Contradictory cases of Ireland and Chilean samples

Before dealing with apparently contradictory studies, we comment on some necessary conditions to find the SGC. 1) The sample should be large from an important industrial city so as to include individuals from extreme SES; if there are not persons from very high and very low SES the cline is difficult to find. 2) The socioeconomic classification should be based on power, prestige, income, life style, ownership and education; if these variables are not included the SGC will not be found. When the classification is founded on consumption or having home electronic or mechanical apparatus, strata are confounded because now all people consume everything and have any apparatus; the difference is in the quality (life style). Thus, only marginal or very poor people can be classified in the lowest SES, but these persons are seldom blood donors. The variable education taken alone may be misleading. In Chile, by the late 1960's and early 1970's, no more than 15% of people had post-high-school or university studies; now it is 50%; thus education now provides little information on SES. 3) The source of sampling may bias the representation of SES. Blood donors do not well represent the extreme SES, and may be a biased sample of blood groups because rare blood groups are sought for transfusions. Random or total samples of blood donors are surely biased as we have showed previously (see also Herrera et al., 2010). To avoid this bias, blood donors should be selected first by their socioeconomic stratum, and several private and public services should be ascertained to be sure that all SES are represented. We overcame this bias in Chile by sampling mother-newborn pairs (that yield unbiased estimates), blood receptors, medical students and random samples (unbiased) of children. All these samples showed the same pattern of sociogenetic distribution. When the sample is taken from only one medical service (homogenization of life style and health insurance), the SGC will probably not be found. This was the case with a sample from the public hospital of Valdivia (Troncoso, 2007). 4) It is difficult to find the cline in highly democratic societies where power is homogeneously distributed and anyone may own a large enterprise (or be president, a brigadier or major general, admiral or university president). Societies where royal, noble and hierarchical distinctions are considered important could present the SGC (social prestige).

This SGC has not been found in two Irish samples (Dawson and Hackett, 1957; Dawson, 1958; Kelleher et al., 1990, see APPENDIX 3). Fortunately (for the possibility of being a blind researcher), I know almost nothing about socioeconomic stratification in Ireland, or of its history (except of the founding people and possible gene frequencies already mentioned). According to our hypothesis, the fact that no SGC was found in the Irish studies is expected if that sample: 1) belongs to a population with a low proportion of extremely high and low SES, or persons of these extreme strata are not blood donors, or the region attended by this blood bank is a rural; 2) the Irish population is highly democratic and power, ownership, life style, education and prestige are universally distributed and anyone can access almost any social level; 3) there is little or no nobility or royalty; 4) no racism, no socioeconomic (or social class) discrimination and no discrimination by social prestige are present in the population; 5) the socioeconomic classification of the first study is clearly not based on power, prestige or income. Although the socioeconomic classification of the second study is apparently the same as in the study in England, time could change the accuracy for classifying people. As in Chile, the frequency of professionals (the educational variable is not so discriminating for SES) could have increased between the two studies. Moreover, if the proportion of women, for whom the SGC is lees evident, in professional occupations increased in the period between the studies, a decrease in the SGC can be expected. Gene frequencies for the Irish samples are found in APPENDIX 3. It is worth noting the lower frequency of A (0.159) and higher frequency of O (0.765) in the sample from southern Ireland (Munster region) in relation to that from County Dublin and Dublin. This agrees with the different origin of populations; in southern Ireland most people are probably from Celtic origin, while in Dublin there are Irish with an important migration from England (Dawson and Hackett, 1957). The authors of the more recent Irish study considered the result of Beardmore and Karimi-Booshehri (1983) as a puzzle, but they did not cite our studies (Valenzuela and Harb, 1977; Valenzuela, 1984a, 1988; Valenzuela et al., 1987) that agrees with the English study. They cited an article proposing that the relationship between manual work with the O group and intellectual work with A group was rather premature (Valenzuela, 1984b).

#### ACKNOWLEDGEMENTS

I am grateful to my colleagues Zuraiya Harb and Mónica Acuña who worked with me in several of the studies and publications on this subject.

#### REFERENCES

- ACUÑA M, VÁSQUEZ H, VERA M, ZAVANDO V (1980) Estratos socioeconómicos y grupos sanguíneos ABO y Rh en Santiago, Chile (manuscript). Scientific method work to obtain the graduation of Medical Technician. Facultad de Medicina, Universidad de Chile (data published in Valenzuela et al., 1987).
- ACUÑA M (1982) Marcadores genéticos y estimación de mezcla en una población de Santiago-Chile (presented to be incorporated to the Sociedad de Genética de Chile, unpublished; data published in Valenzuela et al., 1980 and Valenzuela, 1984)
- ACUÑA M, JORQUERA H, CIFUENTES L, ARMANET L (2002) Frequency of the hypervariable DNA loci D18S849, D12S1090 and D1S80 in a mixed ancestry population of Chilean blood donors. Gen Mol Res 1:139-146.
- ALVIAL BI, HENCKEL C (1963) Estudio de los grupos sanguíneos en la población hospitalaria de Concepción. Bol Soc Biol Concepción (Chile) 38: 35-40.
- ARCOS-BURGOS M, VALENZUELA CY, HERRERA P, PANDEY JP (1997) Alotipos Gm y Km en una muestra de población chilena. Rev Med Chile 125: 161-164
- ARDIEL EL, RANKIN CH (2009) C. elegans: social interactions in a "nonsocial" animal. Adv Genet 68: 1-22.
- BEARDMORE JA, KARIMI-BOOSHEHRI F (1983) ABO genes are differentially distributed in socio-economic groups in England. Nature 303: 522-524.
- CAMPILLO F (1976) Estudio de los grupos sanguíneos en la población española. An Real Acad Nac Med (España) Tomo XCIII, Cuad 3º: 1-22.
- CIFUENTES L, MORALES R, SEPÚLVEDA D, JORQUERA H, ACUÑA M (2004) DYS19 and DYS199 loci in a Chilean population of mixed ancestry. Am J Phys Anthrop 125: 85-89.
- COHN P, ROTHHAMMER F, CRUZ-COKE R (1985) Correlación entre estructura genética y estratificación social en Chile. Rev Med Chile 113: 470-471.
- DAWSON GWP (1958) The blood group frequencies in some occupational groups in County Dublin. Ann Hum Genet (London) 22: 315-322.
- DAWSON GWP, HACKETT WER (1957) A blood group survey of the County and City of Dublin. Ann Hum Genet (London) 22: 97-110.
- ETCHEBERRY R (1997) Razas humanas y hemato-sero-antropología. Orígenes de los indígenas de Chile y nativos pascuenses en el concierto de las razas humanas. Rev Med Chile 125: 1073-1081.

FISHER RA, FRASER-ROBERTS JA (1943) A sex difference in blood-group frequencies. Nature 151: 640-641.

FOWLER JH, SETTLE JE, CHRISTAKIS NA (2011) Correlated genotypes in friendship networks. PNAS 108: 1993-1997.

- GIBSON JB, HARRISON GA, CLARKE VA, HIORNS RW (1973) IQ and ABO blood groups. Nature 246: 498-500.
- HARB Z, VALENZUELA CY (1976) Aplicación de la matriz estocástica madre-hijo en el cálculo de frecuencias génicas. Rev Med Chile 104: 139-142.
- HERRERA C, MARTÍNEZ C, ARMANET L, CÁRCAMO A, BOYE P, LYNG C (2010) Blood donation in Chile: Replacement and volunteer donors. Biologicals 38:36-38.
- HERRERA P, VALENZUELA CY, ARIAS HP, OLIVARI FP, TERAN CE, UBILLA CP, BRAVO PM, FARÍAS P, OVIEDO I (1992) Fiebre tifoidea en el niño. Asociaciones de los fenotipos sanguíneos ABO, Rh y MNSs. Rev Med Chile 120:986-993.
- KELLEHER C, COOPER J, SADLIER D (1990) ABO blood group and social class: a prospective study in a regional blood bank. J Epidemiol Community Health 44: 59-61.
- LI CC (1976) First course in Population Genetics. Pacific Grove, California, The Boxwood Press.
- MARTÍNEZ H, RODRÍGUEZ-LARRALDE A, IZAGUIRRE MH, DE GUERRA DC (2007) Admixture estimates for Caracas, Venezuela, based on autosomal, Y-chromosome, and mtDNA markers. Hum Biol 79: 201-213.
- MATSON GA, SUTTON HE, ETCHEBERRY RB, SWANSON J, ROBINSON A (1969) Distribution of hereditary blood groups among Indians in South America. Am J Phys Anthrop 27:157-194.
- OFFICE OF POPULATION CENSUSES AND SURVEYS (1970) Registrar-General's classifications of occupations. London: Her Majesty's Stationery Office.
- PINTO-CISTERNAS J, FIGUEROA H, LAZO B, CAMPUSANO C (1971) Genetic structure of the population of Valparaiso. Hum Hered 21: 431-439.
- RODAS C, GÉLVEZ N, KEYEUX G (2003) Mitochondrial DNA studies show asymmetrical Am-Ad in Afro-Colombian and Mestizo populations. Hum Biol 75: 13-30.
- RONA R (1972) Influencia genética y ambiental en la edad de menarquia en adolescents de Santiago. Thesis to obtain an academic position. Facultad de Medicina, Universidad de Chile.
- SEPÚLVEDA O (1960) Clasificación nacional jerarquizada de las ocupaciones expresadas en grandes estratos (manuscript). Facultad de Sociología, Universidad de Chile.
- SUADICANI P, HEIN HO, GYNTELBERG F (2000) Socioeconomic status, ABO phenotypes and risk of ischaemic heart disease: an 8 years followup in the Copenhagen Male Study. J Cardiovasc Risk 7:277-283
- THAYER-OJEDA L (1919) Elementos étnicos que han intervenido en la población de Chile. Santiago, Chile: Imprenta, Litografía y Enc. "La Ilustración".

- TRONCOSO E (2007) Composición genética y gradiente socioeconómico de una muestra del Hospital Base de Valdivia, Chile, utilizando los marcadores genéticos ABO y Rh. Undergraduate Thesis, Facultad de Ciencias, Universidad Austral de Chile.
- VALENZUELA CY (1975) Dimorfismo sexual pondoestatural en una población chilena. ¿Evidencia de genes para estatura en los cromosomas sexuales? Rev Med Chile 103: 322-326.
- VALENZUELA CY (1983) Pubertal origin of the larger sex dimorphism for adult stature of a Chilean population. Am J Phys Anthrop 60: 53-60.
- VALENZUELA CY (1984a) Marco de referencia sociogenético para los estudios de Salud Pública en Chile. Rev Chil Pediat 55: 123-127.
- VALENZUELA CY (1984b) Blood group and socio-economic class. Nature 309: 398.
- VALENZUELA CY (1988) On sociogenetic clines. Ethol Sociobiol 9: 259-268.
- VALENZUELA CY (1997) Evaluación de la estatura como indicador nutricional poblacional. Rev Med Chile 125: 595-604.
- VALENZUELA CY (1998) Sociogenetic structure of the Chilean population. In: SANTOS JL, ALBALA C, PÉREZ F (eds) Genetic Epidemiology of Diabetes in Chile. Santiago, Chile, INTA, Universidad de Chile pp: 72-77.
- VALENZUELA CY (2010) Sexual orientation, handedness, sex ratio and fetomaternal tolerance-rejection. Biol Res 43: 347-356.
- VALENZUELA CY, HARB Z (1977) Socioeconomic assortative mating in Santiago, Chile: a demonstration using stochastic matrices of motherchild relationships applied to ABO blood groups. Soc Biol 24:,225-233
- VALENZUELA CY, ROTHHAMMER F, CHAKRABORTY R (1978) Sex dimorphism in adult stature and sex chromosome composition in four Chilean populations. Ann Hum Biol 5: 533-538.
- VALENZUELA CY, AVENDAÑO A, HARB Z, ACUÑA M (1980) Grupos sanguíneos en escolares de un estudio longitudinal: un extraño serendipismo. Rev Chil Pediatr 51: 433-441.
- VALENZUELA CY, PURATIC O, ACUÑA M, HARB Z, AVENDAÑO A, BRAVO M (1983) Patrones y valores de proteínas plasmáticas y erotrocitarias en escolares de 9 a 12 años. Rev Chil Pediatr 54: 243-245.
- VALENZUELA CY, ACUÑA MP, HARB Z (1987) Gradiente sociogenético en la población chilena. Rev Med Chile 115: 295-299.
- VALENZUELA CY, PASTENE CS, PÉREZ CM (1998) Intelligence and genetic markers in Chilean children. Biol Res 31: 81-92.
- VALENZUELA J, DÍAZ E, KLAGGES B (1976) Empleo de un nuevo método de clasificación social. Cuad Med Soc (Santiago, Chile) 17: 14-22.
- WORKMAN PL (1973) Genetic analyses of hybrid populations. In CRAWFORD MH, WORKMAN PL (eds) Methods and theories of Anthropological Genetics. Albuquerque, NM: University of New Mexico Press. pp 117-151.
- ZEMELMAN V, VON BECK P, ALVARADO O, VALENZUELA CY (2002) Dimorfismo sexual en la pigmentación de la piel, color de ojos y pelo y presencia de pecas en adolescentes Chilenos en dos estratos socioeconómicos. Rev Med Chile 130: 879-884.

#### **APPENDIX** 1

Socioeconomic stratum (SES) and ABO gene frequencies in two Chilean cities: 1) from Valparaiso (Pinto-Cisternas et al., 1971, N = 790 students); 2) from Santiago (Valenzuela et al., 1987, N = 1,542 blood donors)

Valparaiso					Santiago				
SES*	fA p	fO r	fB q	SES*	fA p	fO r	fB q	f(AB+B)	
1	0.280	0.674	0.046	1	0.422	0.577	0.000	0.000	
2	0.242	0.745	0.013	2	0.366	0.633	0.000	0.000	
3	0.216	0.748	0.036	3	0.184	0.728	0.088	0.167	
4	0.227	0.739	0.034	4	0.259	0.699	0.042	0.082	
5	0.239	0.729	0.032	5	0.214	0.732	0.055	0.106	
6	0.169	0.777	0.054	6	0.176	0.763	0.061	0.119	
7	0.246	0.710	0.044	7	0.173	0.777	0.050	0.098	
8	0.117	0.848	0.035	8	0.180	0.767	0.053	0.104	
9	0.206	0.763	0.031	9	0.121	0.824	0.055	0.106	
				10	0.171	0.776	0.054	0.104	
r	-0.638	0.632	-0.023	11	0.147	0.805	0.048	0.093	
t	2.19	2.16	0.06	12	0.114	0.800	0.086	0.164	
df	7	7	7	13	0.181	0.779	0.040	0.078	
Prob	0.065	0.068	0.952	r	-0.777	0.839	0.444	0.451	
				t	4.09	5.12	1.65	1.67	
				df	11	11	11	11	
				Prob	0.0018	0.00034	0.1281	0.1222	

\*SES ordered from the highest to the lowest one; f = frequency; r = Pearson's correlation coefficient; t = t test for r; df = degrees of freedom; Prob = probability

#### **APPENDIX 2**

Comparisons of ABO phenotypic and gene frequencies of mother-newborn pairs in private (CAL) and public maternity wards (HSJ) and between mothers and their newborns within both maternity wards (from Valenzuela and Harb, 1977)

	CAL (Private Clinic)					HSJ (Public Hospital)					
ABO groups		AB	А	В	0	Tot	AB	А	В	0	Tot
Mothers	Ν	60	856	235	1210	2361	17	279	83	589	968
	%	2.5	36.3	10.0	51.2		1.8	28.8	8.6	60.8	
Newborns	Ν	50	884	240	1187	2361	13	275	88	592	968
	%	2.1	37.4	10.2	50.3		1.3	28.4	9.1	61.2	
		$\chi^2_{3} = 1.6 \text{x4} = 6.4$ ; P = .094						$\chi^{2}_{3} =$	0.7x4=2.8; F	°=.424	
			Mothers						Newborns		
ABO groups	AB	А	В	0	Tot	AB	А	В	0	Tot	
CAL	60	856	235	1210	2361	50	884	240	1187	2361	
HSJ	17	279	83	589	968	13	275	88	592	968	
		$\chi^{2}_{3} =$	= 24.9; P=1.6	x10 <sup>-5</sup>			$\chi^2_3 = 34.3; P = 2.9 \times 10^{-7}$				
				GENE FRE	QUENCIES	5					
			CAL			HSJ					
Estimation Metl	hod	p(fA)	q(fB)	r(fO)	p(fA)	q(fB)	r(fO)	-			
Mothers ML		0.218	0.065	0.718	0.167	0.053	0.780				
Newborns ML		0.223	0.064	0.713	0.162	0.054	0.784				
Total T matrix ML 0.221 0.063 0.716 0.166		0.055	0.779								
Mothers O		0.231	0.061	0.708	0.158	0.065	0.777				
Receptors-Donors* 0.222 0.063 0.715 0.164 0.055 0.781											

ML = maximum likelihood; Total T matrix = all mother-newborn pairs; Mothers O = fathers' genetic frequencies from O mothers (backcross, see text); \* Receptors in CAL, Donors in HSJ.

## **APPENDIX 3**

ABO gene frequencies according to the socioeconomic stratum (SES) of two samples of Irish blood donors: 1) from County Dublin (Dawson, 1958; N = 6,806); 2) from 35 regional centres in Southern Ireland (Kelleher et al., 1990; N = 2,204)

	Southern Ireland						
SES	fA p	fB q	fO r	SES	fA p	fB q	fO r
Professional	0.207	0.066	0.727	Ι	0.169	0.071	0.760
Clerical	0.200	0.080	0.720	II	0.151	0.074	0.775
Skilled manual	0.205	0.069	0.726	IIINM	0.148	0.074	0.778
Unskilled manual	0.211	0.070	0.719	IIIM	0.168	0.076	0.756
Not classifiable	0.185	0.064	0.751	IV	0.171	0.078	0.772
				V	0.139	0.089	0.772

NM = non-manual.