Table 1. Results of sensitivity tests.

Rare-earth ion	$H_2C_2O_4$ (M^{+3} μg/ml)	Cupferron (M^{+3} μg/ml)
Lanthanum	6.3	2.4
Cerium (III)	6.4	1.6
Praseodymium	6.4	1.6
Neodymium	6.6	2.5
Samarium	6.9	5.1
Gadolinium	17.8	17.8
Yttrium	10.2	10.2

The results of the sensitivity tests are given in Table 1. In general, cupferron appears to be a more sensitive reagent for the detection of the metal ions than oxalic acid. The sensitivity of the oxalic acid tests are greater than those previously found (*1*) but this is perhaps attributable to the absence of a mineral acid. The sensitivity of both reagents decreases with an increase in metal ion atomic number.

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Blood Groups in Pituitary Adenoma—"Suspected Correlation" Reexamined

Mayr, Diamond, Levine, and Mayr (*1*) have recently presented data on ABO blood groups in 123 patients with chromophobe adenoma of the pituitary gland. Of these patients, 57 were from three Boston hospitals and 66 from two hospitals in New York City—23 from the New York Hospital and 43 from the Presbyterian Hospital. Boston and New York patients alike showed marked deviations—more group O, less group A—from the distributions (i) estimated for the total Boston population and (ii) found among 637 Boston patients with brain tumors other than chromophobe adenoma. Distributions i and ii were virtually identical. When the Boston brain-tumor patients were compared with all 123 patients with chromophobe adenoma, the χ^2 test gave a p value < 0.001, but when they were compared with the 57 Boston adenoma patients, $0.02 > p > 0.01$ (my calculation).

Mayr *et al.* wisely considered their findings as tentative, in view of the smallness of their pituitary adenoma sample, despite the statistical significance of the deviation and the concordance of data from four of the five hospitals.

Their investigation has been extended for two reasons. A previous compilation (*2*) on a larger sample of Presbyterian Hospital patients with chromophobe adenoma of the pituitary had shown a blood group distribution unlike that of Mayr *et al.* from the same hospital and one which, in fact, did not differ from that of the Presbyterian Hospital as a whole (*3*). Moreover, the adequacy of a Boston population as a control can be questioned, in view of the high proportion, in certain New York hospitals, of Negroes, with a greater than 2 to 1 preponderance of blood group O over A (*4*), and in view of the different ancestry of the Boston and New York white populations. Not only cities but hospitals within a city and even services within the same hospital may vary widely in genetic composition. It was therefore decided to review (*5*) all cases of chromophobe adenoma at the Presbyterian Hospital for the past 20 years, as far back as records are readily available, and to compare their ABO incidence with that for the Presbyterian Hospital as a whole. This was based on all persons (2259 in number) who received blood transfusions during a 6-month period in 1953. Although the hospital population may have changed over the 20-year period, the transfusion series was deemed an adequate control group for the purpose.

After exclusion of mixed chromophobe and eosinophilic adenomas and of cases where the diagnosis was doubtful or where a microscopic tumor was encountered incidentally at autopsy, 321 cases of adenoma were found. The diagnosis rested on tissue examination or on firm clinical grounds (including enlarged sella turcica, encephalograms, endocrinological and visual abnormalities, and response to x-ray therapy), or on a combination of the two. Of the 321 patients, blood had been typed in 203. There was no difference in ancestry between those who had and those who had not blood-group determinations ($p = 0.60$) or in blood-group frequencies between the 132 with and the 71 without tissue diagnosis ($0.05 > p > 0.02$). The patients with blood-group determinations included 18.2 percent Jews, 7.4 percent Italians, 46.4 percent other whites, and 17.2 percent Negroes. Corresponding figures for the "transfusion group" were quite comparable—16.1 percent, 5.7 percent, 60.0 percent, and 16.4 percent.

In ABO frequency (Table 1), neither whites, Negroes, nor the adenoma series as a whole, which also included eight Puerto Ricans, ten other Latin Americans, and one Chinese, differed from the corresponding "transfusion" group. Chi-square tests gave the respective p values of 0.40, 0.40, and 0.60. While there was a slight percentage preponderance of group O and deficit of A, it is not permissible statistically to compare such subtotals when the complete distributions do not differ (*6*). Neither the total Presbyterian Hospital adenoma series nor the white subgroup within it differed from the Boston brain-tumor series of Mayr *et al.*—p values are 0.25 and 0.40, respectively. Thus, a sizable Presbyterian Hospital series affords no basis for the "suspected correlation" between blood-group frequency and pituitary adenoma.

Should a comparable anlysis of the New York Hospital data yield similar results—a not unreasonable supposition—the "suspected correlation" would rest solely on a probability, based on 57 Boston patients, between the 1-percent and 2-percent significance levels—far from the 0.001 level recommended by Fraser Roberts (*7*) for blood-group correlations.

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Table 1. ABO blood groups in Presbyterian Hospital patients receiving blood transfusion and those with chromophobe adenoma of the pituitary.

	Blood group								
	O		A		B		AB		Total
	No.	%	No.	%	No.	%	No.	%	No.
Whites									
"Transfusion group"	802	43.4	751	40.6	213	11.5	82	4.4	1848
Adenomas	71	47.3	50	33.3	21	14.0	8	5.3	150
Negroes									
"Transfusion group"	187	50.5	101	27.3	67	18.1	15	4.0	370
Adenomas	20	58.8	8	23.5	6	17.6	0	0	34
Total series									
"Transfusion group"	1011	44.5	865	38.3	286	12.6	97	4.6	2259
Adenomas	101	49.8	66	32.5	28	13.8	8	3.9	203

References and Notes

1. E. Mayr *et al.*, *Science* 124, 932 (1956).
2. A. Damon, unpublished study.
3. This was determined by John Scudder and R. H. Osborne, who kindly allowed access to their unpublished data and permission to quote.
4. E. B. Miller, R. E. Rosenfield, P. Vogel, *Am. J. Phys. Anthropol.* 9, 115 (1951).
5. This work was done during the tenure of a research fellowship of the American Heart Association.
6. D. Mainland, *Elementary Medical Statistics* (Saunders, Philadelphia, Pa., 1952), pp. 142–143.
7. J. A. Fraser Roberts, *Proc. Roy. Soc. Med.* 48, 143 (1955).

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The deviations from the control group found by Albert Damon for a sample of 203 patients with chromophobe adenoma of the pituitary are smaller than those found by Mayr *et al.* in smaller Boston samples. They are, in Damon's sample, for group 0, +9 percent among whites and +16 percent among Negroes, and for group A, −18 percent among whites and −14 percent among Negroes (controls = 100 percent). Yet it is gratifying to learn that the direction of all of these deviations is exactly the same as that found in the Boston samples, even though in this rare disease it is difficult to obtain sufficiently large samples to substantiate the significance of the deviations statistically.

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Standard Human Beings versus Standard Values

A fact which is highly pertinent to the thinking of many scientists has received very little or no attention in the application of statistical methods to the study of human beings—namely, that the expected number of individuals in any standard group diminishes, and may diminish greatly, when a *series* of measures is applied. If one uses as standards (i) the medial 50 percent, (ii) the medial 95 percent, or (iii) the medial 99.8 percent, the fractions of a given group that remain after specific numbers of independent measures are shown in Table 1.

In our thinking, we often carry the concept of "standard" or "normal" individuals. If such a "standard individual" means one who is in the medial 50-percent range in every measurable way, then, making the simplifying assumption that only ten independent measurable items exist, we must arrive at the conclusion that only one person in 1024 is "standard." Seldom are there published data which are sufficiently detailed so that this idea can be applied. However, such data are to be found in an article entitled "Plasma lipids of normal men at different ages" (*1*).

There are 65 individuals for whom complete data are given with respect to seven items: (i) total lipid C, (ii) total lipid P, (iii) total lipid N, (iv) lipid amino N, (v) total cholesterol, (vi) free cholesterol, and (vii) esterified cholesterol, each present in 100 ml of plasma. Selection of the medial 50 percent of the individuals after each measurement yields the results given in Table 2. If the measures were independent ones (which they obviously are not), the number remaining in the medial group would have been two after five measures instead of after seven measures, as in this actual case. On the basis chosen, two individuals out of 65 turn out to be standard with respect to the seven somewhat related measures.

If we wish to think of a standard individual in terms of the medial 95 percent with respect to every measurement (making the assumption that there are only ten measurable items), we find that about six out of ten individuals are standard. If, however, we do not make this simplifying assumption and recognize that human beings are of such complexity that hundreds of relatively independent measures are possible (anatomical, histological, physiological, pharmacological, biochemical, psychological, and so on), we are faced with the fact that even in a large sample every individual may be nonstandard with respect to some of the measures in which we may choose to be interested, even at the 95-percent level under consideration. We certainly could not expect any randomly selected individual to be standard in terms of our initial definition.

If we choose to expand our concept of "standard individual" to include the medial 99.8 percent, we will be able to find a substantial number of individuals who are standard, even though many independent measures are made. Some have assumed that selection of 99.8 percent as the standard would result in the exclusion of only 200,000 individuals from a population of 100 million (roughly the adult population of the United States) (*2*). Actually, however, approximately this many are excluded by *each* successive measurement, so that on the basis of 100 measurements, about 18 million would be excluded. If we make the conservative assumption that only 100 measurable items exist for each individual human being, there is about one chance in five that a randomly selected individual will be nonstandard with respect to some of the items, even on the 99.8-percent basis. The use of the concept of a standard man (in contrast to the search for standard values) thus becomes difficult to justify on any definitive basis. If we expand our concept to encompass practically the whole of the population, then the usefulness of the standard vanishes.

Table 1. Results of successive independent measures.

Size of medial group (%)	No. of measures	Fraction of original group remaining in medial group
50	1	0.50
50	5	0.03
50	10	0.001
95	1	0.95
95	10	0.60
95	15	0.468
95	100	0.0059
99.8	1	0.998
99.8	10	0.98
99.8	100	0.82

There are many areas where the afore-mentioned ideas are applicable and where the concept of standard individuals is inherent, whether or not it is overtly expressed. The one which comes closest to the field of my professional competence is that of nutrition. The Food and Nutrition Board and the U.S. Food and Drug Administration have set up "Recommended daily allowances" and "Minimum daily requirements," respectively, for standard or normal human beings. At the present time, 12 items are included in these lists; as further information becomes available, these lists will be expanded. The "recommended allowances" are, in general, more generous than the "minimum daily requirements" and are designed to be "suitable for the maintenance of good nutrition in essentially the whole population."

The point which our data (*3*) emphasize is that, if the level for each nutrient is satisfactory for a specified percentage of the population, the levels *taken as a group* would be satisfactory for a smaller percentage. If 12 levels are individually satisfactory for 90 percent of the population, the 12 levels taken as a group (on the assumption that they are independent of one another) would be satisfactory for only about 28 percent of the population. These needs are not completely independent of one another; hence, the 28-percent figure is low by an unknown amount. As the number of items on the list increases, the discrepancy between the validity of the indi-

Table 2. Size of medial 50-percent group after successive measurements.

Number of measures	1	2	3	4	5	6	7
Individuals in medial group	33	21	14	10	8	3	2