

## *Genetic Effects of Population Size Reduction*

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For evolutionary thought, the proof by Wright that nonadaptive differentiation can occur as the result of genetic accident appears in retrospect to be among the most important results of the application of mathematical analyses to the facts of genetics. Random processes, to whose results the term "genetic drift" has come to be applied, play a part in determining the character of populations. In theory, their role is particularly important in small and entirely isolated groups, whereas with a larger population distributed uninterruptedly over a wide territory their effects tend to be overshadowed by those of selection. The argument that random drift can occur is, however, different from establishing the fact that it has occurred in any given instance; the latter has proved unexpectedly difficult, even in human populations which according to Mayr<sup>1</sup> provide some of the best evidence for random fluctuations of gene frequency. Indeed, it has been argued (for example, refs. 1-3) that drift is of inconsequential influence in the evolution of populations.

Part of the difficulty lies in the way in which the term "random drift" is used to cover various interrelated genetic phenomena. More than two decades were required to appreciate their variety and elucidate their effects. The importance of random factors in the balance of those bringing about evolutionary advance was recognized by Wright<sup>4</sup> in 1932, though not fully. Random fluctuation in intensity or direction of selection had been touched on the year before<sup>5</sup>, but was not stressed until 1935 (ref. 7). In 1938 Wright<sup>6</sup> published a method for dealing with several different types of random processes mathematically. The practically complete indeterminacy of events that are unique was not recognized until 1949 (ref. 8). Today "random drift" is taken to represent the cumulative effects of all the random processes affecting gene frequencies. These may be summarized as follows. (a) The random variation that occurs in the sampling process of passing on gametes from one generation to the next. This is the component to which the term "drift" is frequently restricted in common parlance. (b) Random variation in the magnitude and direction of selective and other systematic forces; these include random fluctuations in mutation rate, in selection pressures, and in rates of population movement. (c) Random unique events. These comprise category I 3 of Wright's<sup>9</sup> classification; here are included novel favourable mutations, unique hybridiza-

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tions, swamping of a population by mass immigration, unique selective incidents, and unique reductions in numbers. The last of these is often termed the "founder" effect or the "bottleneck" effect, which represent the one phenomenon but at different points in a population's history in a given territory.

#### *Studies of Drift*

Discussion of drift as a mechanism for genetic differentiation in human groups has come from three different types of studies. (1) Variations in gene frequency between local populations, and between offshoot and parent populations, have been attributed to drift. For example, Birdsell's<sup>10</sup> survey in south-west central Australia of forty-two tribes showed sharp blood group gene frequency differences which he attributed to drift, recognizing, however, that it could "be no more than suggested in terms of broad probabilities." Glass *et al.*<sup>11</sup> showed in their Dunker study what seemed to be drift of *MN* gene frequencies. Giles *et al.*<sup>12</sup> demonstrated differences in several blood group systems between New Guinea villages of common history and environment, differences which they felt to be due to drift. In these studies, drift has merely been invoked, not proved or measured; there are at best only pointers to the type of random process involved. In the third study, it was felt that the founder principle, or population size reduction by epidemics, was the cause of the differences, though no numerical details were given. In the second study, the authors recognized the difficulty of distinguishing the founder effect from that of accumulated gamete sampling over several generations, and their subsequent attribution to the latter<sup>13</sup> of part of the *MN* frequency change was later questioned<sup>14</sup>.

(2) The demographic and mating structures of particular societies have been examined to show the magnitude of drift that could occur (for example, refs. 15-19). Here the restriction was to random variation that occurs in gamete sampling from one generation to the next. The net outcome of these was to show that the mating structure of the societies examined

would only allow drift of very small degree to occur, though there were extremely segmented societies where the effect might be stronger.

(3) Mathematical models have been applied to populations for which genetic, numerical and mating data are available to enquire whether the observed variations in gene frequencies are explicable by drift alone. For example, Cavalli-Sforza *et al.*<sup>20</sup> found that in North Italy they are greater than might be expected by drift alone, and attributed this extra dispersion to overestimation of the effective size of the population concerned. But because what was measured was the accumulated effects of intergenerational gamete sampling, the finding could have reflected other components of drift. None of these studies, however, has yet demonstrated conclusively that drift has occurred; only the last has attempted to compare observed variation with expected drift magnitude. None, moreover, gives sufficient attention to the category (c) of drift processes, the random unique events. These are almost completely indeterminate statistically, and are therefore not adequately covered in any models so far applied, being treated as negligible components of  $\delta q$ , the random portion of gene frequency change per generation, by Wright<sup>9</sup>. The genetic effects of these processes are illustrated and quantified in this article. It concerns the effects of accidents on the genetic constitution of a population, and in particular how these effects have been brought about through the resulting diminution of numbers, the "bottleneck" phenomenon.

#### *Population and Procedure*

To identify the effects of a bottleneck in terms of the frequency of, say, blood group genes, the investigator would have to be extremely fortunate. He would have to know the gene frequencies in the population immediately before, and immediately after, the bottleneck occurred. He would require foresight to know that the size of the population is about to change, and hindsight to know that it had finished changing. The same results, however, can be demonstrated if the genetic constitution of the population is specified in a way other than by the usual array of frequencies of particular alleles and genotypes. This can be done if the population pedigree is known.

A parent passes to his child half of his chromosomes and therefore virtually half of his genes. When the child himself reproduces he again passes on half his genes, so a grandchild derives on average a quarter of his genes from each grandparent. The probability that any autosomal allele present in a grandparent is present in any one of his grandchildren is one quarter, and the probable genetic contribution of any grandparent to the gene pool of his grandchildren is a quarter. The genetic constitution of any generation of descendants can therefore be specified in terms of the contributions to it from particular ancestors, and, by extension, the same method can be applied to any group of individuals but covering more than one gener-

ation. Thus the genetic constitution of a population at any moment is regarded as comprising a pack of probable ancestral contributions which can be calculated. They reflect the relative fertilities of the ancestors concerned and their descendants. Allowance can be made for the effects of mortality and migration, though not for other mechanisms of gene frequency change, notably for the random variation that occurs in the sampling process of passing on gametes from one generation to the next, for mutation, or for selection through differential mortality. Thus calculation of these probable contributions at a series of points in time, tracing their secular variation, shows how the genetic constitution of the population so defined varies during the period. The calculations are simple, and multiple lines of descent must be allowed for where the population is in any way inbred.

This procedure has been applied to the population of Tristan da Cunha. From the detailed data that are available for this population, from the records kept by the earliest settlers, the observations of visitors and official reports, the lists that at periods were kept of births, deaths, baptisms and marriages, and the investigations of genealogies by Dr Woolley, Dr Loudon and Dr Munch, it is possible to obtain the necessary data for the analysis. First, a complete, albeit highly complex pedigree of the whole population since its founding can be established. Second, the numerical evolution of the population from its founding can be traced. Fig. 1 shows the size of the population on December 31 of each year from 1816 to 1961. There have

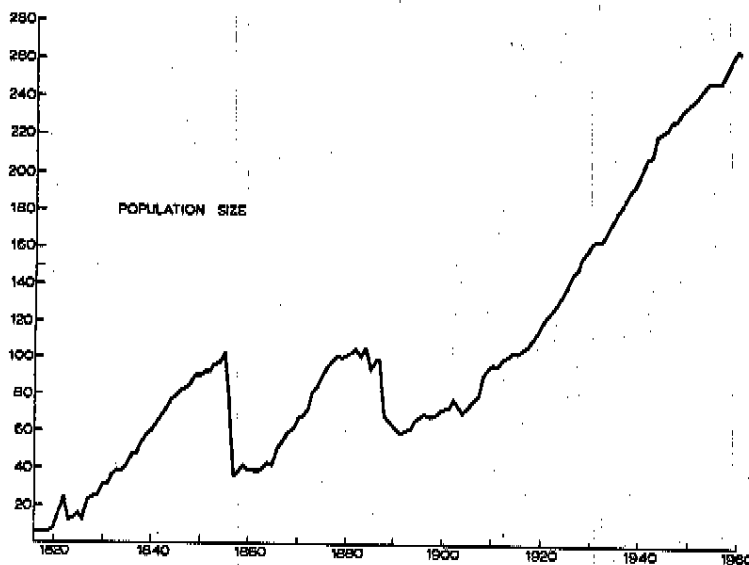


Fig. 1. The size of the population of Tristan da Cunha on December 31 of each year from 1816 to 1960.

been three phases of increase in the population, one lasting until 1855, one until 1884 and one until October 1961, these three periods being separated by sudden and drastic population reductions—true bottlenecks.

#### *Bottlenecks at Tristan da Cunha*

In the first of these the numbers dropped from 103 at the end of 1855 to thirty-three in March 1857 (these figures include men temporarily absent from the island). This massive reduction seems to have been due to a combination of two principal factors, the death of one man and the presence of another. In 1851 the first missionary arrived, and in 1853 the founder, W. G., died. After his death the cohesion of the community appears to have relaxed, and twenty-five of his descendants left for America in 1856. The pastor who remained on the island until 1857 became increasingly convinced that emigration was necessary for the population. Whether this was true, or whether it was a projection of his discontent with his own lot there, will never be known, but he noted that there were "more than a dozen adult females here, with no prospect of a comfortable provision for life" and "it will be a happy day when this little lonely spot is once more left to those who probably always were . . . its only fit inhabitants—the wild birds of the ocean." Under his influence, when he departed, another forty-five islanders left with him for the Cape, settling at Mossel Bay and Riversdale. The presence of a pastor of this opinion at a time when the population was reorganizing itself after the death of its dominant character can only be regarded as a chance combination of chance occurrences. The growth curve of population size to this date shows no sign of flattening, and no indication that numbers were approaching the limit that the island could support.

The second bottleneck was neither quite so extreme nor quite so abrupt. It was triggered by a disaster. The island has no natural harbour, and any vessels that called stood offshore while the islanders put out to them in their small boats. Sometimes they also put out to board passing vessels, for trade. On November 28, 1885, a boat manned by fifteen adult males set off to intercept a passing vessel but, in full view of the watching remaining islanders, vanished beneath the waves. Not one man was saved. This disaster made Tristan an "island of widows" and depleted the population of its adult providers. It left on the island four adult men, of whom one was insane and two were very aged, to support the remaining population. Despite the considerable distress that immediately followed, by August of the next year the population as a whole had accommodated to the situation—for example, adolescent boys had taken over crew duties in the boat—and a petition, organized by those who had emigrated to South Africa, formally to evacuate the island was rejected. During the next few years, however, many of the widows and their offspring left the island of their own accord, and the population declined to a second minimum in 1891. The reduction in

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numbers this time was not by two-thirds but by a little less than half, from 106 to 59. Again, this reduction is a direct result of accident. The population thereafter began its most recent phase of increase.

*Effects on the Gene Pool*

The genetic constitution of the population in 1855 is shown in the second column of Table 1. Twenty ancestors had contributed genes, their respective probable contributions to the gene pool varying from 0.005 to 0.137; the two greatest contributions were from the two original settlers, W. G. and his wife, M. L., and the next three from two of the women from St Helena, S. W. and S. K., and from R. R., the earliest of the men to arrive after the founding of the settlement. These five individuals contributed more than half the genes in the gene pool of the population at the end of 1855.

TABLE 1. PROBABLE CONTRIBUTIONS TO THE GENE POOL OF THE POPULATION IN 1855, 1857, 1884, 1891 AND 1961

ANCESTOR	1855	1857	1884	1891	1961
W.G. 1	0.1275	0.0625	0.0548	0.0657	0.0691
M.L. 2	0.1373	0.0625	0.0548	0.0657	0.0691
T.S. 3	0.0662	0.1389	0.0943	0.1441	0.1339
S.W. 4	0.0907	0.1910	0.1392	0.1864	0.1602
F.M.W. 5	0.0245	0.0521	0.0448	0.0424	0.0263
R.R. 6	0.0637	—	—	—	—
S.K. 7	0.0858	—	—	—	—
T.R. 8	0.0049	0.0139	0.0177	0.0424	0.0382
M.W. 9	0.0637	0.1389	0.1380	0.0805	0.0424
A.C. 10	0.0637	0.1389	0.1285	0.0636	0.0424
P.G. 11	0.0490	0.1042	0.0896	0.0847	0.0526
C.T. 12	0.0490	—	—	—	—
P.M. 13	0.0441	—	—	—	—
W.D. 14	0.0588	—	—	—	—
M.F. 15	0.0049	—	—	—	—
G. 16	0.0049	—	—	—	—
A.H. 17	0.0245	0.0833	0.0684	0.0890	0.0365
F.R.C. 18	0.0049	0.0139	—	—	—
F.F.K. 19	0.0221	—	—	—	—
B. 20	0.0098	—	—	—	—
J.B. 21	—	—	0.0472	—	—
S.P. 22	—	—	0.0613	0.1186	0.1045
F.R. 23	—	—	0.0283	0.0170	—
R.A.B. 24	—	—	0.0142	—	—
M.J. 25	—	—	0.0142	—	—
F.S.G. 26	—	—	0.0047	—	—
A.R. 27	—	—	—	—	0.0625
E.S. 28	—	—	—	—	0.0445
G.L. 29	—	—	—	—	0.0435
G.C. 30	—	—	—	—	0.0126
A.S. 31	—	—	—	—	0.0543
R.L. 32	—	—	—	—	0.0037
F.P.S. 33	—	—	—	—	0.0019
J.B. 34	—	—	—	—	0.0019

The effect of the first reduction in population is shown by comparison of the third with the second column of Table 1. The primary effect was deprivation of the population of eight of its founder ancestors and a recent arrival whose total contributions in 1855 had been more than one-third—genes from only eleven were to be found in the new gene pool. Second, there was a change in their relative contributions. Genes from two of the principal contributors were among those that completely disappeared. The greatest contribution now was from S. W. (0.191), and the next three largest were from her husband, T. S., her sister, M. W., and her husband, A. C. (0.139 each)—the contributions from these three individuals were more than doubled. These four individuals together now contributed 60 per cent of the genes in the new population compared with their previous total of less than 29 per cent. The contributions of the first two settlers were halved, and that of a former minor contributor (T. R.) multiplied nearly threefold (from 0.005 to 0.014).

In the phase of increase that followed this first reduction, the contribution of one further ancestor was lost, but new contributions to the island's gene pool came from six more arrivals. The relative contributions from the original ancestors correspondingly declined with the exception of one (T.R.). By the end of 1884 the gene pool derived from sixteen individuals. It was relatively little affected by the boat disaster itself—the greatest changes were in the contributions of S. P. (0.061 to 0.071), W. G. and M. L. (0.055 to 0.047)—but the subsequent population size reduction had a much more pronounced effect, shown by comparison of columns 4 and 5. Again, there was loss of all the genes from several contributors, and again there was a rearrangement of the relative contributions of the remainder. The contributions (totaling some 8 per cent) lost were from four relatively recent arrivals, so that in 1891 the gene pool derived from only twelve individuals. The greatest contribution was still that from S. W., increasing from 0.139 to 0.186, the second largest from her husband T. S., increasing from 0.094 to 0.144. But the third largest was from a much later immigrant woman, S. P., which nearly doubled, from 0.061 to 0.119, while the former principal contributors, M. W. and A. C., dropped to fifth and eighth places, respectively, from 0.138 to 0.081 and from 0.129 to 0.064.

#### *The Gene Pool in 1961*

The final column of Table 1 shows the probable contributions to the gene pool in October 1961, when the island was evacuated. In the intervening period all the genes from one earlier arrival had been lost, and eight new arrivals had contributed 22.4 per cent of the total to the gene pool, which thus derived from nineteen ancestors. The principal changes were the diminution in the contributions of A. H. and M. W. by about half, and of P. G. and A. C. by about one-third, and the great contributions (sixth and

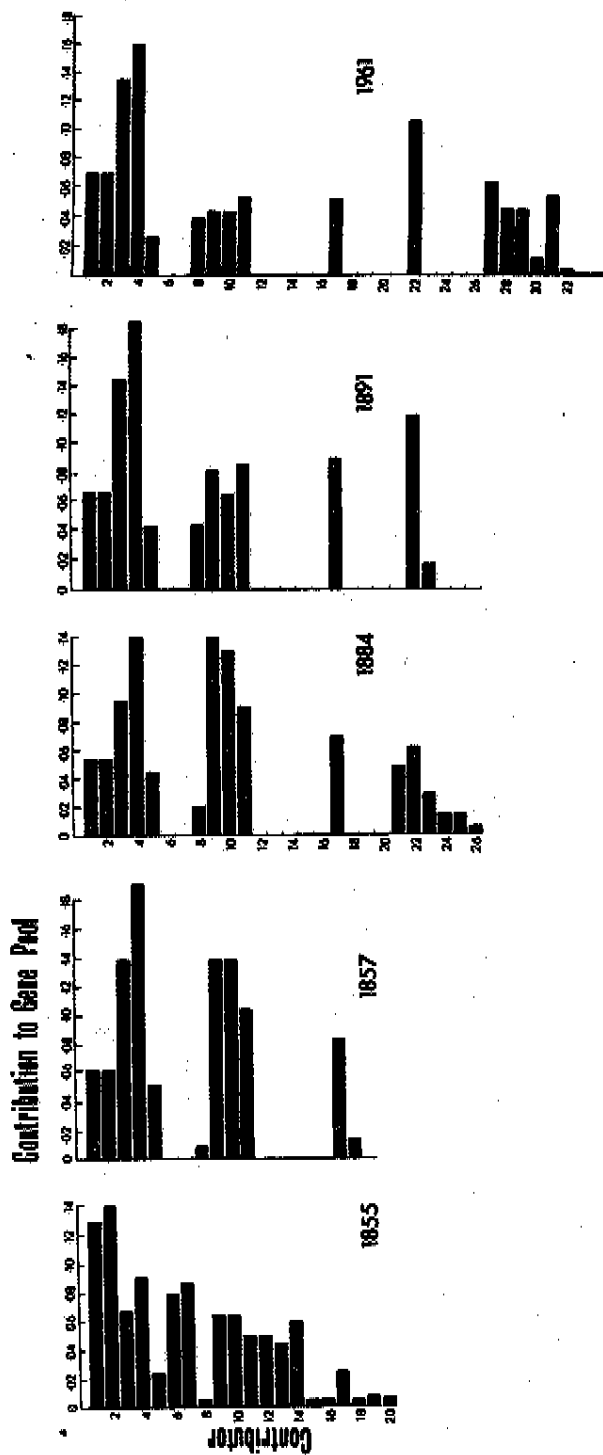


Fig. 2. Contributions of particular ancestors to the gene pool.



seventh in order of size) made by two of the new arrivals. But the three greatest contributions were made by the same individuals as in 1891. Indeed, there is a marked overall similarity between the figures for 1961 and those for 1891.

Tracing the contributions of particular ancestors (Fig. 2), it was the first exodus that halved the contributions of the first two settlers, and then, after a period of slight decline, the second size reduction increased them to nearly the 1961 figure. The predominance of the two principal contributors to the 1961 population is traceable to the first exodus that doubled their original contribution, and then, after a decline, to the second exodus that elevated them to the 1961 values. From the minor contributor, T. R. (No. 8), nearly 4 per cent of the 1961 gene pool derives, largely because the first exodus nearly trebled his contribution and the second exodus multiplied it by another 2.5 times. Two of the most prolific of the early settlers, M. W. and A. C. (Nos. 9 and 10), contribute only a little more than 4 per cent each to the 1961 gene pool; their contribution was doubled by the first exodus and then halved again by the second.

The overall effect is shown in Fig. 3. The gene pool of the population is taken as unity, and the proportion of it derived from each ancestor is shown to scale by the width of the band; time along the abscissa is not to scale. Both the exoduses exerted a considerable effect on the genetic constitution. This effect was two-fold: (a) the elimination of all genes derived from an appreciable proportion of the ancestors and (b) alteration of the actual and relative sizes of the contributions from other ancestors. Immigration in the periods 1857-84 and 1891-1961, although diminishing the contribution of each pre-existing ancestor, did not, it seems, appreciably change the size of these contributions in relation to each other, although further work is required to establish this point. But at the present state of the analysis it seems to be chiefly the two reductions in population size which bring this about. Furthermore, the effects of these size reductions persist, as comparison of the 1961 figures with those for each other year shows. The general similarity of the 1961 figures to those for 1891 implies that, apart from the contributions of the recent immigrants, the gene pool of the 1961 population derives in its major features principally from the reduction in population that occurred between 1884 and 1891, and the modification that occurred then acted on the gene pool the features of which had been chiefly derived from the effects of the earlier exodus.

#### *Reduction of Population and Genetic Drift*

I have documented here, perhaps for the first time in a human population, the effects of drastic population reduction on the genetic constitution of the population. In both of the bottlenecks there are two primary effects: (a) deprivation of the population of the genetic contribution of some founder ancestors, that is, a reduction in the number of contributing an-

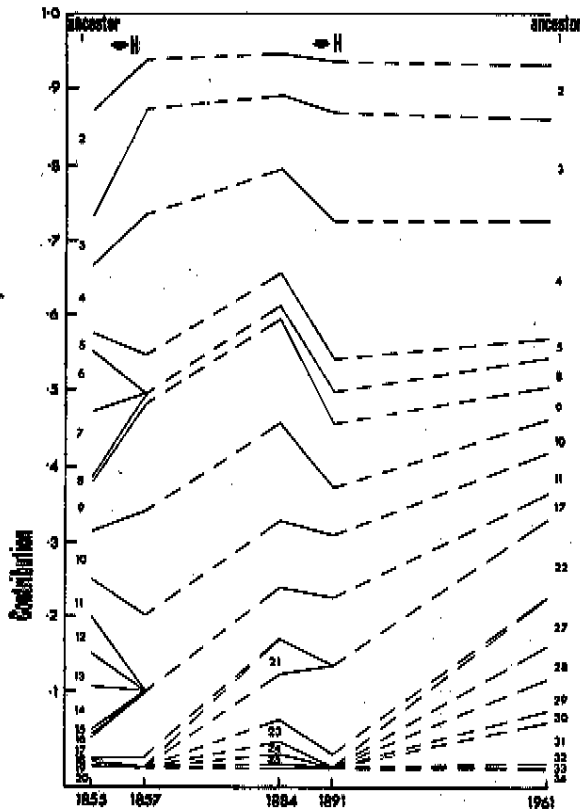


Fig. 3. Overall contributions of ancestors to the gene pool of the population in 1855, 1857, 1884 and 1961. H shows serious bottleneck.

cestors, and (b) change in the relative contributions of the remainder. The effects of these size reductions persist and, in accumulation, shape the profile of ancestral contributions to the gene pool of the present population; this in 1961 bears much more resemblance to the 1891 profile than to that of 1855. The present profile bears little relationship to the fertility of the ancestors, though further analysis is in progress to assess the relative importance of accumulated differential fertility effects. But there can no longer be any doubt that reduction in population size of the magnitude that occurs in nature must have a severe effect on the genetic constitution of a population.

There are, of course, drawbacks to this method of envisaging the gene pool as a pack of probable ancestral contributions. It obviously depends on the reliability of the pedigree. All possible steps were taken to ensure accu-

racy by comparison of the accounts of descent collected by different investigators, by checking these against the known movements of individuals to and away from the island, and by comparing all pedigrees with the information on the large number of genetic markers that is available for this population. In the few cases where paternity remained in doubt, it was possible to assign the most probable father on the basis of the known genotypes. No other population has been so intensively studied and the pedigree information now available can be regarded as the most reliable possible. The second drawback is that the work is couched in terms of probabilities. Although on average a child possesses a quarter of the genes of each grandparent, it is an extremely remote possibility that a given child actually carries no gene derived from a particular grandparent. While this would be quite unlikely taken over all loci, on the other hand, it is much more likely for a single locus. It is therefore interesting to compare observed numbers of genes with the probable numbers expected from the present work. The  $C_3$  serum cholinesterase phenotype occurs in thirty-six individuals out of 213 tested<sup>21</sup>; there is little doubt that this gene was introduced by S. W., whose contribution to the 1961 population was 0.16; this gives an expected number of thirty-four heterozygous carriers in the population, instead of the observed thirty-six. The very slight gain of the  $C_3$  gene is perhaps a result of intergenerational gamete sampling, or perhaps of selection. The pack method taken as a starting point for this analysis of the effects of population size reduction is obviously a powerful one for the elucidation of the effects of other processes on the gene pool.

This example illustrates the difficulty of assigning any given gene frequency change to any one category of evolutionary processes. Although the reduction in population was in both cases brought about by accident, there was a large non-accidental component to the reduction itself. In both cases family groups emigrated, so which genes and what proportions of them were lost from the population's gene pool were a partly random, partly non-random array. The families that departed obviously included individuals who felt they could no longer accept the conditions on the island or its prospects for them, so the non-random component in part may be identified as selective. The fact that man is a social animal, that individuals tend to move and often act as family units, brought about, in this population, what may be termed a "booster" effect, whereby, although the genes lost from the population by accident were in actuality a random sample, the loss of some of them was exaggerated by consequent deliberate emigration of families.

This study therefore shows that there is no doubt as to the importance of drastic reductions of population in shaping the genetic constitution of an isolated population. The gene frequency changes they bring about, however, can only be attributed to drift when drift is defined so as to incorporate all random unique events, for there may be an appreciable selective component

and in man there is also an exaggeration of the effects of both these processes by family ties and relationships. In populations such as that discussed here, drift so defined cannot be regarded as of inconsequential influence on their genetic evolution, at least in the short term.

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