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July 12, 1963

ON THE OCCASIONAL DOMINANCE OF THE "PERCEPTIBLE PHENOTYPE" IN MAN*

by

Leo Szilard
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People generally believe, on the basis of everyday experience, that sons and daughters frequently resemble one, or the other, of the parents. Frequently, people remark that a boy or a girl is the "split image" of the father or the mother. It is by no means self-evident, however, how such striking resemblances come about as frequently as people, rightly or wrongly, believe that they do.

It is, of course, conceivable that people might be wrong and such striking resemblances might be much less frequent than they believe them to be. In the circumstances, a valid determination of just how often a boy or a girl shows a marked resemblance to one of the parents would appear to be very desirable at this point and I intend to describe elsewhere a method that would permit this to be accomplished.

In the meantime I propose to assume the validity of the generally held belief that a marked resemblance of a child to one of the parents is rather frequent. I shall also assume that a really striking resemblance between unrelated individuals is extremely rare; in my whole life I have come across only one or two cases where a boy or a girl appeared to be the "split image" of someone whom I knew and to whom they were not related.

The way a person looks, moves, and the quality of his voice, make up most of what may be called the "perceptible phenotype" of the individual. Because of the very great variety of perceptible phenotypes within a population, it seems reasonable to assume that the perceptible phenotype is determined by a fairly large number of genes. In order to be able to explain a high frequency for a girl or boy to appear to be the split image of the father or the mother we shall

* This work was performed under a research grant of the National Institutes of Health

first of all assume that all the relevant genes form a single linkage group which we shall designate as the "PP (perceptible phenotype) linkage group". This assumption would appear to be a necessary condition for a high frequency of marked resemblances between a child and one of the parents. It cannot by itself explain, however, why such resemblances should occur with a high frequency, because each individual carries two homologous copies of the PP genes, one copy inherited from the father and one copy inherited from the mother and one would expect the presence of two different PP groups to blur any resemblance of an individual to either of its parents.

In order to explain a striking resemblance of an individual to one of its parents, one would have to postulate that the PP group of genes, derived from that parent, has somehow acquired dominance over the PP group inherited from the other parent. Thus the question arises whether it may be possible to think of a plausible mechanism which could account for the occasional dominance of the perceptible phenotype.

We are led to postulate a particular mechanism which could account for this phenomenon on the basis of the following considerations:

It appears to be well established that in many of the somatic cells of the female only one of the two X-chromosomes is functional and the other X-chromosome undergoes heterochromatinisation, becomes heteropycnotic, and forms the so-called sex-chromatin body. It appears that this heterochromatinisation is induced in a large part of one of the X-chromosomes of the somatic cells at an early embryonic stage. Generally speaking, the two X-chromosomes of a female have an equal probability to undergo heterochromatinisation in her somatic cells, but once one of the X-chromosomes has undergone heterochromatinisation in a somatic cell, then thereafter that chromosome will form the sex-chromatin body in all of the descendants of that somatic cell.[1,2,3]

Recently, however, there have been found exceptions to this general rule.[4] In the cases of two female patients, each of whom carried an X-chromosome which was structurally abnormal, it was found that in all the somatic cells of the patient this abnormal X-chromosome was consistently heteropycnotic and late

replicating. In these two cases one might choose to say that the X-chromosome which had the abnormal structure happened to be "weaker" than the other, normal, X-chromosome, and that the normal X-chromosome established its dominance by suppressing the abnormal X-chromosome.

These two examples show that, at least in the case of the X-chromosome, there is known to exist a mechanism which may occasionally permit one of two homologous chromosomes to establish its dominance by rendering the other chromosome non-functional.

The PP linkage group of genes cannot be assumed to be located on the X-chromosome, because if it were so located, then boys would always show a striking resemblance to their mother and never to their father. Therefore we must assume that the PP group is located on one of the autosomes, which we may designate as the PP-autosome. In order to explain the occasional dominance of the perceptible phenotype of the father or of the mother, we propose to postulate that each PP linkage group of genes possesses a certain "strength". We further postulate that if the PP linkage group of genes which an individual inherits from, say, the father has a much greater "strength" than the homologous group of genes which that individual inherits from its mother, then during early embryonal development the stronger PP linkage group suppresses the weaker one (in the same manner as the normal X-chromosome appears to have suppressed the abnormal X-chromosome in the case of the two patients mentioned above) and, accordingly, this individual would then be the ~~split image~~ "spitting image" of its father.

The mechanism described above might have evolved because of the evolutionary advantage that would be possessed by a population in which the dominance of the perceptible phenotype is a frequent occurrence, over a population in which it is not.

In Man there appears to be a strong "aesthetic selection" at work in the choice of the mate which is guided by the perceptible phenotype. If there were no correlation, or only a very weak correlation, between the perceptible phenotype and the genotype of the individual, then such an aesthetic selection could not make any constructive contribution, either to the development of new evolutionary

traits, or even to the prevention of the deterioration of the genotype which may result from spontaneous mutations.

If the dominance of the perceptible phenotype is sufficiently frequent, then there is a strong correlation between the perceptible phenotype and the genotype of the individual and because the aesthetic selection may be assumed to be a very powerful one, PP-autosomes, which may have undergone major changes through spontaneous mutations, could spread rapidly through the whole inter-breeding population, when this autosome undergoes a further mutation, resulting in an aesthetically attractive perceptible phenotype.

There is one type of conspicuous "exception" which gives the appearance of contradicting the above described general scheme of things, and which represents a paradox that needs to be resolved.

This exception is exemplified by the colour of the eye. In contemporary populations we find both dark eyed and blue eyed individuals, "blue eyes" being recessive and "dark eyes" being dominant. The eye colour is determined by a single gene locus which has a conspicuous effect on the perceptible phenotype of the individual and which must consequently also affect the "aesthetic selection" in the choice of the mate. Yet, this gene locus cannot be part of the PP linkage of genes, otherwise "dark eyes" could hardly be always dominant.

This paradox may be resolved as follows: In early prehistoric times different populations, living in geographically adjacent areas, lived in comparative isolation from each other. Let us now assume that such a population was homozygous for "blue eyes" while another population, living in an adjacent area, was homozygous for "dark eyes". Let us further assume, that at some point in time cross-breeding between these two, previously isolated, populations has occurred and has led to a mixed population which was heterozygous for eye colour. Because aesthetic selection for "blue eyes" or "dark eyes" may be assumed to be exceedingly rapid, the period of time which it would have taken for the mixed population to become homozygous either for "blue eyes" or for "dark eyes" may be assumed to have been so short as to be negligible, from an evolutionary point of view. After a short transitional period of time, the mixed population would have

become homozygous for eye colour and thereafter aesthetic selection would have again been solely guided by the PP linkage group of genes.

The contemporary populations, which include both blue eyed and dark eyed individuals have resulted from cross-breedings which have taken place comparatively recently - as the consequence of the high mobility of populations, newly acquired in historic, and late prehistoric, times.

Until I saw a way of resolving the above described paradox it has formed for me a mental block, which kept me from finding any plausible explanation for the occasional dominance of the perceptible phenotype.

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by

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People generally believe, on the basis of everyday experience, that sons and daughters frequently resemble one, or the other, of the parents. Frequently, people remark that a boy or a girl is the "spitting image" of the father or the mother. It is by no means self-evident, however, how such striking resemblances might come about as frequently as people, rightly or wrongly, believe that they do.

It is, of course, conceivable that people might be wrong and such striking resemblances might be much less frequent than they believe them to be. In the circumstances, a valid determination of just how often a boy or a girl shows a marked resemblance to one of the parents would appear to be very desirable at this point and I intend to describe elsewhere a method that would permit this to be accomplished.

In the meantime I propose to assume the validity of the generally held belief that a marked resemblance of a child to one of the parents is rather frequent. I shall also assume that a really striking resemblance between unrelated individuals is extremely rare; in my whole life I have come across only one or two cases where a boy or a girl appeared to be the "spitting image" of someone whom I knew and to whom they were not related.

The way a person looks, moves, and the quality of his voice, make up most of what may be called the "perceptible phenotype" of the individual. Because of the very great variety of perceptible phenotypes within a population, it seems reasonable to assume that the perceptible phenotype is determined by a fairly large number of genes. In order to be able to explain a high frequency for a girl or boy to appear to be the "spitting image" of the father or the mother we shall first of all assume that all the

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*This work was performed under a research grant, administered by The University of Chicago, of the General Medical Sciences Division of the National Institutes of Health.

+ Purple: July 12, 1963 (some titles) Jan 25, 1957
" " 25, 1963 (Aging + Comp. Sperm) (Vacc. Del Type)
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relevant genes form a single linkage group which we shall designate as the "PP (perceptible phenotype) linkage group". This assumption would appear to be a necessary condition for a high frequency of marked resemblances between a child and one of the parents. It cannot by itself explain, however, why such resemblances should occur with a high frequency, because each individual carries two homologous copies of the PP genes, one copy inherited from the father and one copy inherited from the mother and one would expect the presence of two different PP groups to blur any resemblance of an individual to either of its parents.

In order to explain a striking resemblance of an individual to one of its parents, one would have to postulate that the PP group of genes, derived from that parent, has somehow acquired dominance over the PP group inherited from the other parent. Thus the question arises whether it may be possible to think of a plausible mechanism which could account for the occasional dominance of the perceptible phenotype.

We are led to postulate a particular mechanism which could account for this phenomenon on the basis of the following considerations:

It appears to be well established that in many of the somatic cells of the female only one of the two X-chromosomes is functional and the other X-chromosome undergoes heterochromatinisation, becomes heteropycnotic, and forms the co-called sex-chromatin body. It appears that this heterochromatinisation is induced in a large part of one of the X-chromosomes of the somatic cells at an early embryonic stage. Generally speaking, the two X-chromosomes of a female have an equal probability to undergo heterochromatinisation in her somatic cells, but once one of the X-chromosomes has undergone heterochromatinisation in a somatic cell, then thereafter that chromosome will form the sex-chromatin body in all of the descendants of that somatic cell. [1,2,3].

Recently, however, there have been found exceptions to this general rule.[4] In the cases of two female patients, each of whom carried an X-chromosome which was structurally abnormal, it was found that in all the somatic cells of the patient this abnormal X-chromosome was consistently heteropycnotic and late

replicating. In these two cases one might choose to say that the X-chromosome which had the abnormal structure happened to be "weaker" than the other, normal, X-chromosome, and that the normal X-chromosome established its dominance by suppressing the abnormal X-chromosome.

These two examples show that, at least in the case of the X-chromosome, there is known to exist a mechanism which may occasionally permit one of two homologous chromosomes to establish its dominance by rendering the other chromosome non-functional.

The PP linkage group of genes cannot be assumed to be located on the X-chromosome, because if it were so located, then boys would always show a striking resemblance to their mother and never to their father. Therefore we must assume that the PP group is located on one of the autosomes which we may designate as the PP-autosome. In order to explain the occasional dominance of the perceptible phenotype of the father or of the mother, we propose to postulate that each PP linkage group of genes possesses a certain "strength". We further postulate that if the PP linkage group of genes which an individual inherits from, say, the father has a much greater "strength" than the homologous group of genes which that individual inherits from its mother, then during early embryonal development the stronger PP linkage group suppresses the weaker one (in the same manner as the normal X-chromosome appears to have suppressed the abnormal X-chromosome in the case of the two patients mentioned above) and, accordingly, this individual would then be the "spitting image" of its father.

The mechanism described above might have evolved because of the evolutionary advantage that would be possessed by a population in which the dominance of the perceptible phenotype is a frequent occurrence, over a population in which it is not.

In Man there appears to be a strong "aesthetic selection" at work in the choice of the mate which is guided by the perceptible phenotype. I f there were no correlation, or only very weak correlation, between the perceptible phenotype and the genotype of the individual, then such an aesthetic selection could not make any constructive contribution, either to the development of new revolutionary

traits, or even to the prevention of deterioration of the genotype which may result from spontaneous mutations.

If the dominance of the perceptible phenotype is sufficiently frequent, then there is a strong correlation between the perceptible phenotype and the genotype of the individual and because the aesthetic selection may be assumed to be a very powerful one, PP-autosomes, which may have undergone major changes through spontaneous mutations, could spread rapidly through the whole inter-breeding population when this autosome undergoes a further mutation resulting in an aesthetically attractive perceptible phenotype.

There is one type of conspicuous "exception" which gives the appearance of contradicting the general scheme of things, described above, and which represents a paradox that needs to be resolved.

This exception is exemplified by the colour of the eye. In contemporary populations we find both dark eyed and blue eyed individuals, "blue eyes" being recessive and "dark eyes" being dominant. The eye colour is determined by a single gene locus which has a conspicuous effect on the perceptible phenotype of the individual and which must consequently also affect the "aesthetic selection" in the choice of the mate. Yet, this gene locus cannot be part of the PP linkage of genes, otherwise "dark eyes" could hardly be always dominant.

This paradox may be resolved as follows: In early prehistoric times different populations, living in geographically adjacent areas, lived in comparative isolation from each other. Let us now assume that such a population was homozygous for "blue eyes" while another population, living in an adjacent area, was homozygous for "dark eyes". Let us further assume, that at some point in time cross-breeding between these two, previously isolated, populations has occurred and has led to a mixed population which was heterozygous for eye colour. Because aesthetic selection for "blue eyes" or "dark eyes" may be assumed to be exceedingly rapid, the period of time which it would have taken for the mixed population to become homozygous either for "blue eyes" or for "dark eyes" may be assumed to have been so short as to be negligible, from an evolutionary point of view. After a short transitional period of time, the mixed population would have

become homozygous for eye colour and thereafter aesthetic selection would have again been solely guided by the PP linkage group of genes.

The contemporary populations, which include both blue eyed and dark eyed individuals have resulted from cross-breedings which have taken place comparatively recently - as the consequence of the high mobility of populations, newly acquired in historic, and late prehistoric, times.

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References

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