



Joshua Lederberg

Human Mutation Can Scramble The Coded Genetic Message of DNA

IN THE NORMAL cycle of generations, every individual receives his endowment of genetic information in equal portions of DNA from his two parents. Each portion of DNA is represented by a set of 23 chromosomes, allotted at random from the 23 pairs of the parent in the formation of an egg or a sperm. For better or worse, the DNA message is a faithful copy of what was inherent in the parent, except for the mishaps that we call genetic mutations.

Many environmental fac-

tors are either known to add to our burden from mutational mishaps, as in the case of radiation, or suspected of doing so, as in the case of many chemicals. It is important that the complexities of such insults be carefully examined and more widely understood, and to do this demands an orderly classification of a wide range of events and their consequences.

THE KIND of cell in which a mutation occurs is all-important. Every cell of the body is programed by a

copy of the individual's DNA and is subject to mutation. Only if the cell in question is a germ cell, leading to an egg or sperm, is there a possibility of transmitting the mutation to the offspring. And then it will have no effect on the person himself.

Alternatively, mutations may occur in body cells, which can have no effect on later generations. Their effect on the person is problematical; however, there is grave concern that some cancerlike diseases such as leukemia stem from mutations in blood-forming tissues. In addition, the disorganization of an increasing proportion of body cells by mutation is one of the plausible theories of aging.

The main evidence for these concerns is that large doses of radiation will induce leukemias and accelerate aging as well as produce mutations in a proportion of all exposed cells.

Germ-cell mutations are what we commonly think of as genetic effects. (They must be distinguished from direct effects on the growing fetus, such as those of thalidomide. The deformations caused by this drug involved only the limbs, and not the germ cells, and will not be transmitted to further generations.)

Mutations are quite indiscriminately scattered over different genes and chromosomes. Up to the present time, we have not encountered any chemicals or agents that can alter one variety of the DNA and leave other messages intact. It is reasonable to predict that

some viruses will be found to act in this way, or that virus-like molecules will be fabricated that might cause specific mutations—perhaps even beneficial ones. But we do not know this now.

MUTATIONS are classified along several lines. The function or organ affected may range from color vision to thought, from toenail to scalp. The severity of effect may be a cosmetic nicety like a white forelock, a monstrosity incapable of surviving or, most tragic of all, a physical deformity or mental handicap. The mutation may be dominant, immediately expressed in one generation, or recessive, reshuffled through posterity until it appears simultaneously in a uniting egg and sperm.

In recent years, we have also become more aware of the significance of chromosome mutations where a whole chromosome or a large segment of one is imperfectly transmitted and mimics a dominant mutation.

Except for dominant mutations, we have little direct evidence of new occurrences of these various events in man. We live under a substantial burden of a historic legacy: the simplest way to describe the genetic load is to say that a third of fertilized eggs fail to complete a normal life cycle. Fortunately, most of these events are manifest as spontaneous abortions; but all too much misery already spills over into the lives of born children and their families.

© 1969, The Washington Post Co.

Joshua Lederberg

Human Mutation Can Scramble the Coded Genetic Message of DNA

IN THE NORMAL cycle of generations, every individual receives his endowment of genetic information in equal portions of DNA from his two parents. Each portion of DNA is represented by a set of 23 chromosomes, allotted at random from the 23 pairs of the parent in the formation of an egg or a sperm. For better or worse, the DNA message is a faithful copy of what was inherent in the parent, except for the mishaps that we call genetic mutations.

Many environmental factors are either known to add to our burden from mutational mishaps, as in the case of radiation, or suspected of doing so, as in the case of many chemicals. It is important that the complexities of such insults be carefully examined and more widely understood, and to do this demands an orderly classification of a wide range of events and their consequences.

THE KIND of cell in which a mutation occurs is all important. Every cell of the body is programmed by a copy of the individual's DNA and is subject to mutation. Only if the cell in question is a germ cell, leading to an egg or sperm, is there a possibility of transmitting the mutation to the offspring. And then it will have no effect on the person himself.

Alternatively, mutations may occur in body cells, which can have no effect on later generations. Their effect on the person is problematical; however, there is grave concern that some cancerlike diseases such as leukemia stem from mutations in blood-forming tissues. In addition, the disorganization of an increasing proportion of body cells by mutation is one of the plausible theories of aging.

The main evidence for these concerns is that large doses of radiation will induce leukemias and accelerate aging as well as produce mutations in a proportion of all exposed cells.

Germ-cell mutations are what we commonly think of as genetic effects. (They must be distinguished from direct effects on the growing fetus, such as those of thalidomide. The deformations caused by this drug involved only the limbs, and not the germ cells, and will not be transmitted to further generations.)

Mutations are quite indiscriminately scattered over different genes and chromosomes. Up to the present time, we have not encountered any chemicals or agents that can alter one variety of the DNA and leave other messages intact. It is reasonable to predict that some viruses will be found to act in this way, or that virus-like molecules will be fabricated that might cause specific mutations—perhaps even beneficial ones. But we do not know this now.

MUTATIONS are classified along several lines. The function or organ affected may range from color vision to thought, from toenail to scalp. The severity of effect may be a cosmetic nicety like a white forelock, a monstrosity incapable of surviving or, most tragic of all, a physical deformity or mental handicap. The mutation may be dominant, immediately expressed in one generation, or recessive, reshuffled through posterity until it appears simultaneously in a uniting egg and sperm.

In recent years, we have also become more aware of the significance of chromosome mutations where a whole chromosome or a large segment of one is imperfectly transmitted and mimics a dominant mutation.

Except for dominant mutations, we have little direct evidence of new occurrences of these various events in man. We live under a substantial burden of a historic legacy: the simplest way to describe the genetic load is to say that

a third of fertilized eggs fail to complete a normal life cycle. Fortunately, most of these events are manifest as spontaneous abortions; but all too much misery already spills over into the lives of born children and their families.

© 1969. The Washington Post Co.