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THE FALL IN THE RATE OF DEATH FROM HEART DISEASES

by

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Abstract

A self limiting interaction between heart disease producing factors and genetic factors is postulated. Such an interaction could be responsible for the fall in rate of death from ischemic disease observed in the United States.

Key words: Heart disease; Death rate; Operator.

The reasons for the spectacular fall in rate of death from heart (ischemic) diseases in the United States and other countries[1] since about 1960 have not as yet been satisfactorily explained. The correlation between the changes in this rate and the suspected causes of the heart diseases, such as high fat diet, cigarette smoking, lack of physical exercises, etc. is not fully convincing. I would like to suggest here a possible influence of an interplay between environmental and genetic factors on this problem.

The possibility that mutations coupled to adaptive mechanisms could influence these rates is extremely remote, since it is well known that a large number of generations is required to fix a mutation by selective pressures. The observed changes in the rate of death (fig.1) are occurring too rapidly for such a process.

One can however visualize the following situation. Assume X is an external agent involved in the production of arterioschlerosis. We consider that the rate of death is proportional to the concentration of X in organism, and death will occur for $X > X_{threshold}$. Assume also that the DNA of human cells codes for an enzyme, α, which interferes with the activity of X, effectively neutralizing it. In the steady state condition, implying an approximately constant concentration of X as well as of α in the cells, the rate of death would be reasonably constant.

At some point in time the amount of X starts increasing (increased cigarette smoking, changes in dietary habits, increase in air pollution, etc.). Assume that X interferes with, or acts directly and negatively on the regulation of the production of

α protein. This could be envisaged as a direct action of X on the α operator as an inducer, or any more complicated step in the transcription process. The increase in the concentration of X produced by the many known factors can lead to an increase in the production of α.

As an example α could be coded by an amplified, multiple copy gene, with individual operons for each gene. The gradual increase in X would activate stepwise the α genes. This implies that the harmful agent either acting directly, or via some other agent, controls its own fate, and that the organism defends itself through this control system (fig.2).

Such mechanisms are not novel[2,3], hence they are biologically plausible. They could also explain the geographic differences in the rates of death from heart diseases. It has been observed, for instance, that in California the decrease in the death rate anteceded that in other parts of the United States[1]. This could simply signify that the concentration of X in California was higher than elsewhere, hence X reached the value of $X_{threshold}$ sooner than elsewhere, and the protection mechanism started operating sooner.

The actual situation is bound to be more complex. There exist certainly many X type molecules, as well as many α's partaking in the process.

We simply want to call attention to the fact that the regulatory mechanism in protein production maybe playing a decisive role in the observed decrease of the death rate, and may not allow for an interpretation based purely on the analysis of possible causative agents.

REFERENCES

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FIGURE CAPTIONS

1 - The changes in the rate of death from heart diseases in the United States (by permission: R. Stallone Scientific American, 243, 43 (1980)).

2 - Hypothesis of multiple α gene copy. Increase in the concentration of X activates stepwise the operators of the 1st, 2nd, ... nth α gene, increasing (also stepwise) the production of α protein. The scales of X and α concentrations are not identical.

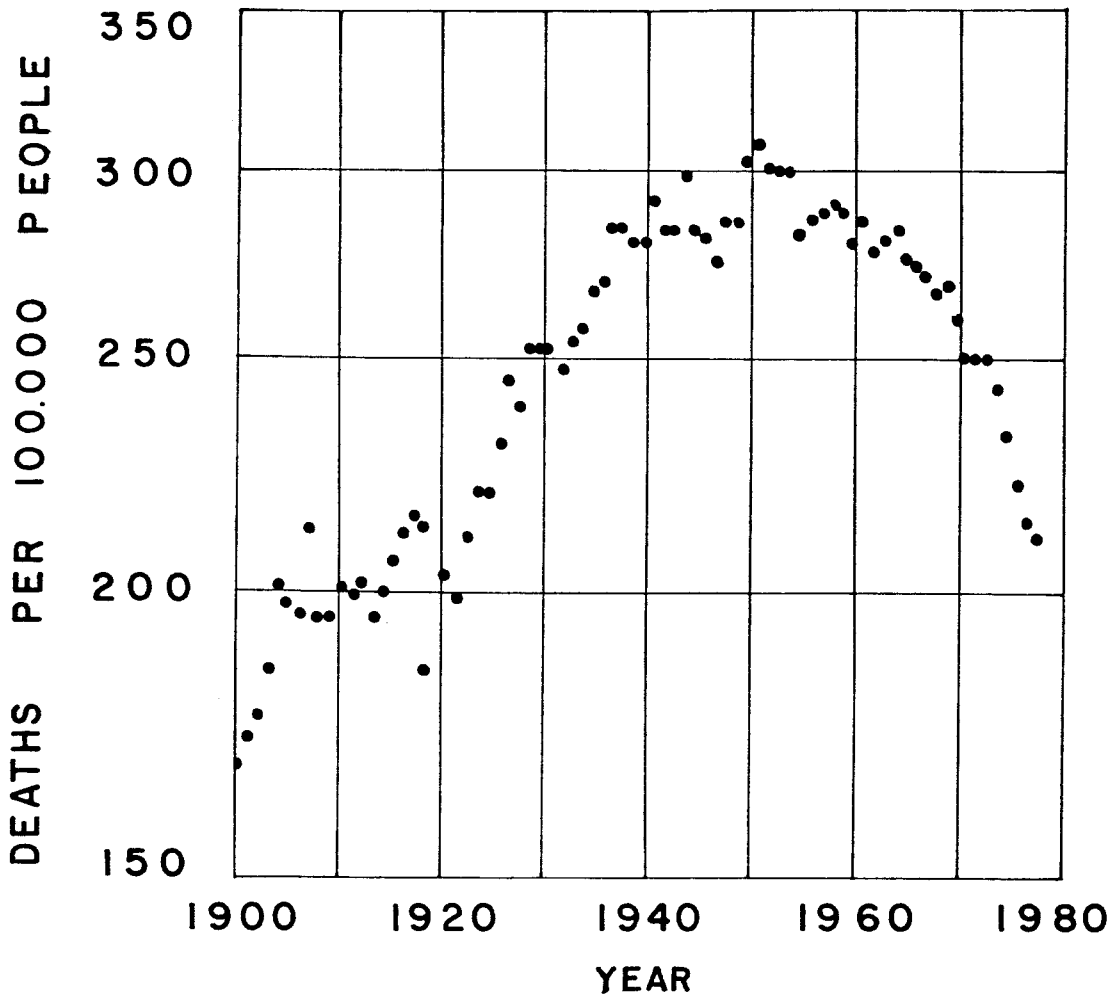
DEATHS PER 100.000 PEOPLE
350
300
250
200
150
1900
1920
1940
1960
1980
YEAR

FIG. 1

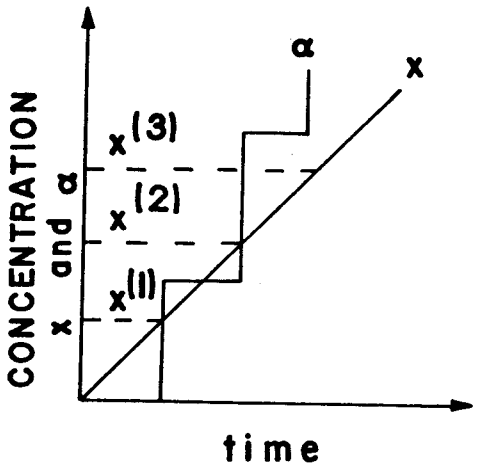

FIG. 2