formed but are much *smaller* than expected shows that *partial* repulsion exists between the two yellow variations. In the origin of the 55 yellow rats which have been tested, 110 gametes were involved. Inspection of the results shows that in 92 of these gametes the factors for red-eye and pink-eye remained apart, as they were originally; but in 18 of them a cross-over must have occurred producing a gamete which contained both factors. This ratio of 92 unchanged to 18 cross-over gametes (or 5.1 to 1) among the gametes which produced the yellow rats, should give nearly, though not quite, the gametic ratio among *all gametes* produced by the F_1 rats. This true gametic ratio may be shown by the foregoing figures to be about 4.6 to 1 and the per cent. of cross-overs to be about 18.

Animals of class 3 (*pprr*), homozygous for both kinds of yellow, should produce gametes in which these two characters would show positive coupling instead of repulsion. This matter is now being investigated with the idea of finding a quantitative expression for the strength of the coupling and comparing it with the strength of the repulsion already demonstrated.

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TOXICITY AND MALNUTRITION[1]

THE concept denoted by the word "toxicity" contains an element essentially physiological in its nature and describes primarily not so much a chemical property of a given substance as the result of a chemical reaction of this substance with one or more constituents of a given organism. Thus the effects produced by the chemical substance on the organism are obviously due to the chemical properties both of the substance itself and of the tissues of the organism. Hence, while derived in part from the chemical properties of the substance, toxicity does not exist apart from the organism and can be asserted of any given substance only after fitting experiments have been carried out on the organism in question. In contrast to this property, the purely chemical properties, such as acidity or alkalinity, exist apart from any relation to the organism. When a given chemical substance possessed of specific properties comes in contact with an organism which of course is essentially made up of substances having likewise definite chemical properties, the reactions which follow in accordance with the laws governing chemical behavior are capable of description by means of chemical terms, but from the standpoint of the organism a physiological result has occurred defined not in terms of ions and molecules, but in terms of function. When, as a result of the chemical reaction, the organism is so modified as to cause the non-performance or imperfect performance of function a more or less marked physiological injury is recognized. If the injury involves sufficiently important functions and the reaction is irreversible, death results. Should functional activity be impaired only in nonessential particulars or should the reaction be reversed, life may persist in spite of permanent injury or recovery may take place. If the arrest or derangement of function is sufficiently thorough and prompt, the organism is said, in popular phrase, to be "poisoned" and the chemical substance entering into the disturbing reaction is said to be a "toxic" substance. In view of these considerations there seems to be no scientific ground for limiting the term "toxicity" to the popular conception.

"Toxicity" results in functional impairment due to chemical reaction and, accurately speaking, is more a matter of kind than of degree. If this impairment proceeds to the point of death there might seem to be a basis for distinction between this result and that of a less serious injury not so terminating. However, if death takes place indirectly and remotely through secondary changes initiated by the chemical reaction, the organism would still have been "poisoned." If functional injury, however slight and remote, should follow from the chemical reaction, it would still be in kind a "toxic" action.

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The terms "toxic" and "poisonous," as used popularly in characterizing chemical substances, are subject to still another consideration. Substances like corrosive sublimate, copper salts, hydrochloric acid and phenol, are popularly called "toxic" substances because, in concentrations familiarly used, they produce such marked chemical reactions in organisms as to cause serious impairment of function and perhaps death. It should be borne in mind, however, that these substances lose their ability to act toxically on sufficient dilution, and even the so-called harmless chemical agents when sufficiently concentrated, if still soluble, become harmful. The question of toxic action, therefore, comes down finally not only to a matter of the chemical properties of substances, but equally to a question of the concentration of the solution in which they encounter the organism. It would follow that perhaps all substances acting singly are potentially toxic.

It might seem that water, at least, would escape the suspicion of being "poisonous." Of course, pure water is practically unknown to biology and little can be asserted concerning its action on organisms. When this substance is referred to, distilled water, a dilute solution of various substances, is usually meant. The work of a host of investigators on distilled water has led to a great variety of results, a fact due on the one hand, doubtless, to the great variation in the water used, and, on the other, to the varying susceptibility of the experimental organisms employed. It has, however, been repeatedly shown that very minute traces of salts are able to profoundly modify the physiological properties characteristic of highly purified water.

It has been shown that distilled water withdraws small quantities of electrolytes from various organisms of both plant and animal origin, with the result that as this process advances, the water becomes an increasingly concentrated solution of ions. The ability of *Fundulus* eggs to resist the action characteristic of water rendered in a scientific sense even approximately pure, as claimed by Loeb, seems to be very unusual. It would be of interest to know accurately what the ion concentration of the distilled water used in these investigations might have been at the beginning of the experiment and after it had been occupied by the *Fundulus* eggs.

If toxicity is indicated by functional derangement due to chemical reactions, then clearly nothing can be toxic in its action that can not produce chemical change in the organism. In other words, mere absence can not furnish a ground for charges of toxicity against any substance. If the solution from which a necessary substance is lacking causes the development of toxic properties (*i. e.*, functional derangement due to chemical modifications produced in the organism by the external medium) the reaction causing the derangement must proceed from the substances in position to affect the organism. Hence, incomplete nutrient media or unbalanced solutions, both producing functional derangement, bring about this effect through the reactions performed by the substances present, certainly not by those not present. Perhaps the most satisfactory approach to the situation is seen through the relation supposed by Loeb and others to exist between ions and proteins in the living organism. For normal functioning certain affinities in the proteins of the organism must be occupied by certain ions in a rather definite way. When one such ion is lacking to the medium, the affinities normally occupied by it are satisfied in a chemical way by ions present without, however, satisfying the corresponding physiological requirement. While, therefore, the absence of a necessary ion gives the opportunity for the harm-bringing reaction to take place, the actual damage is wrought within the cell by constituents actually there present. Thus, a medium characterized as deficient or unbalanced becomes actively injurious through the effects produced by the ions that are present, and malnutrition, starvation, or even a more violent type of chemical injury may appear.

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