Experimental Argyrosis: II. Treatment of Rats Receiving Silver With 2,3-Dimercaptopropanol (BAL)

CHARLES T. OLCOTT and WALTER F. RIKER, JR.
Departments of Pathology and Pharmacology, Cornell University Medical College, New York City

In a previous communication (*3*) it has been reported that silver pigment is deposited in the experimental rat in a way essentially similar to that in which it is deposited in man. In view of the efficacy of 2,3-dimercaptopropanol (BAL) in the treatment of poisoning with arsenic (*1*, *4*) and mercury (*2*), it appeared desirable to study the effect of this agent on the experimental argyrosis of the rat.

The experiment was carried out on four rats, grouped in pairs and placed on a diet of dog pellets. The first pair received a solution of 1:1,000 silver nitrate in place of drinking water for a period of 456 days. During this time a total amount of 23.2 grams of silver nitrate was consumed by the two animals, or an average of 11.6 grams each. On the 457th day the silver nitrate solution was discontinued and replaced by water. At this time the eyes of both rats were distinctly pigmented, one slightly more so than the other. Eighteen days later the more deeply stained rat was started on treatment with intramuscular BAL. The BAL was given in a 1:50 dilution in cottonseed oil. A total of nine injections was given on alternate days, covering a period of 18 days. Each single dose was 0.2 mM/kg. (10 times the minimal effective dose for the treatment of acute arsenic poisoning in the cat). The other rat was maintained as a control. The treated animal showed a weight loss of 30 grams over the period of therapy, but otherwise appeared healthy. The control animal lost 6 grams. Both animals were sacrificed on the 21st day, at which time the eyes of the treated rat were still darker than those of the control.

On histological examination, the eyes, thyroid, liver, pancreas, spleen, and kidneys contained an apparently identical amount of silver deposit. No lesions were found in either rat.

The second pair of rats received for a period of 514 days a 1:1,000 solution of silver chloride with added sodium thiosulfate (approximately 1:300) in place of drinking water. The total average silver chloride intake for each of the two animals was 12.9 grams. On the 515th day the silver chloride solution was replaced by drinking water. The eyes of the pair were also distinctly pigmented. Eighteen days later the more deeply stained rat was started on BAL therapy. The dose and manner of administration was as described above, with the exception that a total of 18 injections of BAL was given, covering a period of 38 days. The cage mate was kept as a control. During the period of treatment the treated animal lost 25 grams in weight, but otherwise appeared healthy; the control showed a 3-gram gain. On the 42nd day both were sacrificed, at which time the eyes of the treated rat still appeared darker than those of the control.

On histological examination, there were apparently identical amounts of silver deposits in the thyroid, kidneys, eyes, and choroid plexus of each rat. There were no lesions indicating any toxic effect in either rat.

It appears from these observations on a limited number of animals that BAL is incapable of mobilizing silver, which is deposited in the tissues as metallic silver or silver oxide. It seems likely, therefore, that BAL should prove of little or no value in the treatment of argyria in man. It is interesting to note the marked resistance of the rat to poisoning by BAL. No acute symptoms resulted from the injection of 0.2 mM/kg., and there were no chronic effects from the repeated administration of this quantity of BAL.

References

1. EAGLE, H., MAGNUSON, H. J., and FLEISCHMAN, R. The systemic treatment of experimental arsenic poisoning with 2,3-dimercaptopropanol (BAL). (To be published.)
2. LONGCOPE, W. T., and LUETSCHER, J. A., JR. *J. clin. Invest.*, in press.
3. OLCOTT, C. T. *Experimental argyrosis.* New York: New York Pathological Society, 1944.
4. RIKER, W. F. *J. Pharm. exp. Therap.*, 1946, **87**, 66.

The Movement of Substances Through a Two-phased Solution System[1]

T. C. BROYER
University of California, Berkeley

A thermodynamically sound treatment is essential to an understanding of the movement of substances through solutions. Manifestations of flux are common in aqueous biological systems. These phenomena are logically expressed on the basis of the concept of escaping tendency or free energy of a constituent component. Certain fundamentals of the process are presented in the hope that the free-energy concept, as it applies to this movement, will be adopted generally by biologists. The tendencies for movement of water will be discussed first, followed by that of a solute in an aqueous solution system.

WATER MOVEMENT

Pure water possesses an internal energy representing the sum of its internal kinetic and potential energies. At thermodynamic equilibrium, a steady state, the free energy of the water is equal throughout the phase. The free energy or escaping tendency of the water molecules may be modified by the application of certain chemical or physical influences. The addition of a solute to water lowers the free energy of the solvent in the resultant solution. The application of a pressure to water increases its free energy. At thermodynamic equilibrium within a solution consisting of two components,

[1] Detailed treatises will be printed in *Botanical Review* (1947), comprehending the movement of water and of a solute. In these, references are made to earlier publications pertinent to the subject.

Symbols used are defined as follows: p is an applied pressure, in a given state of the system, necessary to make $\bar{f}$ equal to $\bar{f}^o$; p^o is an applied pressure, in a reference or standard state of the system; $\bar{f}$ is the partial molal free energy of a constituent component of a solution in a given state; $\bar{f}^o$ is the partial molal free energy of a constituent component of a solution in a reference or standard state—here, at infinite dilution; $\bar{v}^o$ is the partial molal volume of a constituent component of a solution in a reference or standard state—here, at infinite dilution; F is a specific (volumed) free energy of a constituent component of a solution in a given state; subscripts i and e refer to the separate phases of a two-phased solution system—here, internal and external, respectively; and subscripts (Δf) or ($-\Delta f$) refer to influences in or on a system, which increase or decrease, respectively, the free energy of a constituent component of a solution from that in a reference or standard state to that in a given state.