Its action would be analogous in this respect to the increase of sugar in the blood stream following the administration of adrenalin.

After adrenalin injections the fibrin values remain high for several hours, and probably would have to be considered in interpreting nitrogen metabolism studies such as have been reported recently by Watkins and Smith.[7]

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Oxidation of Cobaltous Cysteine.

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Michaelis and Barron[1] and Michaelis and Yamaguchi[2] have shown that cobalt reacts with cysteine to form a product which has a high reduction intensity. They also showed that this reaction product can be oxidized with air, ferri-cyanide, and phenolindophenol to a brown cobaltic cysteine complex. We have found that cobaltous cysteine reacts in a different manner toward each one of these oxidants. Indigo disulfonate produces a quantitative conversion of cobaltous cysteine to the cobaltic cysteine complex. All other oxidants except those which contain a quinone group result in the formation of the cobaltic cysteine complex and cystine in different proportions.

Oxidation with ferricyanide produces a unique type of electrometric titration curve because all of the cobaltous cysteine is removed from solution by addition of a half of the total amount of oxidant. The last half of the curve represents oxidation of cysteine to cystine.

Cysteine reacts with quinone and with the quinone group of dibromophenol-indophenol with the formation of an addition product between the dye and the thiol group similar to the addition of an aromatic thiol group to quinone. One molecule of cysteine reacts with 1 molecule, that is, 2 equivalents of the dye. Ninety per cent of cobaltous cysteine is oxidized to the cobaltic cysteine complex with dibromophenolindophenol, and 10% of the cysteine combines with the dye. The amounts of cobaltic complex and cystine

[7] Watkins, O., and Smith, George Van S., *Am. J. Physiol.*, 1931, **96**, 28.

[1] Michaelis, L., and Barron, E. S. C., *J. Biol. Chem.*, 1929, **83**, 191.

[2] Michaelis, L., and Yamaguchi, S., *J. Biol. Chem.*, 1929, **83**, 367.

formed by each oxidant are such that the amounts of ferricyanide, oxygen, and indophenol required for a given amount of cysteine are all equal to two-thirds the amount of the cysteine.

The conversion of cobaltous cysteine into the cobaltic cysteine complex is not a straight forward oxidation such as occurs in the oxidation of cobaltocyanide to cobalticyanide. Slight variations in the velocity of addition of the oxidizing agent bring about significant variations in the proportions of cobaltic cysteine complex and cystine which are formed. The cobaltous ion is not oxidized to the cobaltic state at pH 7.4 by any of the oxidants which have been used. The results indicate that in the presence of the thiol group the cobalt is oxidized to cobaltic tricysteine. This is not stable and rearranges into a cobaltic dicysteine complex which is the brown complex described by Michaelis and coworkers. The rearrangement of cobaltic tricysteine to the complex results in the liberation of a negatively charged $^{-}$SR group.

The quantitative relations in the oxidation of cobaltous cysteine with the different oxidants can be explained by variations in the relative velocities of 4 reactions:

1. Oxidation of cobaltous cysteine to cobaltic tricysteine.
2. Conversion of cobaltic tricysteine into the cobaltic dicysteine complex.
3. Oxidation of the $^{-}$SR group to cystine or addition to the quinone group of a dye.
4. Recombination of the $^{-}$SR group with cobalt ion.

Cystine, oxidized glutathione, sodium hydrosulfite, and sodium sulfite convert cobaltous cysteine into a cobaltic cysteine complex. Sodium thiosulfate has no effect on cobaltous cysteine. Glutathione will not form a complex with cobalt.

Formaldehyde, acetaldehyde, heptaldehyde, cyanide, and ferrocyanide decompose cobaltous cysteine and prevent its oxidation to the cobaltic complex.

Although indigo disulfonate cannot oxidize cysteine to cystine a small percentage of the total cysteine is converted into cystine with this dye if cobalt is present in less than half the molar concentration of the cysteine. This indicates activation of the thiol group which may be explained by the presence in solution of a negatively charged $^{-}$SR group during oxidation of cobaltous cysteine.