rier, on the one hand the oxidation systems which utilize oxygen, and on the other the foodstuffs which are the source of hydrogen.

The enzyme responsible for the rapid and reversible oxidation of hexuronic acid has been called "hexoxidase." Its properties are different from the properties of other known oxidizing enzymes. Study of the kinetics of this enzyme has clearly shown that this enzymic function is a complicated one and that the hexuronic acid is not immediately oxidized by the enzyme. The enzyme contains a special substance or grouping, "x," which is first oxidized by the oxygen. This oxidized "x" then in turn oxidizes the hexuronic acid and is itself reduced again. No cyan-sensible oxygen activation is involved in the oxidation of "x," so that this oxidation probably goes hand in hand with the formation of hydrogen peroxide. This would explain the presence of the highly active peroxidase which would complete the system, utilizing the peroxide thus formed.

Extending these studies to the suprarenal gland, it was found that the suprarenal cortex contains a strong reducing agent, the high concentration of which is sharply characteristic for this organ. This substance has been isolated in crystalline form and has been found to be identical with the hexuronic acid from plants.

Hexuronic acid completely inhibits formation of pigment in all systems in which a "melanoid" pigment is formed through the oxidation of a phenol. In biologic systems a minimal concentration of hexuronic acid is sufficient to give complete inhibition. The absence of hexuronic acid in Addison's disease could give thus a clear explanation of the mechanism of formation of pigment.

Experiments, however, performed on animals after extirpation of the suprarenal glands, have shown that hexuronic acid is unable to prolong life. Hexuronic acid given in two cases of Addison's disease seemed to have some beneficial effect but did not restore the patients to full activity. It seems to be certain, therefore, that besides hexuronic acid some other substance is elaborated by the suprarenal cortex to which this organ owes its vital importance. The formation of pigment, however, which in Addison's disease is not dependent on the gravity of the case, seems to be connected with hexuronic acid. It seems to be highly probable that the other hitherto unknown product of the cortex plays in the animal tissue a part analogous to that of the "x" substance of the oxidation system of the cabbage leaf, which has been mentioned.

The careful survey from a chemical standpoint of reducing substances of the suprarenal gland also has brought out the fact that the medulla contains, besides epinephrin, a strong reducing agent which is specific for the medullary tissue. The substance has not yet been isolated. In many ways its behavior is analogous to that of hexuronic acid, but it seems not to be identical with it. This substance also inhibits formation of pigment, and it is possible that its absence also is a factor in the production of pigmentation in Addison's disease. It is possible that both reducing substances, hexuronic acid and the reducing substance of the medulla, play an important part in the stabilization of the other active principles present (epinephrin and the unknown hormone of the cortex). It can easily be shown *in vitro* that epinephrin is highly autooxidizable at the hydrogen-ion concentration of the tissue. The oxidized molecule rapidly undergoes irreversible secondary changes. In the presence of hexuronic acid or in the presence of the reducing substance of the medulla the oxidized molecule of epinephrin is at once reduced again and is protected in this way from secondary irreversible changes.

There are thus four specific substances elaborated by the whole suprarenal gland. In the medulla are found epinephrin and a strongly reducing substance. In the cortex are found hexuronic acid and the probable presence of another active principle, the existence of which seems to be established by the recent work of Hartman and his collaborators, of Stewart and Rogoff and by the most recent investigation of Swingle.

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