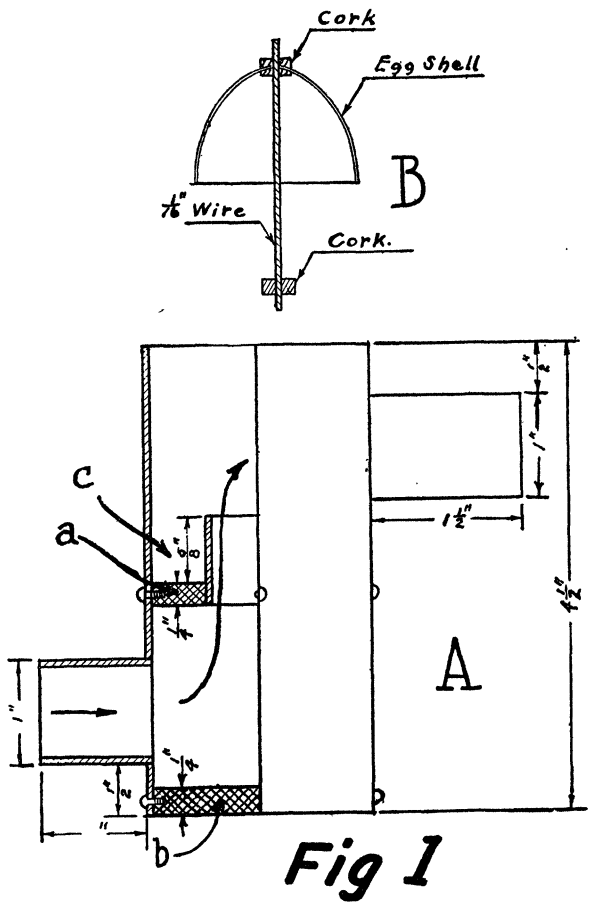

Fig 1

The valve chamber, Figure 1, *A*, consists of a short length of nickeled brass pipe cut from what plumbers designate as a two-inch tank L. This pipe is fitted with two brass discs, *a* and *b*, the latter of which closes the lower end of the chamber while the former forms the floor of the circular mercury well, *c*. As shown in the figure, a short length of one-inch brass pipe soldered in place serves for the inner wall of the mercury well. The discs, *a* and *b*, may be held in place by means of round head brass screws or may be soldered.

The direction of the air current is shown by means of the arrows. The entrance and exit tubes are of one-inch brass tubing. Before assembling for use the interior of the valve chamber must be thoroughly coated with hard paraffin or beeswax to prevent the mercury from corroding the soldered joints. The valve chamber may be readily held in its proper position by means of one or more screws passed through the disc *b*. In this laboratory the two valve chambers and the absorber chamber are compactly assembled upon a brass plate which in turn is supported by short pipe legs and mounted upon a wooden base by means of stove bolts. The upper end of the valve chamber is closed by means of a No. 11 rubber stopper. This allows for convenient examination and adjustment.

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SPECIAL ARTICLES

THE HEME COMPOUNDS IN NATURE AND BIOLOGICAL OXIDATIONS[1]

THE new knowledge of the existence and function of the heme compounds in aerobic tissues generally brings together two problems which at first sight seem far apart, the problem of the peculiar biological distribution of the hemoglobins, which are found only in a few groups of unrelated animals, and the problem of the nature of the iron compounds which catalyze biological oxidations.

Heme is the iron pyrrol complex which is joined to the protein, globin, in hemoglobin. It may be prepared in the form of its crystalline chloride, hemin. The blood of every vertebrate contains hemoglobin. Without such a pigment the large active vertebrates could not exist. But outside of the vertebrates hemoglobin occurs only here and there and in the most widely different animals. Its completely haphazard distribution does not follow at all the genetic relationships. Apparently a very complicated substance has arisen independently in nature again and again. Apparently when an individual species requires hemoglobin it can create heme to fill its need.

The ordinary fuel substances which are very stable when exposed to air *in vitro* are burned in the living organism with great ease due to the aid of catalysts. It has been believed that heavy metal compounds, in particular iron compounds, are concerned in this catalysis. But the only fact that has been known about the nature of the iron compounds which exist in all tissues is that one can not get a test for free inorganic iron. Yet the properties, catalytic and otherwise, of an iron compound depend to a great extent on the nature of the complex to which the iron is attached. Small changes in the nature of the complex can cause big changes in the powers of the catalyst.

The conclusion we wish to present is that the iron pyrrol complex, heme, is present not only here and there as a constituent of hemoglobin, but in the oxygen-consuming tissues of animals and plants generally, and that the heme compounds in nature are intimately concerned with the catalysis of biological

[1] Based on a lecture given in Evanston, Illinois, on August 11, 1928, before the Institute of Chemistry of the American Chemical Society.

oxidations. Hemoglobin, then, is to be regarded as a specialized and occasional derivative of the universal heme. And in the study of biological oxidations we must now operate not with the vague idea of iron compounds, but more specifically and more profitably with the iron pyrrol complexes of the heme family.

The first proof[2] that heme identical with the heme of hemoglobin exists in tissues outside of hemoglobin, was an application of our work on the nature of hemochromogen[3, 4]. Every hemochromogen, as we had shown, is a compound of heme and some nitrogenous substance. The exact properties of a hemochromogen, in particular the exact positions of its sharp absorption bands, depend on what nitrogenous substance it contains. Furthermore, there is always the equilibrium

$$\text{Hemochromogen} \rightleftarrows \text{Heme} + \text{Nitrogenous substance}$$

If there is added to a hemochromogen containing the unknown nitrogenous substance X the known nitrogenous substance pyridine, which has a great affinity for heme, there results

$$X\ \text{Hemochromogen} + \text{Pyridine} \rightleftarrows \text{Pyridine hemochromogen} + X$$

By the addition of enough pyridine the reaction is driven to the right; X is displaced.

If pyridine is added to yeast, a two-banded pigment is obtained which is indistinguishable in respect to the position of its bands from the pyridine hemochromogen obtained by adding pyridine to crystalline hemin prepared from hemoglobin. We conclude that yeast contains heme and that any nitrogenous substance combined with the heme has been displaced by pyridine. Our conclusion has recently been confirmed by Fischer and Schwerdtel,[5] who have isolated hemin from the pyridine extract of yeast.

We were led to this experiment by the demonstration by Keilin[6] that cytochrome is present in a great variety of tissues and that the components of cytochrome have some of the properties of hemochromogens, although they are not identical with the hemochromogen prepared from hemoglobin. MacMunn[7] had likewise previously given evidence that substances related to hemochromogen are present in animal tissues.

Warburg and his fellow workers[8] have recently investigated the rôle of heme compounds in biological oxidations. Not only can heme catalyze oxidations *in vitro*, but the oxidations are stopped by the specific inhibitors of biological oxidations, such as cyanide. And combination of heme with nitrogenous substances influences greatly both the catalysis of the oxidations and their inhibition. For instance, heme combined with nicotine catalyzes the oxidation of cystein fifteen times faster than free heme.

Warburg discovered that carbon monoxide can stop the respiration of yeast in the dark, but not in the light. Based on this discovery and on Einstein's law of photochemical equivalence is Warburg's ingenious method of determining the spectrum of the substance in yeast with which the carbon monoxide combines. This spectrum proved to have the two characteristic bands of the carbon monoxide heme compounds.

Altogether, as a result of knowledge based on *in vitro* experiments with hemoglobin and the easily prepared heme derivatives, the existence of heme in aerobic tissues generally has been demonstrated, and the study of the catalysis of biological oxidations is now approached from the point of view of the iron pyrrol complexes. And because of the facts that the heme pigments have well-defined spectra and that their compounds with carbon monoxide are sensitive to light, biological oxidations can now be studied by new and powerful photochemical methods. In regard to hemoglobin itself, a new insight has been gained into its place in the economy of nature. Hemoglobin is a specialized derivative of the universal heme.

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THE NATIONAL ACADEMY OF SCIENCES. III

The Cambrian in northern Maine: EDWARD S. C. SMITH. A thick series of folded slates and sandstones is found along the banks of the east branch of the Penobscot River in Township 5, Range 8, Penobscot