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Introductory Remarks

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Introductory remarks

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Our present knowledge of the mode of formation in living cells of the porphyrins dates from the classic paper by Shemin & Rittenberg, who showed that the nitrogen atom of glycine was specifically used in the biosynthesis of protoporphyrin. In the following five years it was demonstrated that glycine and succinyl-coenzyme A combine under the influence of a specific enzyme, and in the presence of pyridoxal phosphate, to give 5-aminolaevulinic acid, and the carbon and nitrogen atoms of this compound account for all the carbon and nitrogen atoms in protoporphyrin. The main outlines of the reactions leading to haem are now established.

We have also good reasons to believe that chlorophylls *a* and *b* and others are derived from protoporphyrin. It is also well established that the insertion of magnesium is a first step in the specific biosynthetic pathway of chlorophyll, and this insertion is followed or associated with the esterification of one of the carboxyl groups of one of the two propionic acid side-chains. Full details of these reactions and particularly the sequence of the various steps are still a matter for further investigation.

The present Discussion Meeting will concentrate on those aspects of the biogenesis of these compounds, about which we are still relatively ignorant. The enzyme catalysing the first step has only been incompletely characterized, and this enzyme is of particular importance in the overall regulation of porphyrin biosynthesis. There is reason to believe that regulation is exerted not only by the rate of formation of the enzyme, but also through activation or inhibition of the enzyme by substances of low molecular mass. There is also some evidence of the presence of two forms of the enzyme of high and low activity respectively. In addition, the formation of aminolaevulinic acid in green plants and algae does not appear to occur by the mechanism found in animal tissues or micro-organisms so far investigated. The second enzyme, aminolaevulinic dehydratase, has recently been carefully investigated by Dr Shemin, who will give an account of his work. The step from porphobilinogen to uroporphyrinogen III, which is promoted by the cooperative action of two enzymes, presents one of the most interesting and challenging problems, and will be discussed in two papers at our Meeting.

The incorporation of iron to give haem is most probably an enzymic process, but the ferrochelatase, the enzyme in question, has not been purified. Enzymic incorporation of magnesium into protoporphyrin has never been demonstrated in a cell-free system to the best of my knowledge. It seems to be associated with the methylation step, and is subject to inhibition by *S*-adenosylethionine. There are many other areas on which this present Discussion Meeting will throw new light, such as the mechanism of biosynthesis of vitamin B_{12}, and the later steps of biosynthesis of various chlorophylls other than chlorophylls *a* and *b*.

Together with the advances which have occurred in the purely biological field, there has also been an impressive increase in our understanding of the structural chemistry of these compounds, the electron density pattern of porphyrins and of their metal complexes, and in the availability of a great variety of new preparative methods. The introduction of new physical tools such as mass-spectrometry has also made a considerable impact. The

cooperation of organic chemists and biochemists in this field is likely to be particularly fruitful, and the choice of both topics and speakers at our meeting gives expression to this basic philosophy.

The organizers would like to express their appreciation for the great help given by Dr Kevin Smith in both arranging the Discussion Meeting and collecting and editing the papers.

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