

as with the variety of nervous stimulations which leads to the discharge of adrenocorticotrophic hormone. The evidence in favour of the alternative views that the release of adrenocorticotrophic hormone is mediated by some neurohumoral substance of unknown chemical nature (the so-called CRF) or by vasopressin, or by melanophore-stimulating hormone, was reviewed by Dr. Guillemin, but there seems little that is precise about these matters, and as the general discussion at the end of the seminar indicated, considerable doubt exists about the assumed localization of hypothalamic function with respect to the control of pituitary function.

The verbatim record of what passes at endocrinological symposia has on occasion detracted from the value of what might otherwise have been regarded as scientific meetings of high quality. On this occasion this is not so. Not only do the papers which were delivered at the seminars of the Collège de France provide a first-rate account of the matters with which they deal, but it is also plain from the record of the discussions that Prof. Courrier kept the several sessions of the two seminars very much to the point. He is to be congratulated for having inaugurated a series of seminars which will, one is certain, continue to enjoy the high standard of the two now published.

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## HÆMOGLOBIN: NORMAL AND ABNORMAL

### Hemoglobin and Its Abnormalities

By Prof. Vernon M. Ingram. (A Monograph in American Lectures in Living Chemistry.) Pp. xiv+153. (Springfield, Ill.: Charles C. Thomas; Oxford: Blackwell Scientific Publications, 1961.) 60s.

**H**ÆMOGLOBIN is the most intensively studied of proteins. Many of the techniques available to the physiologist, biochemist, biophysicist and geneticist have at one time or another been applied to hæmoglobin. All this work has led to spectacular progress in our understanding of the structure and function of hæmoglobin and its near relative, myoglobin.

Last year saw the publication of papers that represent the culmination of long and detailed analysis by the investigators concerned. Kendrew and his colleagues have extended the resolution of data from their X-ray diffraction patterns of myoglobin to the 2 Å.-level, so that for the first time the helical arrangement in the polypeptide chain of a protein can be unequivocally demonstrated. At the same time, Perutz *et al.* published the structure of hæmoglobin at a resolution of 5.5 Å. Because of its very great similarity to the myoglobin structure, they have been able to infer considerably more than the actual resolution allows. From these X-ray diffraction patterns detailed information about the secondary and tertiary structure of proteins in crystalline form can be deduced. There is already correlation of structures deduced from X-ray patterns with the amino-acid sequences which are now known for the human hæmoglobin chains and nearly all known for horse hæmoglobin chains and myoglobin.

In 1949, Pauling *et al.* demonstrated that the basic defect in sickle-cell disease is an abnormal hæmoglobin. The term 'molecular disease' introduced by

Pauling for conditions of this kind has caught the imagination of many research workers and provided a great stimulus to research in the field. Eight years later Ingram applied Sanger's technique of peptide analysis to normal adult and sickle-cell hæmoglobins. He found that the two molecules differ only in a single peptide, and later this difference was shown to be due to the substitution of the amino-acid valine for glutamic acid which occupies the sixth position from the amino-terminus of the  $\beta$ -polypeptide chain of the normal molecule. Ingram and his co-workers, and later others, have shown that several other abnormal hæmoglobins differ from the normal by single amino-acid substitutions in the  $\beta$ - or  $\alpha$ -chain. There was formal evidence that genes controlling the synthesis of normal and abnormal  $\beta$ -chains were allelic with one another but not with genes controlling synthesis of  $\alpha$ -chains.

Ingram's important discovery could not have come at a more opportune time. The importance of proteins in mediating genetic effects transmitted by nucleic acid had emerged from the publications of Crick and others, and there was a great need to know the sort of effects on protein structure produced by mutation of the genes controlling their synthesis. The studies of Ingram and his colleagues provided precisely the required information. The technique of peptide analysis, re-named by Ingram 'fingerprinting', came to be used in many laboratories for establishing exact structural differences between related proteins.

In the book under review Ingram gives a general account of these developments, beginning with the structure and function of the normal hæmoglobin molecule and describing the structural differences in some of the known abnormal molecules. The arguments are well presented and easy to read. There are few mistakes (in caption 2 to Fig. 46 *S* should be replaced by *F*). Diagrams and references have been carefully selected and provide an excellent introduction to the field. So much has been done that it is, of course, impossible to expect a book of this length to serve as a comprehensive reference work. Although the main emphasis of the book is biochemical, the diseases associated with the abnormal hæmoglobins are briefly discussed and a few of the interesting problems in population genetics raised by the high frequency of certain abnormal hæmoglobin genes in some human populations are mentioned. In connexion with the latter, Ingram quotes the extraordinary and unfounded suggestion that "hæmoglobin E might have a selective advantage because in the presence of this gene the likelihood of an allelic thalassaemia disease occurring in homozygous form is removed".

This book is likely to be read by many people with an interest in biochemistry and genetics, and it seems a pity that, although only 150 pages long, it should cost £3.

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## ADVANCED ORGANIC CHEMISTRY

### Advanced Organic Chemistry

By Prof. G. W. Wheland. Third edition. Pp. xi+871. (New York and London: John Wiley and Sons, Inc., 1960.) 17.50 dollars; 140s.

**T**HIS book constitutes an extended, revised edition of Prof. G. W. Wheland's well-known book, *Theoretical Organic Chemistry*, which, for more than a decade, has been of such considerable value to