be a number of different classifications, each based on different characters, and each equally valid for its own purpose.

It is true that there will be one, as it were, general-purpose classification, more natural than others, in the sense that more inductive generalizations can be made about its classes—and this general-purpose classification is, of course, the normal taxonomic arrangement into species, genera, families and so on. This classification should not, however, be regarded as an approximation towards a single, ideal scheme, but as a permanently flexible arrangement, changing as new knowledge is acquired and incorporated in it. It can be called phylogenetic only in a secondary sense, namely, that the reason why a particularly natural biological classification can be made at all is of living things—and, further, phylogenetic studies can, of course, be made regarding the origin and development of its groups; but both these considerations are very different from regarding a natural classification as essentially and primarily phylogenetic.

One may well ask, what difference does it make in practice whether we regard a natural classification of living things as—to put it briefly—'logically' natural or 'phylogenetically' natural. Are we not just splitting hairs, with no practical result? I do not believe that this will prove to be the case. I believe it is possible that, if we can once and for all lay the bogey of the existence of true relationship and realize that there are, not one, but many kinds of relationship —genealogical relationship, morphological relationship, cytological relationship, and so on—we shall release ourselves from the bondage of the absolute in taxonomy and gain enormously in flexibility and adaptability in taxonomic practice. Instead of the present rigid separation between the normal categories on one hand and those of experimental taxonomy on the other, we shall realize that they differ in degree and purpose only, and are all equally valid for the overall purpose of making inductive generalizations about living things. To take a concrete example, Turesson's genecological classification and its later modifications, or Danser's categories of *Comparium*, *Convivium*, etc., based on capacity to interbreed, should not be regarded as possible rivals of the orthodox categories, but as special classifications equally valid for their own particular purposes. In the same way, a truly phylogenetic classification, based on known lineages, would also take its place as a special classification constructed for its own particular purpose.

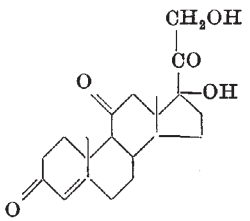
An ever-increasing volume of data is now being produced in the field of experimental taxonomy, data showing the great complexity of the units comprising the ebb and flow of evolutionary change. Recently, Dr. W. H. Camp, in a stimulating paper entitled "Biosystematy" (*Brittonia*, 7, 113; 1951), has emphasized forcibly the difficulty of fitting the dynamic concepts of modern experimental taxonomy into the orthodox categories of genus and species, conceived, as they were, against the static background of special creation. He hints that these categories may have to be abandoned completely for the special purpose of classifying the actual units of evolutionary change, and I would strongly support this view. Such a course would seem almost sacrilegious if we regard the orthodox taxonomic categories as an attempt at expressing 'true relationship'; but on the view that I have been outlining, that they are human contrivances constructed for human purposes, there is, of course, nothing shocking in abandoning them if they do not serve the particular purpose we have in mind at the moment.

I do not claim that what I have said here is more than the outline of an approach to present taxonomic problems, and I hope that others may be persuaded to join in working out its implications more fully.

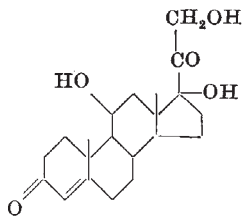
ORGANIC CHEMISTRY IN THE SERVICE OF MEDICINE

ONE of the sessions of Section B (Chemistry) of the British Association, during the recent Edinburgh meeting, was devoted to a symposium on "Organic Chemistry in the Service of Medicine." Notwithstanding the title, two of the three papers which were presented had a distinctly biochemical flavour, which perhaps serves to emphasize that organic chemistry and biochemistry are inextricably intermingled, in spite of those who would have it otherwise. The chair was taken by Prof. G. F. Marrian, who suggested that one of the main reasons for the selection of the subject of the discussion was a desire to honour the memory of the late Prof. George Barger, his predecessor in the chair of chemistry in relation to medicine in the University of Edinburgh. Prof. Marrian recalled some of Barger's outstanding chemical contributions to medical science, and referred also to the important work carried out by some of the pupils whom he inspired.

The first paper in the symposium was read from the chair by Prof. Marrian, who described recent work on the adrenocortical steroids. He pointed out that the discovery by Hench, Kendall and their collaborators of the treatment of rheumatoid arthritis and certain related diseases by cortisone, or by administration of the adrenocortical stimulating hormone of the anterior pituitary, no longer seems to be the great discovery in practical therapeutics that at first it appeared to be. But to the medical scientist, who takes a longer view than his clinical colleague, the discovery appears to be even more important than it did two years ago, on account of the way in which it has stimulated chemical, biochemical and clinical research on the adrenocortical hormones. The work of Kendall and Reichstein, and their collaborators, on the 'life maintenance' principle of the adrenal cortex, led to the isolation, during the period 1936–40, of six active steroids and to the determination of their structures. These are 11-deoxycorticosterone (now known as cortexone), corticosterone, 11-dehydrocorticosterone, and their respective 17-hydroxy derivatives. Two of the latter are cortisone and the related compound cortisol, both of which are therapeutically active in the treatment of rheumatoid arthritis. Cortisol is likely



Cortisone
(17-Hydroxy-11-dehydro-corticosterone)



Cortisol
(17-Hydroxy-corticosterone)

soon to be more readily available, and is believed to be preferable to cortisone in some respects.

Cortisone appears to influence rheumatoid arthritis and related diseases by suppressing the inflammatory symptoms in the mesenchymal tissues; this is in contrast with the function of adrenocortical hormones in the treatment of Addison's disease, where the effect is to make good a deficiency or absence of the endogenous hormones.

Prof. Marrian thought that, from a biochemical point of view, one of the most interesting and challenging facts about the adrenocortical hormones is the multiplicity of the physiological and pharmacological effects which they are able to produce. He suggested that there may be some common biochemical factor underlying these, possibly the interaction of the hormone with some particular chemical grouping which is present in a number of different enzymes. Several groups of workers have demonstrated effects *in vitro* of some of the hormones on the carbohydrate metabolism of preparations of liver and muscle tissue. It has also been found that granulation tissue from healing wounds or embryonic tissues maintained *in vitro* are able to fix sulphate in insoluble organic combination, possibly due to the synthesis of sulphated mucopolysaccharides. This fixation of sulphate can be entirely inhibited by the addition of cortisone to the culture medium. Another group of workers has found that hyaluronidase can be inhibited by cortisone.

One of the most outstanding recent achievements has been that of Pincus and his collaborators, who have shown conclusively, by using cholesterol labelled at C_3 with carbon-14, that under the influence of adrenotrophic hormone the adrenal gland is able to manufacture the adrenocortical hormones by degradation of cholesterol. By using various steroids these workers were also able to show that the gland (without adrenotrophic hormone) can effect hydroxylation at positions 11, 17, and 21, and they obtained evidence that progesterone is an intermediate in the conversion of cholesterol to the adrenocortical hormones. Thus progesterone, which has been isolated from the adrenal gland, was converted into corticosterone and cortisol.

In conclusion, Prof. Marrian referred to current work aimed at the total synthesis of cortisone, which may conceivably satisfy the requirements of the hormone for clinical use. He recalled the recently announced total synthesis of *epi*androsterone by Sir Robert Robinson and his collaborators, an achievement which also represents the total synthesis of androsterone and testosterone. Almost simultaneously, Woodward and his collaborators announced the total synthesis of the methyl ester of *dl*-3-keto-$\Delta^{4,9(11),16}$-*aetio*cholatrienic acid. This has since been resolved and converted into cholestan-3β-ol, which had already been converted into cholesterol. Among other steroids the total synthesis of which has been completed by this work is the adrenocortical hormone cortexone (the total synthesis of cortisone has also just been reported (Woodward *et al.*, *J. Amer. Chem. Soc.*, **73**, 4057; 1951)).

Dr. F. L. Rose followed with an interesting and authoritative account of the extensive co-operative researches carried out during the Second World War on the synthesis of new antimalarial drugs. The most outstanding advances in this field were those of Dr. Rose himself and the late Dr. F. H. Curd and their collaborators, culminating in the discovery of the most effective antimalarial drug so far known, namely, 'Paludrine'. The importance of this service to medicine and to mankind may be gauged by Prof. Marrian's comment that it has been estimated that a quarter of the population of the world suffers from malaria. In his contribution, Dr. Rose pointed out that malaria is unique among the diseases of micro-organismal origin in that it has a history of chemotherapy extending over the past three hundred years, arising from the use of the cinchona alkaloids. Quinine is not the perfect antimalarial drug, however, and the search for improved synthetic agents began in the past century. Dr. Rose showed how the observation by Ehrlich and Guttman in 1891 of the slight therapeutic effect in man of methylene blue opened the way for future developments. Exploitation of this early lead was delayed until new preparations, based on this dyestuff, could be assayed in the laboratory. This came in the early part of the present century with the discovery and use of the avian malarias. By then, the significant features of the structure of quinine had become clear, and this knowledge led in 1926 to the synthesis in Germany of the related 6-methoxyquinoline derivative pamaquin (originally called 'Plasmoquine'). The continued search for a drug having schizonticidal activity resulted, a few years later, in the acridine derivative mepacrine ('Atebrin'), and it was this substance that was selected for process study in Britain in 1938 as an insurance against a break in quinine supplies resulting from war, which then seemed imminent. At that time, the use of mepacrine was still in the experimental stage, and although its availability from 1940 onwards was of vital military significance, careful clinical investigations established its limitations and disadvantages. As a result, intensive co-operative searches for new and improved agents were begun, co-ordinated in Great Britain by the Medical Research Council, and in the United States by the National Research Council. The objectives were freedom from colour (skin pigmentation) and reduced toxicity, ease of manufacture, and an action at the exoerythrocytic phase of the life-cycle of the causative parasite. This last had by the early 1940's assumed paramount importance in the minds of workers looking for new antimalarial drugs, since only through the control of the tissue forms could true causal prophylaxis be obtained.

A vast screening programme in the United States dealt with some fourteen thousand compounds, and led to the discovery of antimalarial activity in experimental infections (including prophylactic action) in a number of previously unconsidered chemical types. The most important outcome of this search was the establishing of the therapeutic value of the 4-aminoquinoline derivative chloroquin, a substance which under its name 'Resochin' is now known to have been undergoing field-trials at the hands of its German discoverers in 1939.

In Britain, a more modest programme led to the preparation and assay of, perhaps, two thousand substances in all. The majority of these were based on the discovery, early in the work, of laboratory activity in a chloroanilinopyrimidine. Exploitation of this lead also resulted in the elaboration of a wide variety of compounds, mostly heterocyclic, exhibiting similar behaviour, of which one at least, *p*-chlorophenylguanidinopyrimidine, was active clinically. An attempt to get away from the use of heterocyclic systems, while yet retaining other features considered structurally significant, led in 1944 to an investigation of certain diguanide derivatives. These

proved active, not only against erythrocytic but also against the exoerythrocytic forms of the experimental avian parasites, and one such derivative, proguanil ('Paludrine' : N^1 - *p* - chlorophenyl - N^5 - *iso*propyldi - guanide), has passed into extensive clinical use on this basis.

As a result of these war-time endeavours, the objectives initially postulated have been largely attained. The causative organisms of malaria are so numerous in variety and drug susceptibility, however, that some forms of the disease inevitably remain resistant to therapy if only in degree, and the existence of these, together with the problem of relapse in certain cases, provide the challenge for the future.

In the concluding paper of the session, Mrs. R. V. Pitt-Rivers described recent work on the thyroid gland. She pointed out that the biosynthesis of thyroxine depends on the ability of the thyroid gland to collect iodide from the plasma and to fix it in organic combination. In the normal animal, the iodine-concentrating mechanism is largely controlled by the thyrotrophic hormone of the anterior pituitary, and fails in hypophysectomized animals. Thiocyanate inhibits the iodine-concentrating mechanism and, in fact, causes the discharge of iodide already collected by the gland. The second function of the thyroid, the synthesis of thyroxine, is generally assumed to occur in three stages : (*a*) oxidation of iodide to iodine, (*b*) iodination of tyrosine, and (*c*) coupling of two molecules of di-iodotyrosine. The first stage requires enzymic activity, but this is not necessarily so for the coupling reaction, as coupling can occur *in vitro* in the absence of any enzyme system. Dr. Pitt-Rivers has found that if the amino group is protected by acylation and the carboxyl group by peptide combination, then the yield of thyroxine formed by incubating diiodotyrosine aerobically can be raised to 35 per cent. The coupling is an oxidative one, but its mechanism is not known, nor is the fate of the three-carbon chain which is lost from one molecule of diiodotyrosine.

Dr. Pitt-Rivers outlined experiments with anti-thyroid drugs of the thiourea group and also with aniline derivatives which include *p*-aminobenzoic acid and some of the sulphonamides ; these have led her to conclude that the formation of thyroxine from diiodotyrosine is an oxidative reaction brought about *in vitro* by small amounts of iodine liberated from the diiodotyrosine. In *in vivo* experiments, too, the formation of thyroxine is invariably accompanied by loss of iodine from diiodotyrosine. The remarkable inhibition of thyroid function by iodide is possibly due to an inhibition by excess of iodide of the enzyme system which is responsible for its own oxidation.

Finally, Dr. Pitt-Rivers showed how the use of new techniques, in particular the use of radioactive iodine and partition chromatography, has enabled several groups of workers to localize reactions in which iodine plays a part, and to detect iodo compounds which are present in the gland only in traces. Apart from diiodotyrosine and thyroxine, the only iodine compound present in the gland which has been unequivocally characterized is monoiodotyrosine. All three compounds are present in the thyroid in very small amount as free amino-acids, and three new iodine-containing compounds of unknown constitution have been detected in the gland. Evidence has been provided that the circulating hormone in the plasma is free thyroxine.

AUTOMATIC CONTROL

A CONFERENCE organized by the Department of Scientific and Industrial Research, on the subject of developments in the field of automatic control, was held at the College of Aeronautics, Cranfield, during July 16–21, under the presidency of Sir Ben Lockspeiser. It was attended by some three hundred engineers, mathematicians and teachers of engineering, including members from most of the leading industrial countries.

The purpose of the present article is to give an impression of the state of developments in the field of automatic control as revealed by the papers and the discussion at the conference. The broad principles of automatic control involving feed-back are now very well known, and many useful methods for the analysis of the behaviour of control systems are quite familiar. The conference was concerned with those aspects of the subject that go beyond these well-established principles and methods and in which further progress is required. The chief topics may, perhaps, be broadly classified as follows : first, educational problems arising from the growing importance of feed-back systems, and the rapid increase in the demand for personnel having specialized knowledge and skills in this field at all technical levels ; second, the development and co-ordination of improved methods of mathematical analysis for such systems ; third, the extension of the methods to a widening range of technical and other problems ; and finally, the attempt to deal more adequately with such problems as systems with non-linearities and with intermittent data. In attempting to give a summary of the present state of progress as revealed by the conference, it will be convenient to consider these four topics in turn.

Educational problems. New requirements in respect of instruction in the principles of automatic control are arising over the whole educational spectrum, from the shortage of instrument mechanics in the chemical industries to the need for more men of the highest engineering and mathematical competence to carry on development work in such fields as the control of aircraft or the development of combined analogue-digital calculators.

The opening paper of the conference by Prof. Gordon Brown, of the Massachusetts Institute of Technology, made a striking plea for the recognition of the "feed-back engineer" as a new professional category corresponding with a new type and perhaps a new standard of professional competence. The specification for a feed-back engineer is for a man capable of synthesizing many technical specialisms and capable of eliciting co-operation at all technical levels. Prof. Brown described the postgraduate school in control engineering at the Massachusetts Institute of Technology, which has an annual output of approximately fifty postgraduate students. This figure was referred to by a member from a leading American instrument firm as "merely a drop in the ocean of America's requirements". Prof. Brown described how students are trained at the Massachusetts Institute as working engineers participating in large-scale research projects, accepted by the Institute on contract. Such forms of advanced technical training are unknown in Great Britain, where it is noteworthy that the research establishments of government departments and of the research associations have no specific educational functions and not even in organized liaison with higher education.