THE FOURTH INTERNATIONAL GOITRE CONFERENCE

THERE is a growing body of opinion in favour of replacing the large international conferences, attended by three or four thousand people, by smaller gatherings of an international character, and devoted to more specialized topics. At such meetings there should be better opportunity for expert discussion of communications, less overlapping of programmes and, above all, a chance of seeking out and talking with specific participants. Confirmation of the correctness of such expectations was afforded by the very successful meeting of the Fourth International Goitre Conference held in London during July 4–8. In all, about 600 endocrinologists, clinicians and biochemists, drawn from more than forty countries, took part. More than a hundred papers were delivered, and a book of abstracts of about 500 words each, in four languages, was provided at the time of registration.

A very large part of the subject-matter reported at the Conference was devoted to endemic goitre, and papers were read which surveyed its incidence in various parts of the world, the genetic aspects of the subject, and the part which goitrogens and other factors might play in its etiology. That iodine deficiency, in the opinion of Perinetti *et al.* and Kicic *et al.*, is the most important cause of endemic goitre was shown by the reliable effects which iodized salt had brought about in the disappearance of the condition in such different areas as Mendoza in Argentina and Gornja Josanica in Yugoslavia. On the other hand, Kilpatrick *et al.* suggested that iodine deficiency probably plays only a part in the development of goitre in an area to the west side of Sheffield, which was compared with a coastal district near Edinburgh. Although the iodine content in the water supply in the two districts is not dissimilar, there was a higher incidence of goitres in Sheffield. More fish was consumed in Scotland. It was further noticed that there was a definite familial linkage in the disease. An examination of the iodine content of goitrous thyroids did not reveal consistently low values as compared with normal thyroids. Observations of the seasonal incidence of goitre in sheep and cattle and the similar seasonal variation in anti-thyroid activity of milk (even in dried milk) suggests that though iodine may play a part in the incidence of goitre in the Sheffield area, goitrogens may also be a contributory factor.

Similar views were put forward by Costa *et al.*, who conclude that endemic goitre is a process which goes beyond mere alteration in thyroid function and that it is not a simple adaptation by the gland to iodine shortage. In a very careful examination by Koenig in Switzerland of nineteen endemic cretins, ranging in ages between 46 and 93 years, a number of interesting facts arose. It is difficult to find cretins born in Switzerland after 1910, which is at least ten years prior to the inception of iodine prophylaxis. Results of determinations of protein-bound iodine and the uptake of thyroidal iodine-131 show wide individual variation. In most cases these values were low, but in some they were normal and in others high. Some cretins responded well to exogenous thyroid-stimulating hormones, while others did not. The basic metabolic rate was a most unreliable indication of the state of affairs.

Cassano *et al.* believe that iodine deficiency may arise from excessive renal loss. They found that a high rate of excretion of iodine normally occurs in puberty and pregnancy and, significantly, in Cushing's disease and acromegaly, suggesting a hormonal basis for the increased renal excretion. The hormone most active on renal clearance of iodine is aldosterone. In any areas where iodine deficiency is likely, increased renal clearance of iodine, as in pregnancy and puberty, might favour the development of goitre.

A number of *Brassicae* are goitrogenic when fed to animals. Astwood *et al.*[1] isolated L-5-vinyl-2-thiooxazolidone (goitrin) from yellow turnip, but this cyclized derivative of an *iso*thiocyanate does not exist as such in the plant but is formed enzymically from progoitrin, identified by Greer as a mustard oil glycoside. It is now reported (Greer *et al.*) that the conversion to goitrin can be accomplished by microorganisms in the animal gastrointestinal tract. Both cooked and raw brassicaceous vegetables are therefore potentially goitrogenic, the effect being an iodine-blocking one.

Endemic goitre is not always associated with a deficiency of iodine in the soil and a relation to pasture has been suspected. Thus, in Tasmania endemic goitre occurs and it has been shown that cows fed on the brassica 'chou-mœllier' secrete an active goitrogen in their milk which is consumed in quantity by school children. Peltola reports a somewhat similar situation from Finland, where endemic goitre areas exist. Recently published researches of Bachelard and Trikojus[2] go far to elucidate this problem. They find the turnip weed *Rapistrum rugosum*, which grows abundantly in certain areas of Australia, to contain a glycoside of cheiroline (γ-methylsulphonylpropyl-*iso*thiocyanate). Cheiroline had a variable goitrogenic effect when administered to rats, suggesting its possible transformation into an effective goitrogen in the animal body. Incubation of cheiroline with cows' ruminal contents afforded *sym*-di-cheiroline thiourea $(CH_3SO_2[CH_2]_3NH)_2C=S$. This interesting transformation may occur more generally with *iso*thiocyanates and be of importance in bringing about endemic goitre.

Dimitriadou *et al.* believe that there may be a defective synthesis and storage of fully iodinated hormones in some cases of non-toxic goitre and that this might be due to a defective iodinating mechanism. By means of their 'supplemented iodine-131 test' it was possible to calculate the amount of iodine-127 available to the thyroid, the rate at which iodine-131 became fixed organically into the various iodinated amino-acids in the gland, and also to estimate the size of the thyroid iodine stores. Results indicated little difference in urinary iodine excretion between patients with thyrotoxicosis, those with non-toxic goitre (with or without avid uptake of iodine) and euthyroid individuals. Stores of iodine compounds in the thyroid were diminished in cases of non-toxic goitre and the rate of transfer of iodine-131 into heavily iodinated compounds, that is to say, diiodotyrosine and the iodinated thyronines, was slower in such persons. This defective or slowed iodinating mechanism can be compensated for, however, by iodine supplements even though, by normal standards, these persons were not deficient of iodine in the diet.

A number of authors reported studies in which family pedigrees were examined to discover the incidence of abnormal thyroid behaviour. Fraser *et al.* and Thould and Scowen reported on the condition known as Pendred's syndrome, the main features of which are bilateral deafness, observed early in life, and goitre developing from about eight years onwards. The defect, which is probably congenital lack of a peroxidase enzyme system in the thyroid, results in inadequate organic binding of iodine. The condition is rare, and genetic data suggest that the syndrome is inherited in a recessive manner.

Other genetic studies were reported on simple goitre. One pedigree of 250 individuals was studied (Van Wyk *et al.*) which suggested that the occurrence of goitre in this family was a simple dominant trait which is more commonly overt in the female. Serologically there was a characteristic abnormality which consisted of a protein-bound iodinated constituent migrating electrophoretically with the albumin fraction. Other studies in a different family provided evidence of defective peripheral dehalogenation of iodotyrosines.

Elucidation of the process of biosynthesis of its hormone by the thyroid gland has proved to be a peculiarly baffling problem. The process may be divided into the three stages of concentration of iodide from the blood (the 'trapping' mechanism), iodination of thyroglobulin and release of thyroxine or triiodothyronine from the gland. Such a subdivision, although convenient, is somewhat arbitrary since it becomes increasingly clear that the metabolism of iodine must be considered within the thyroid gland as a whole.

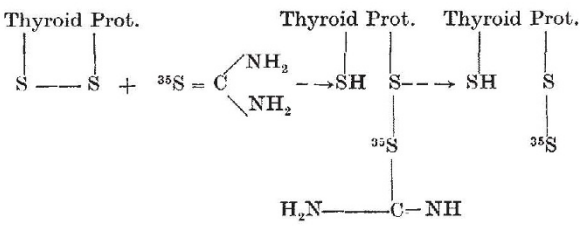
Thiocyanate and perchlorate are both known to prevent the accumulation of radioiodine by the thyroid. Wollman and Reed reported experiments designed to ascertain whether thiocyanate can, in addition, affect the iodination process and involving measurements of the binding-rate and thyroid/serum ratio (T/S) of injected radioiodide computed for different levels of serum thiocyanate. If two thyroidal compartments, an iodinating and a non-iodinating, respectively, were envisaged and the concentration of radioiodide in the latter was assumed to parallel that of serum, binding-rate constants became independent of serum thiocyanate-levels, consistent with the hypothesis that thiocyanate acts solely by decreasing the concentration of radioiodide at the binding site.

Perchlorate is excreted virtually unchanged (Lewitus *et al.*). Administration of $K^{36}Cl^{18}O_4$ showed that it is distributed in the body as is the iodine ion, being similarly concentrated in the thyroid gland. The supposed antagonism between perchlorate and iodide is of a competitive nature. These two ions have nearly the same ionic volume. Monofluorosulphonate, difluorophosphate and fluoroborate also have approximately the same ionic volume and are isoelectronic with perchlorate, and trial shows that they also inhibit the uptake of iodine by the thyroid. These studies lead to the conclusion that the 'trapping mechanism' may be merely a specifically adapted protein with a spatial arrangement that will chelate those ions which will fit into its spatial structure.

The synthesis of thyroglobulin in the mouse has been followed autoradiographically after injection of labelled leucine (Nadler *et al.*). Maximum activity was seen in the epithelium within 0·5 hr., followed by a decline as activity rose in the colloid (maximum in 35 hr.). These results are interpreted as indicating synthesis of a pre-thyroglobulin in the epithelium followed by secretion as thyroglobulin into the colloid, where it is iodinated prior to breakdown and release of thyroxine and amino-acids. The number of cells in the epithelium controls the rates of these processes. De Groot reported upon the early stages of *in vitro* hormonogenesis in sheep thyroid slices and in living rats. A homogenate of the thyroid tissue was separated into mitochondrial, microsomal and soluble fractions which were then analysed. Soluble fraction protein-bound iodine-131 as per cent of total protein-bound iodine-131 increased rapidly, then plateaued and was apparently all thyroglobulin. No thyroxine was identified in slice homogenates. It seems that in the iodination of thyroglobulin, iodine-131 may be transferred from a particulate fraction.

There is still much discussion concerning the possible role of a thyroid peroxidase in oxidizing iodide to iodine available for iodination. This chemical reaction can occur *in vitro* and therefore seems attractive, but it will be recalled that, among others, Glock[3] has severely criticized the evidence purporting to show the presence of a true peroxidase in the thyroid gland. Alexander reports that thyroid and salivary gland homogenates oxidize iodide in the presence of hydrogen peroxide added as such or generated by auto-oxidation of flavin. Catalase or anaerobiosis prevents flavin activation. The iodine formed by oxidation will iodinate tyrosine and to a lesser extent histidine, but the presumed natural acceptors, thyronine and di- and tri-iodothyronine, are *not* iodinated by this system.

That biological iodination may, in fact, be brought about by a different mechanism is suggested by a most interesting communication from Maloof and Soodak. These authors had previously demonstrated the desulphuration of sulphur-35-labelled thiourea by a cytoplasmic particulate system of thyroid. Thiouracil and thioacetamide are similarly desulphurated, the products being about 50 per cent protein-bound sulphur-35, 27 per cent thiosulphate, 10 per cent sulphate and 10 per cent an unknown compound. The protein-bound sulphur-35 is non-dialysable and stable to acid, but 80 per cent of it is displaced by such alkaline reagents as cyanide, sulphite, sodium hydroxide or by thiols such as cysteine, reduced glutathione and diethyldithiocarbamate. The desulphuration of thiourea is strongly inhibited by sulphite and cyanide, nucleophilic anions which are known to split disulphide bonds forming a thiol and an S-alkyl thiosulphate or alkyl thiocyanate, respectively. Using $Na_2{}^{35}SO_3$, it is found that it also forms protein-bound sulphur-35, which is quantitatively and qualitatively similar to that arising from labelled thiourea. The results suggest that both react with thyroid protein disulphide bonds forming a new mixed disulphide linkage as follows :



Free sulphydryl groups do not play a part in the desulphuration of thiourea since pre-incubation with SH reagents is not inhibitory. Parallel observations

on the iodination reaction in this *in vitro* system suggest that a disulphide bond may be involved in the formation of an active iodinating intermediate. Hence, cleavage of an S—S bond in thyroid tissue by thiourea may be a factor in the inhibitory action of this compound. The desulphurating effect appears to be specific since it did not occur with liver tissue preparations.

Anti-thyroid drugs are not only of great therapeutic value, but also the study of their action continues to throw light upon the mechanism of biosynthesis of thyroxine, as the last-mentioned contribution clearly shows. For the medical treatment of thyrotoxicosis in the United States, according to McClintock and Gassner, propylthiouracil, 1-methyl-2-mercaptoimidazole and 5-iodo-2-thiouracil are most commonly used, while the British 'Carbimazole' has only been introduced there during the past year. The trend is to use these drugs for pre-operative preparation although their use as the sole method of curative therapy still has adherents. The first three have been compared for involutional activity. 5-Iodo-2-thiouracil appeared superior and gave less trouble during subsequent surgery. All the compounds are, however, associated with toxic reactions (4–8 per cent). It may be mentioned in this connexion that one of the advantages of 'Carbimazole' is its comparatively low toxicity.

The mode of action of anti-thyroid drugs has been investigated by Rimington. Recent work shows that where thiol $\rightleftharpoons$ thione tautomerism is possible, involving carbon and nitrogen, compounds exist mainly in the thione form (hydrogen on nitrogen not on sulphur); configuration may be 'fixed', however, by alkylation. Using 'Neo-mercazole' ('Carbimazole': 1-methyl-3-carbethoxy-2-thioglyoxalone) for standard reference, a series of compounds were compared including derivatives of 3-mercapto-1,2,4-triazole and the alkyl-fixed thiol and thione form corresponding to 'Neo-mercazole' itself, namely, 1-methyl-3-ethylglyoxaline-2-thione and 2-ethylmercapto-1-methylglyoxoline. None was as potent an anti-thyroid in rats as 'Neo-mercazole' and the thione configuration appeared to be that responsible for anti-thyroid action. Measurement of the inhibitory effect of these drugs upon a horseradish peroxidase system *in vitro* showed no correlation with anti-thyroid activity.

Mayberry and Astwood have used propylthiouracil to study the intrathyroidal metabolism of iodine in rats. The distribution of iodine-131 in controls 24 hr. after dosing was triiodothyronine 2·6 per cent, thyroxine 21·2 per cent, iodide 2·7 per cent, monoiodotyrosine 25·2 per cent, and diiodotyrosine 42·4 per cent, and these proportions varied little during six days while 53 per cent of the iodine-131 left the gland. In the propylthiouracil-treated group, 92 per cent of activity left the gland in the same time, while the proportion of thyroxine steadily diminished. If recycling of iodine-131 was prevented by a large dose of iodide following the isotope, rate of loss of iodine-131 was only slightly greater than in the controls and the distribution was similar except for a slow drop in monoiodotyrosine. These results suggest that propylthiouracil not only blocks iodination but may also inhibit coupling of iodotyrosines.

The lipid metabolism of the thyroid has been investigated using phosphorus-32. Experiments on rats of depletion of sialic acid, iodine-131 and iodine-127 from the gland indicate that the concentration of the former affords a measure of the thyroglobulin content. Histochemical methods have been used in investigations of prolonged dietary iodine deficiency and of normal and pathological glands. Lindsay and Jenks studied a number of dehydrogenases, diphosphopyridine nucleotide and triphosphopyridine nucleotide diaphorases, monoamine and cytochrome oxidases and found most of these enzymes increased in animals treated with propylthiouracil, but greatly decreased after hypophysectomy or thyroid feeding. Tricarboxylic acid cycle enzymes are present in thyroid glands, but in lower concentrations than in sheep liver (Dumont). They are not inhibited by anti-thyroid drugs and are raised in glands from treated thyrotoxicosis patients. Blood pyruvic acid is high in toxic goitre but normal in non-toxic goitre (Gasiorowski). It remained high after attainment of the euthyroid state.

The firmness of binding of thyroxine in sera has been measured by determining the proportion held back on a suitable resin; enhanced binding is found in myxœdema, after propylthiouracil and in pregnancy but weak binding in hyperthyroidism (Mitchell *et al.*). Attention was, however, directed by Hamolsky *et al.* to the effects of factors such as carbon dioxide tension, buffers and *p*H on thyroxine binding in sera. At *p*H 8·6 an irreversible increase in binding occurs. The pattern of thyroxine binding in normal and pathological conditions has been the subject of several investigations. The pre-albumin shows a greater elective affinity for triiodothyronine than for thyroxine (Andreoli *et al.*).

The discovery of triiodothyronine has turned attention to the deiodinating enzymes and the metabolism of the thyroid hormones. Thus, Lissitzky *et al.* reported that thyroxine bound to specific binding protein is protected from deiodination and that in cells there is competition for thyroxine between deiodinase and thyroxine bound protein.

The tadpole has long been used for the study of thyroxine. With its development into a frog, concomitant alterations occur in responsiveness to thyroid hormone and the manner or rate at which it is metabolized (Galton and Ingbar). The results presented are consistent with, but do not prove, the hypothesis that hormonal response is linked to hormonal degradation. The fate of the doubly labelled sulphuric ester of triiodothyronine in the rat is rapid hydrolysis followed by deiodination. It appears to be either a storage or transport form of the hormone (Roche *et al.*). Radioactive 'Triac' and 'Tetrac', the acetic acid analogues of triiodothyronine and thyroxine, respectively, are found by Green and Ingbar to be metabolized differently in man.

Peripheral biochemical anomalies as well as thyroidal disturbances are thought to be present in sporadic cretinism from studies by Klein of the half-value times of thyroxine metabolism.

The relationship of pituitary to thyroid function has been studied by Becker *et al.* Patients with active or inactive Graves's disease did not show an immediate decrease of thyroid function following total hypophysectomy.

One of the most difficult conditions commonly associated with thyrotoxicosis to understand, and also one of the most unpredictable in its course, is exophthalmos. A number of interesting papers were read on the subject. Bartels and Irie showed, by studying patients suffering from severe progressive exophthalmos, that there was no close relationship between the development of the condition and the functional state of the thyroid or the type of treatment given for hyperthyroidism. Hitherto the course, degree and severity of exophthalmos have often been

regarded as being influenced by the type and extent of the treatment offered for thyrotoxicity. A significant minority of patients developed exophthalmos before hyperthyroidism, and in five cases of severe exophthalmos no hyperthyroidism was noted at any time.

Dobyns described the use of fish (*Fundulus heteroclitus*) for the measurement of the level of an exophthalmos-producing substance in serum. Only in patients with active, progressive exophthalmos was exophthalmos-producing substance clearly demonstrable. Condliffe *et al.* provided evidence, from work with ion-exchange chromatography, that thyroid-stimulating hormone and an exophthalmos-producing substance are separate entities.

Contributions to our knowledge of the relationship between pituitary and thyroid activity, as well as a further understanding of those substances circulating in the blood stream which affect the activity of the thyroid gland, both in health and disease, were made by a number of authors. Two important papers (Purves and Adams, and J. M. McKenzie) described an abnormal thyroid-stimulating agent present in the blood of hyperthyroid persons. It appears not to be present in normal persons; the substance differs from normal thyrotrophin, for example, in the duration of its effect on the thyroid of guinea pigs and mice. It is active far longer than thyroid-stimulating hormone. The substance is active in hypophysectomized animals, thus demonstrating that it acts directly on the thyroid. The amount in serum appears to be correlated more closely with the degree of exophthalmos present than the severity of hyperthyroidism. Halmi *et al.* showed that thyroid-stimulating hormone stimulates rapidly the output of iodide from the thyroid, but the uptake of iodide more slowly.

El Kabir reports a reliable assay method for thyroid-stimulating hormone based on release of iodine-131 in incubated guinea pig thyroid slices. Generally speaking, thyroid-stimulating hormone values were high in patients with thyrotoxicosis and untreated primary myxœdema, whereas in exophthalmic ophthalmoplegia the values did not differ appreciably from normal.

Hellman *et al.* pointed out that apart from the differences in thyroxine-levels to be found in myxœdema and hyperthyroidism, there were also profound differences in the metabolism of androgens. If the thyroid dysfunction is corrected, disturbances in the androgens return to normal. Androsterone, of which low levels are found in hypothyroidism and high levels in hyperthyroidism, can be shown to produce to some extent the actions of thyroxine itself (thyromimetic effect).

No significant thyroxine formation was found by Taurog *et al.* in thyroidectomized rats. On the other hand, large daily injections of iodide had a stimulatory effect on growth. Since no thyroxine can be detected in the plasma, the possibility must be considered that iodide itself may have a thyroxine-like effect on tissues when given in high concentrations.

The connexion between serum cholesterol-levels, hyperthyroidism, hypothyroidism and the incidence of myocardial infarction has fascinated many, and a number of papers were devoted to these subjects.

One of the most interesting concepts which has arisen in recent years in connexion with the etiology of disease is that of auto-immunization, namely, the production by the body of antibodies against one of its own tissue components. That this could be a mechanism has often been suspected, but not clearly demonstrated, until Doniach and Roitt's work on Hashimoto's thyroiditis. Positive serological reactions can be obtained with the serum of such patients. Trotter and Belyavin observed complement fixation reactions between thyroid extracts and sera from patients of nearly all cases of Hashimoto's thyroiditis. The antigen is probably derived from the thyroid cells and appears to reside in the microsome fraction. Most cases of spontaneous myxœdema and about one-third of patients with thyrotoxicosis afford serum with a relatively low titre, as do occasional cases with non-toxic goitre, thyroid carcinoma or normal subjects. This cellular antigen can be detected in extracts of all types of thyroid, but is most abundant in thyrotoxic glands. Fixation of complement by the antigen and its corresponding antibody may be prevented by an inhibitory factor. The serum from patients with Hashimoto's disease commonly contains antibodies also against thyroglobulin. These are demonstrable by precipitation reactions and are distinct from those to the 'cellular antigen'.

A striking objective demonstration of the cytotoxicity of Hashimoto's sera was presented in a film by Pulvertaft *et al.* Primary cultures of human thyroid cells put up in fresh Hashimoto's serum showed few, if any, surviving cells at 18 hr. Substitution of Hashimoto's serum for normal serum in an 18-hr. old culture was followed by immediate darkening of the filamentous mitochondria and their gradual dissolution followed by rapid death of the cell. On the other hand, cultures grown for 36 hr. appeared to remain unaffected. The factor in Hashimoto's serum is thermolabile and specific; it does not kill all cells in a dense culture. Somewhat conflicting evidence was presented by Irvine, who argues that Hashimoto humoral antibodies are of secondary etiological importance. He considers that the basic pathology of Hashimoto's disease may be damage to the basement membrane, possibly due to cell-bound antibodies. Humoral antibodies, secondary to the escape of colloid, would then be an effect, rather than a cause, of the disease. However, since serological reactions are frequently demonstrable in thyroid disease, even in a small percentage of cases of unequivocal thyrotoxicosis according to Alexander *et al.*, and since some patients without Hashimoto's disease have a few clinical features of thyroid over-activity, screening tests for Hashimoto's thyroiditis should always be undertaken.

Two papers were presented in which the incidence of cancer was related to the use of radioactivity therapeutically. Winship and Rosvoll discussed an attempt which had been made over twelve years to examine the past history of children who, prior to the age of fifteen years, developed cancer of the thyroid. Where it has been possible to interrogate the parents of the children very fully, in 81 per cent of the cases there was a history of irradiation having been given therapeutically for a variety of reasons. Commonly, X-ray therapy had been given to try to treat an enlarged thymus. Sometimes similar treatment had been given for enlarged tonsils and adenoids; in others, for hæmangiomata and nævi. The latent period for the development of malignancy appears to be 7–12 years, and in most cases 400–700 r. had been given. The most common type of carcinoma encountered was the papillary type. Another investigation of a not dissimilar character was reported by Pochin. Careful analysis of the actual incidence of

leukæmia in patients treated with radioactive iodine for cancer of the thyroid, when compared with the incidence of the disease in the healthy population at large, suggests that leukæmia may have to be regarded as a calculated risk (even if only a small one) when this treatment is used for thyroid cancer. Pochin, however, suggested that when smaller dosages are given for the treatment of thyrotoxicosis, the present known incidence of leukæmia does not appear to be greater than that which could have been said to have arisen by chance. Nevertheless, it is clearly desirable to watch this situation carefully and to extend observation over a longer period.

Ackerman *et al.* reported a simple and accurate test for the diagnosis of thyroid cancer. This consists of giving orally 500 mc. of phosphorus-32. Twenty-four hours later, multiple counts are taken of the radioactivity from suspicious nodules. In six cases uptake of phosphorus-32 was increased markedly. These were afterwards shown to be malignant tumours. It was very interesting to find that one case of Hashimoto's disease also suggested malignancy by this test. Thirty-four negative tests were produced and in all those operated upon (22), except one, benign tumours were diagnosed.

It is twenty-two years since the last International Goitre Conference, and although striking advances in both knowledge and technique have occurred during this time, it will be apparent that many fundamental problems still remain unresolved.

The late Edwin Ramsdell had prepared an address which was read at the opening of the conference. In it he reminded the members that at the third conference there had been no mention even of anti-thyroid drugs, let alone of radioactive isotopes. How completely the position has changed will be evident from the wide compass of topics dealt with in 1960.

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[1] Astwood, E. B., *et al.*, *J. Biol. Chem.*, **181**, 121 (1949).
[2] Bachelard, H. S., and Trikojus, V. M., *Nature*, **185**, 80 (1960).
[3] Glock, G. E., *Nature*, **154**, 460 (1944).

THE BRITISH COMPUTER SOCIETY

HARROGATE MEETING

SOME 400 delegates attended the second annual conference of the British Computer Society, held at Harrogate during July 4–7. The president, Dr. M. V. Wilkes, noted with satisfaction that the Society, with one annual meeting behind it, was indeed flourishing.

In his opening address, Dr. Wilkes announced the formation of an International Federation of Information Processing Societies, in which the British Computer Society would represent the United Kingdom. The Federation has elected its secretary-treasurer (A. Speiser, Switzerland), president (I. Auerbach, United States) and vice-president (A. Walther, Germany), and has announced that its next conference will be in Munich in September 1962.

Dr. Wilkes referred to the activities of the publication committees of the British Computer Society, and especially to the technical committees on automatic programming. He thought that scientific auto-coding was now generally accepted, but that the break-through in auto-code language for commercial applications, the results of which could be devastating, was still to come. One of the most important current problems was that of data-transmission, and he compared the rather slow teleprinter circuit, with difficult checking facilities, with the telephone circuit with forward error-detecting codes and automatic repeat when necessary. An interesting point was that 100 per cent accuracy is not essential, the aim being to make the transmission of information as accurate as any further processing thereof. He envisaged the less-pecunious universities ringing round to their more fortunate brethren, sending their problems by telephone to the fastest and cheapest service. Again, however, he warned that the solution of the problem, though imminent, was not yet effected.

The second session discussed a common computer language. C. Strachey (formerly of the National Research Development Corporation) outlined the problems arising in the construction of such language and its advantages to programmers, and mentioned important advances made by the United States in the technique of 'list processing'. He made a plea for humans to regard their time as valuable, and to refrain from relapsing into slavery to the machine. R. Brooker (University of Manchester) spoke in technical terms of some recent work in constructing translating routines, carried out at Manchester, for any 'computer-oriented' language, and reported success with regard to the autocodes of *Pegasus* and *Mercury*. These methods apparently need a machine with a fairly large store, though K. Tocher (United Steel) reported success in devising restricted autocodes for smaller machines.

Business applications also have their auto language, and R. Paine (I.C.T.) outlined the desirable features of such a language and some attempts made to meet them. He warned that management cannot yet dispense with its programming staff, that the language of the accountant is not yet that of the computing machine, and envisaged the evolution of long-hand and short-hand versions of the language. This contribution included the comments that a computer conference might be described as a "meeting of contiguous word-noises", and that machine manufacturers' advertisements of business computer autocodes rarely err on the side of modesty.

At about this stage one notes with sorrow the transformation of certain features of the English language, and too often its mutilation which, in these vulgar times, seems to accompany the development of any new scientific field, and in which computer terminology is second to none. One finally applauded the question, "What exactly, please, is a programmer ?", and listened with regretful admiration to the chairman's "Since it is now time for coffee, I shall have to treat that question as rhetorical !"

The next session was also concerned with language and general-purpose programmes, this time for market research (A. Douglas, University of Leeds, and R. Cook, Elliott Bros.), which provided facilities