

that these special stains proceed from the brown pigment in the cells of the Malpighi layer and internal epithelial hair sheath in the original skin. This pigment becomes fixed by mineral matter so that decomposition in the limes is resisted.

The author finds that the common factor in the stains examined is the presence of traces of iron. The persistence of the connective elements, especially the nuclei and epithelial tissues, is proved, and the very slight changes that take place in the connective tissue lead the writer to conclude that bacteria play a very small part in the production of the stains he examined.

In this paper M. Abt, for the stains he has examined, takes up practically the opposite view to that enunciated by Becker, who claims that many of the salt stains are largely caused by bacterial action.

The experiments carried out by M. Abt have been carefully performed, and the hypothesis he draws from the results obtained on the stains he has examined appear to be conclusive. The paper is extremely well illustrated by coloured photographs of prepared sections of normal and salt-stained skin and leather which are very clear, and are much more defined than the illustrations usually given in this type of work; in fact, these microphotographs are from magnificent sections, and are beautifully reproduced in the article. They are the finest reproductions of the structure of the hide and skin that have been published in recent times.

M. Abt's work on this subject is of great importance to leather technologists, and, while the author does not claim to have solved all the various kinds of salt stains, he has certainly solved a portion of the difficult problem, and appears to have definitely proved that what the tanner and leather-dresser call salt stains may originate from more than one cause, and may under different conditions vary in appearance and effect upon the skin.

The paper shows that M. Abt has carried out a very careful and systematic investigation, and it is a most valuable contribution to the elucidation of this problem, but in spite of this the subject is still by no means exhausted, and we venture to hope that M. Abt will investigate some other forms of salt stains which he has not yet dealt with. Although the author has undoubtedly clearly proved the cause, traced the history, and shown the effect of certain forms of salt stains, he has not yet described any practical method of avoiding this economic waste which is so vital to the tanners of calf and other similar leathers, but the paper brings us one step nearer this goal.

J. G. P.

THE BRITISH ASSOCIATION AT BIRMINGHAM.

SECTION H.

ANTHROPOLOGY.

OPENING ADDRESS BY SIR RICHARD C. TEMPLE, BART.,
C.I.E., PRESIDENT OF THE SECTION.

Administrative Value of Anthropology.

THE title of the body of which those present at this meeting form a section is, as all my hearers will know, the British Association for the Advancement of Science, and it seems to me therefore that the primary duty of a sectional President is to do what in him lies for the time being, to forward the work of his section. This may be done in more than one way: by a survey of the work done up to date and an appreciation of its existing position and future prospects, by an address directly forwarding it in some particular point or aspect, by considering its applicability to what is called

the practical side of human life. The choice of method seems to me to depend on the circumstances of each meeting, and I am about to choose the last of those above mentioned, and to confine my address to a consideration of the administrative value of anthropology because the locality in which we are met together and the spirit of the present moment seem to indicate that I shall best serve the interests of the anthropological section of the British Association by a dissertation on the importance of this particular science to those who are or may hereafter be called upon to administer the public affairs of the lands in which they may reside.

I have to approach the practical aspect of the general subject of anthropology under the difficulty of finding myself once more riding an old hobby, and being consequently confronted with views and remarks already expressed in much detail. But I am not greatly disturbed by this fact, as experience teaches that the most effective way of impressing ideas, in which one believes, on one's fellow man is to miss no opportunity of putting them forward, even at the risk of repeating what may not yet have been forgotten. And as I am convinced that the teachings of anthropologists are of practical value to those engaged in guiding the administration of their own or another country, I am prepared to take that risk.

Anthropology is, of course, in its baldest sense the study of mankind in all its possible ramifications, a subject far too wide for any one science to cover, and therefore the real point for consideration on such an occasion as this is not so much what the students of mankind and its environments might study if they chose, but what the scope of their studies now actually is, and whither it is tending. I propose, therefore, to discuss the subject in this limited sense.

What, then, is the anthropology of to-day that claims to be of practical value to the administrator? In what directions has it developed?

Perhaps the best answer to these questions is to be procured from our own volume of "Notes and Queries on Anthropology," a volume published under the arrangements of the Royal Anthropological Institute for the British Association. This volume of "Notes and Queries" has been before the public for about forty years, and is now in the fourth edition, which shows a great advance on its predecessors and conforms to the stage of development to which the science has reached up to the present time.

The object of the "Notes and Queries" is stated to be "to promote accurate anthropological observation on the part of travellers including all local observers) and to enable those who are not anthropologists themselves to supply information which is wanted for the scientific study of anthropology at home." So, in the heads under which the subject is considered in this book, we have exhibited to us the entire scope of the science as it now exists. These heads are (1) physical anthropology, (2) technology, (3) sociology, (4) arts and sciences. It is usual, however, nowadays to divide the subject into two main divisions—physical and cultural anthropology.

Physical anthropology aims at obtaining "as exact a record as possible of the structure and functions of the human body, with a view to determining how far these are dependent on inherited and racial factors, and how far they vary with environment." This record is based on two separate classes of physical observation: firstly on descriptive characters, such as types of hair, colour of the eyes and skin, and so on, and actual measurement; and secondly on attitudes, movements, and customary actions. By the combined study of observations on these points physical heredity is ascertained, and a fair attribution of the race or races to which individuals or groups belong can be arrived at.

But anthropology, as now studied, goes very much

further than inquiry into the physical structure of the human races. Man, "unlike other animals, habitually reinforces and enhances his natural qualities and force by artificial means." He does, or gets done for him, all sorts of things to his body to improve its capacities or appearance, or to protect it. He thus supplies himself with sanitary appliances and surroundings, with bodily ornamentation and ornaments, with protective clothing, with habitations and furniture, with protection against climate and enemies, with works for the supply of water and fire, with food and drink, drugs and medicine. And for these purposes he hunts, fishes, domesticates animals, and tills the soil, and provides himself with implements for all these, and also for defence and offence, and for the transport of goods, involving working in wood, earth, stones, bones, shells, metals and other hard materials, and in leather, strings, nets, basketry, matting and weaving, leading him to what are known as textile industries. Some of this work has brought him to mine and quarry, and to employ mechanical aids in the shape of machinery, however rude and simple. The transport of himself and his belongings by land and water has led him to a separate set of industries and habits: to the use of paths, roads, bridges, and halting places, of trailers, sledges, and wheeled vehicles; to the use of rafts, floats, canoes, coracles, boats, and ships, and the means of propelling them, poles, paddles, oars, sails, and rigging. The whole of these subjects is grouped by anthropologists under the term technology, which thus becomes a very wide subject, covering all the means by which a people supplies itself with the necessities of its mode of livelihood.

In order to carry on successfully what may be termed the necessary industries or even to be in a position to cope with them, bodies of men have to act in concert, and this forces mankind to be gregarious, a condition of life that involves the creation of social relations. To understand, therefore, any group of mankind, it is essential to study sociology side by side with technology. The subjects for inquiry here are the observances at crucial points in the life-history of the individual—birth, puberty, marriage, death, daily life, nomenclature, and so on; the social organisation and the relationship of individuals. On these follow the economics of the social group, pastoral, agricultural, industrial, and commercial, together with conceptions as to property and inheritance (including slavery), as to government, law and order, politics and morals; and finally the ideas as to war and the external relations between communities.

We are still, however, very far from being able to understand in all their fulness of development even the crudest of human communities without a further inquiry into the products of their purely mental activities, which in the "Notes and Queries" are grouped under the term "Arts and Sciences." Under this head are to be examined, in the first place, the expression of the emotions to the eye by physical movements and conditions, and then by gestures, signs and signals, before we come to language, which is primarily expressed by the voice to the ear, and secondarily to the eye in a more elaborate form by the graphic arts—pictures, marks and writing. Man further tries to express his emotions by what are known as the fine arts; that is by modifying the material articles which he contrives for his livelihood in a manner that makes them represent to him something beyond their economic use—makes them pleasant, representative or symbolical—leading him on to draw, paint, enamel, engrave, carve and mould. In purely mental efforts this striving to satisfy the artistic or æsthetic sense takes the form of stories, proverbs, riddles, songs, and music. Dancing, drama, games, tricks and amusements are other manifestations of the same

effort, combining in these cases the movements of the body with those of the mind in expressing the emotions.

The mental processes necessary for the expression of his emotions have induced man to extend his powers of mind in directions now included in the term "abstract reasoning." This has led him to express the results of his reasoning by such terms as reckoning and measurement, and to fix standards for comparison in such immaterial but all essential matters as enumeration, distance, surface, capacity, weight, time, value, and exchange. These last enable him to reach the idea of money, which is the measurement of value by means of tokens, and represents perhaps the highest economic development of the reasoning powers common to nearly all mankind.

The mental capacities of man have so far been considered only in relation to the expression of the emotions and of the results of abstract reasoning; but they have served him also to develop other results and expressions equally important, which have arisen out of observation of his surroundings, and have given birth to the natural sciences: astronomy, meteorology, geography, topography, and natural history. And further they have enabled him to memorise all these things by means of records, which in their highest form have brought about what is known to all of us as history, the bugbear of impulsive and shallow thinkers, but the very backbone of all solid opinion.

The last and most complex development of the mental processes, dependent upon all the others according to the degree to which they themselves have been developed in any given variety of mankind, is, and has always been, present in every race or group on record from the remotest to the most recent time in some form or other and in a high degree. Groups of men observe the phenomena exhibited by themselves or their environment, and account for them according to their mental capacity as modified by their heredity. Man's bare abstract reasoning, following on his observation of such phenomena, is his philosophy, but his inherited emotions influence his reasoning to an almost controlling extent and induce his religion, which is thus his philosophy or explanation of natural phenomena as effected by his hereditary emotions, producing that most wonderful of all human phenomena, his belief. In the conditions, belief, faith, and religion must and do vary with race, period, and environment.

Consequent on the belief, present or past of any given variety of mankind, there follow religious practices (customs as they are usually called) based thereon, and described commonly in terms that are familiar to all, but are nevertheless by no means even yet clearly defined: theology, heathenism, fetishism, animism, totemism, magic, superstition, with soul, ghost, and spirit, and so on, as regards mental concepts; worship, ritual, prayer, sanctity, sacrifice, taboo, &c., as regards custom and practice.

Thus have the anthropologists, as I understand them, shown that they desire to answer the question as to what their science is, and to explain the main points in the subject of which they strive to obtain and impart accurate knowledge based on scientific inquiry: that is, on an inquiry methodically conducted on lines which experience has shown them will lead to the minimum of error in observation and record.

I trust I have been clear in my explanation of the anthropologists' case, though in the time at my disposal I have been unable to do more than indicate the subjects they study, and have been obliged to exercise restraint and to employ condensation of statement to the utmost extent that even a long experience in exposition enables one to achieve. Briefly, the science

of anthropology aims at such a presentation and explanation of the physical and mental facts about any given species or even group of mankind as may correctly instruct those to whom the acquisition of such knowledge may be of use. In this instance, as in the case of the other sciences, the man of science endeavours to acquire and pass on abstract knowledge, which the man of affairs can confidently apply in the daily business of practical life.

It will have been observed that an accurate presentation of the physical and mental characteristics of any species of mankind which it is desired to study is wholly dependent on accurate inquiry and report. Let no one suppose that such inquiry is a matter of instinct or intuition, or that it can be usefully conducted empirically or without due reference to the experiences of others; in other words, without sufficient preliminary study. So likely indeed are the uneducated in such matters to observe and record facts about human beings inaccurately, or even wrongly, that about a fourth part of the "Notes and Queries" is taken up with showing the inquirer how to proceed, and in exposing the pitfalls into which he may unconsciously fall. The mainspring of error in anthropological observation is that the inquirer is himself the product of heredity and environment. This induces him to read himself, his own unconscious prejudices and inherited outlook on life, into the statements made to him by those who view life from perhaps a totally different and incompatible standpoint. To the extent that the inquirer does this, to that extent are his observations and report likely to be inaccurate and misleading. To avoid error in this respect, previous training and study are essential, and so the "Notes and Queries on Anthropology," a guide compiled in cooperation by persons long familiar with the subject, is as strong and explicit on the point of how to inquire as on that of what to inquire about.

Let me explain that these statements are not intended to be taken as made *ex cathedra*, but rather as the outcome of actual experience of mistakes made in the past. Time does not permit me to go far into this point, and I must limit myself to the subject of sociology for my illustration. If a man undertakes to inquire into the social life of a people or tribe as a subject apart, he is committing an error, and his report will almost certainly be misleading. Such an investigator will find that religion and technology are inextricably mixed up with the sociology of any given tribe, that religion intervenes at every point not only of sociology but also of language and technology. In fact, just as in the case of all other scientific research, the phenomenon observable by the anthropologist are not the result of development along any single line alone, but of a progression in a main general direction, as influenced, and it may be even deflected, by contact and environment.

If again the inquirer neglects the simple but essential practice of taking notes, not only fully, but also immediately or as nearly so as practicable, he will find that his memory of facts, even after a short time, has become vague, inexact, and incomplete, which means that reports made from memory are more likely to be useless than to be of any scientific value. If voluntary information or indirect and accidental corroboration are ignored, if questions are asked and answers accepted without discretion, if exceptions are mistaken for rules, then the records of an inquiry may well mislead and thus become worse than useless. If leading or direct questions are put without due caution, and if the answers are recorded without reference to the natives' and not the inquirer's mode of classifying things, crucial errors may easily arise. Thus, in many parts of the world, the term "mother" includes all female relatives of the past or passing generation,

and the term "brother" the entire brotherhood. Such expressions as "brother" and "sister" may and do constantly connote relationships which are not recognised at all amongst us. The word "marriage" may include "irrevocable betrothal," and so on; and it is very easy to fall into the trap of the mistranslation of terms of essential import, especially in the use of words expressing religious conceptions. The conception of godhead has for so long been our inheritance that it may be classed almost as instinctive. It is nevertheless still foreign to the instincts of a large portion of mankind.

If also, when working among the uncultured, the inquirer attempts to ascertain abstract ideas, except through concrete instances, he will not succeed in his purpose for want of representative terms. And lastly, if he fails to project himself sufficiently into the minds of the subjects of inquiry, or to respect their prejudices, or to regard seriously what they hold to be sacred, or to keep his countenance while practices are being described which to him may be disgusting or ridiculous—if indeed he fails in any way in communicating to his informants, who are often super-sensitively suspicious in such matters, the fact that his sympathy is not feigned—he will also fail in obtaining the anthropological knowledge he is seeking. In the words of the "Notes and Queries" on this point, "Nothing is easier than to do anthropological work of a certain sort, but to get to the bottom of native customs and modes of thought, and to record the results of inquiry in such a manner that they carry conviction, is work which can be only carried out properly by careful attention."

The foregoing considerations explain the scope of our studies and the requirements of the preliminary inquiries necessary to give those studies value. The further question is the use to which the results can be put. The point that at once arises here for the immediate purpose is that of the conditions under which the British Empire is administered. We are here met together to talk scientifically, that is, as precisely as we can: and so it is necessary to give a definition to the expression "Imperial Administration," especially as it is constantly used for the government of an empire, whereas in reality it is the government that directs the administration. In this address I use the term "administration" as the disinterested management of the details of public affairs. This excludes politics from our purview, defining that term as the conduct of the government of a country according to the opinions or in the interests of a particular group or party.

Now in this matter of administration the position of the inhabitants of the British Isles is unique. It falls to their lot to govern, directly or indirectly, the lives of members of nearly every variety of the human race. Themselves Europeans by descent and intimate connection, they have a large direct interest in every other general geographical division of the world and its inhabitants. It is worth while to pause here for a moment to think, and to try and realise, however dimly, something of the task before the people of this country in the government and control of what are known as the subject races.

For this purpose it is necessary to throw our glance over the physical extent of the British Empire. In the first place, there are the ten self-governing components of the Dominion of Canada and that of Newfoundland in North America, the six colonial States in the Commonwealth of Australia, with the Dominion of New Zealand in Australasia, and the four divisions of the Union of South Africa. All these may be looked upon as indirectly administered portions of the British Empire. Then there is the mediatised government of Egypt, with its appanage the directly British administered Sudan, which alone covers about a

million square miles of territory in thirteen provinces, in northern Africa. These two areas occupy, as it were, a position between the self-governing and the directly-governed areas. Of these, there are in Europe Malta and Gibraltar, Cyprus being officially included in Asia. In Asia itself is the mighty Indian Empire, which includes Aden and the Arabian coast on the west and Burma on the east, and many islands in the intervening seas, with its fifteen provinces and some twenty categories of native states "in subordinate alliance," that is, under general Imperial control. To these are added Ceylon, the Straits Settlements, and the Malay States, federated or other, North Borneo and Sarawak, and in the China Seas Hong Kong and Wei-hai-wei. In South Africa we find Basutoland, Bechuanaland, and Rhodesia; in British West Africa, Gambia, the Gold Coast, Sierra Leone, and Nigeria; in eastern and Central Africa, Somaliland, the East Africa Protectorate, Uganda, Zanzibar, and Nyassaland; while attached to Africa are the Mauritius, Seychelles, Ascension, and St. Helena. In Central and South America are Honduras and British Guiana, and attached to that continent the Falkland Islands, and also Bermuda and the six colonies of British West Indies. In the Pacific Ocean are Fiji, Papua, and many of the Pacific Islands.

I am afraid that once more during the course of this exposition I have been obliged to resort to a concentration of statement that is almost bewildering. But let that be. If one is to grapple successfully with a large and complex subject, it is necessary to try and keep before the mind, so far as possible, not only its magnitude, but the extent of its complexity. This is the reason for bringing before you, however briefly and generally, the main geographical details of the British Empire. The first point to realise on such a survey is that the mere extent of such an Empire makes the subject of its administration an immensely important one for the British people.

The next point for consideration and realisation is that an empire, situated in so many widely separated parts of the world, must contain within its boundaries groups of every variety of mankind, in such numerical strength as to render it necessary to control them as individual entities. They do not consist of small bodies lost in a general population, and therefore negligible from the administrator's point of view, but of whole races and tribes or of large detachments thereof.

These tribes of mankind profess every variety of religion known. They are Christians, Jews, Mahomedans, Hindus, Buddhists, Jains, Animists, and, to use a very modern expression, Animatists, adherents of main religions followed by an immense variety of sects, governed, however loosely, by every species of philosophy that is or has been in fashion among groups of mankind, and current in every stage of development, from the simplest and most primitive to the most historical and complex. One has to bear in mind that we have within our borders the Andamanese, the Papuan, and the Polynesian, as well as the highly civilised Hindu and Chinese, and that not one of these, nor indeed of many other peoples, has any tradition of philosophy or religion in common with our own; their very instincts of faith and belief following other lines than ours, the prejudices with which their minds are saturated being altogether alien to those with which we ourselves are deeply imbued.

The subjects of the British King-Emperor speak between them most of the languages of the world, and certainly every structural variety of human speech has its example somewhere in the British Empire. A number of these languages is still only in the process of becoming understood by our officials and other residents among their speakers, and let there be no

mistake as to the magnitude of the question involved in the point of language alone in British Imperial regions. A man may be what is called a linguist. He may have a working knowledge of the main European languages and of the great Oriental tongues—Arabic, Persian, and Hindustani—which will carry him very far indeed among the people—in a sense, in fact, from London to Calcutta—and then, without leaving that compact portion of the British possessions known as the Indian Empire, with all its immense variety of often incompatible subordinate languages and dialects, he has only to step across the border into Burma and the Further East to find himself in a totally different atmosphere of speech, where not one of the sounds, not one of the forms, not one of the methods, with which he has become familiarised is of any service to him whatever. The same observation will again be forced on him if he transfers himself thence to southern Africa or to the Pacific Ocean. Let him wander amongst the North American Indians and he will find the linguistic climate once more altogether changed.

Greater Britain may be said to exhibit all the many varieties of internal social relations that have been set up by tribes and groups of mankind—all the different forms of family and general social organisation, of reckoning kinship, of inheritance and control of the possession of property, of dealing with the birth of children and their education and training, physical, mental, moral, and professional, in many cases by methods entirely foreign to British ideas and habits. For instance, infanticide as a custom has many different sources of origin.

Our fellow-subjects of the King follow, somewhere or other, all the different notions and habits that have been formed by mankind as to the relations between the sexes, both permanent and temporary, as to marriage and to what have been aptly termed supplementary unions. And finally, their methods of dealing with death and bringing it about, of disposing of the dead and worshipping them, give expression to ideas, which it requires study for an inhabitant of Great Britain to appreciate or understand. I may quote here, as an example, that of all the forms of human head-hunting and other ceremonial murder that have come within my cognisance, either as an administrator or investigator, not one has originated in callousness or cruelty of character. Indeed, from the point of view of the perpetrators, they are invariably resorted to for the temporal or spiritual benefit of themselves or their tribe. In making this remark, I must not be understood as proposing that they should not be put down, wherever that is practicable. I am merely trying now to give an anthropological explanation of human phenomena.

In very many parts of the British Empire, the routine of daily life and the notions that govern it often find no counterparts of any kind in those of the British Isles, in such matters as personal habits and etiquette on occasions of social intercourse. And yet, perhaps, nothing estranges the administrator from his people more than mistakes on these points. It is small matters—such as the mode of salutation, forms of address and politeness, as rules of precedence, hospitality, and decency, as recognition of superstitions, however apparently unreasonable—which largely govern social relations, which no stranger can afford to ignore, and which at the same time cannot be ascertained and observed correctly without due study.

The considerations so far urged to-day have carried us through the points of the nature and scope of the science of anthropology, the mental equipment necessary for the useful pursuit of it, the methods by which it can be successfully studied, the extent and nature

of the British Empire, the kind of knowledge of the alien populations within its boundaries required by persons of British origin who would administer the Empire with benefit to the people dwelling in it, and the importance to such persons of acquiring that knowledge.

I now turn to the present situation as to this last point and its possible improvement, though in doing so I have to cover ground that some of those present may think I have already trodden bare. The main proposition here is simple enough. The Empire is governed from the British Isles, and therefore year by year a large number of young men are sent out to its various component parts, and to them must inevitably be entrusted in due course the administrative, commercial, and social control over many alien races. If their relations with the foreign peoples with whom they come in contact are to be successful, they must acquire a working knowledge of the habits, customs, and ideas that govern the conduct of those peoples, and of the conditions in which they pass their lives. All those who succeed find these things out for themselves, and discern that success in administration and commerce is intimately affected by success in social relations, and that that in its turn is dependent on the knowledge they may attain of those with whom they have to deal. They set about learning what they can, but of necessity empirically, trusting to keenness of observation, because such self-tuition is, as it were, a side issue in the immediate and imperative business of their lives. But, as I have already said elsewhere, the man who is obliged to obtain the requisite knowledge empirically, and without any previous training in observation, is heavily handicapped indeed in comparison with him who has already acquired the habit of right observation, and, what is of much more importance, has been put in the way of correctly interpreting his observations in his youth.

To put the proposition in its briefest form: in order to succeed in administration a man must use tact. Tact is the social expression of discernment and insight, qualities born of intuitive anthropological knowledge, and that is what it is necessary to induce in those sent abroad to become eventually the controllers of other kinds of men. What is required, therefore, is that in youth they should have imbibed the anthropological habit, so that as a result of having been taught how to study mankind, they may learn what it is necessary to know of those about them correctly, and in the shortest practicable time. The years of active life now unavoidably wasted in securing this knowledge, often inadequately and incorrectly even in the case of the ablest, can thus be saved, to the incalculable benefit of both the governors and the governed.

The situation has, for some years past, been appreciated by those who have occupied themselves with the science we are assembled here to promote, and several efforts have been made by the Royal Anthropological Institute and the Universities of Oxford, Cambridge, and London, at any rate to bring the public benefits accruing from the establishment of anthropological schools before the Government and the people of this country.

In 1902 the Royal Anthropological Institute sent a deputation to the Government with a view to the establishment of an official Anthropometric Survey of the United Kingdom, in order to test the foundation for fears, then widely expressed, as to the physical deterioration of the population. In 1909 the institute sent a second deputation to the present Government, to urge the need for the official training in anthropology of candidates for the Consular Service and of the Indian and Colonial Civil Services. There is

happily every reason to hope that the Public Services Commission may act on the recommendations then made. This year (1913) the institute returned to the charge and approached the Secretary of State for India, with a view to making anthropology an integral feature of the studies of the Oriental Research Institute, to the establishment of which the Government of India had officially proposed to give special attention. The institute has also lately arranged to deal with all questions of scientific import that may come before the newly constituted Bureau of Ethnology at the Royal Colonial Institute, in the hope with its cooperation of eventually establishing a great *desideratum*—an Imperial Bureau of Ethnology. It has further had in hand a scheme for the systematic and thorough distribution of local correspondents throughout the world.

At Oxford, anthropology as a serious study was recognised by the appointment, in 1884, of a reader, who was afterwards given the status of a professor. In 1885, it was admitted as a special subject in the final honours school of natural science. In 1904, a memorandum was drawn up by those interested in the study at the University, advocating a method of systematic training in it, which resulted in the formation of the committee of anthropology in the following year. This committee has established a series of lectures and examinations for a diploma, which can be taken as part of the degree course, but is open to all officers of the public services as well. By these means a school of anthropology has been created at Oxford, which has already registered many students, among whom officers engaged in the administration of the British Colonies in Africa and members of the Indian Civil Service have been included. The whole question has been systematically taken up in all its aspects, the instruction, formal and informal, comprising physical anthropology, psychology, geographical distribution, prehistoric archaeology, technology, sociology, and philology.

At Cambridge, in 1893, there was a recognised lecturer in physical anthropology, an informal office now represented by a lecturer in physical anthropology and a reader in ethnology, regularly appointed by the University. In 1904, as a result of an expedition to Torres Straits, a board of anthropological studies was formed, and a diploma in anthropology instituted, to be granted, not for success in examinations, but in recognition of meritorious personal research. At the same time, in order to help students, among whom were included officials of the African and Indian Civil Services, the Board established lectures on the same subjects as those taught at Oxford. This year, 1913, the University has instituted an anthropological tripos for its degrees on lines similar to the others. The distinguishing feature of the Cambridge system is the prominence given to field work, and this is attracting foreign students of all sorts.

In 1909, joint representations were made by a deputation from the Universities of Oxford and Cambridge to both the India and Colonial Offices, advocating the training of Civil Service candidates and probationers in ethnology and primitive religion.

In 1904, the generosity of a private individual established a lectureship in ethnology in connection with the University of London, which has since developed into a professorship of ethnology with a lectureship in physical anthropology. In the same year the same benefactor instituted a chair of sociology. In 1909 the University established a board of anthropology, and the subject is now included in the curricula for the degrees of the University. In and after 1914, anthropology will be a branch of the science honours degree. The degree course of the future covers both physical and cultural anthropology in regard to

zoology, palæontology, physiology, psychology, archæology, technology, sociology, linguistics, and ethnology. There will also be courses in ethnology with special attention to field work for officials and missionaries, and it is interesting to note that students of Egyptology are already taking a course of lectures in ethnology and physical anthropology.

Though the universities have thus been definite enough in their action where the authority is vested in them, it is needless to say that their representations to Governments have met with varying success, and so far they have not produced much practical result. But it is as well to note here that a precedent for the preliminary anthropological training of probationers in the Colonial Civil Service has been already set up, as the Government of the Sudan has directed that every candidate for its services shall go through a course of anthropology at Oxford or Cambridge. In addition to this, the Sudan Government has given a grant to enable a competent anthropologist from London to run a small scientific survey of the peoples under its administration. The Assam Government has arranged its ethnographical monographs on the lines of the British Association's "Notes and Queries" with much benefit to itself, and it is believed that the Burma Government will do likewise. The Colonial Office has appointed a lecturer in anthropology for East and West Africa, and the Government of India is distributing copies of the anthropological articles in its Imperial Gazetteer to successful candidates for its civil services.

Speaking in this place to such an audience as that before me, and encouraged by what has already been done elsewhere, I cannot think that I can be mistaken in venturing to recommend the encouragement of the study of anthropology to the University of such a city as Birmingham, which has almost unlimited interests throughout the British Empire. For it should be remembered that anthropological knowledge is as useful to merchants *in partibus* in dealing with aliens as to administrators so situated. Should this suggestion bear fruit, and should it be thought advisable some day to establish a school of anthropology in Birmingham, I would also venture to point out that there are two requirements preliminary to the successful formation of almost any school of study. These are a library and a museum *ad hoc*. At Oxford there is a well-known and well-conducted anthropological museum in the Pitt-Rivers collection, and the museum of archæology and ethnology at Cambridge contains collections of the greatest service to the anthropologist. Liverpool is also interesting itself in such matters. The Royal Anthropological Institute is forming a special library, and both that institute and the University of London have the benefit of the splendid collections of the British Museum and of the Horniman Museum readily accessible. The libraries at Oxford and Cambridge are, I need scarcely say, of world-wide fame. At all these places of learning, then, these requisites for this department of knowledge are forthcoming.

It were almost superfluous to state why they are requisites. Every student requires, not only competent teachers to guide him in his particular branch of study, but also a library and a museum close at hand, where he can find the information he wants and the illustration of it. Where these exist, thither it will be found that students will flock. Birmingham possesses peculiar facilities for the formation of both, as the city has all over the Empire its commercial representatives, who can collect the required museum specimens on the spot. The financial labours also of those who distribute these men over Greater Britain, and indeed all over the world, produce the means to create the library

and the school, and their universal interests provide the incentive for securing for those in their employ the best method of acquiring a knowledge of men that can be turned to useful commercial purpose. Beyond these suggestions I will not pursue this point now, except to express a hope that this discourse may lead to a discussion thereon before this meeting breaks up.

Before I quit my subject I would like to be somewhat insistent on the fact that, though I have been dwelling so far exclusively on the business side, as it were, of the study of anthropology, it has a personal side as well. I would like to impress once more on the student, as I have often had occasion to do already, that whether he is studying of his own free will or at the behest of circumstances, there is scarcely any better hobby in existence than this, or one that can be ridden with greater pleasure. It cannot, of course, be mastered in a day. At first the lessons will be a grind. Then, until they are well learnt, they are irksome, but when fullness of knowledge and maturity of judgment are attained, there is, perhaps, no keener sense of satisfaction which human beings can experience than that which is afforded by this study. Its range is so wide, its phases so very many, the interests involved in it so various, that it cannot fail to pleasantly occupy the leisure hours from youth to full manhood, and to be a solace, in some aspect or other, in advanced life and old age.

The processes of discovery in the course of this study are of such interest in themselves that I should wish to give many instances, but I must confine myself now to one or two. The student will find on investigation, for instance, that however childish the reasoning of savages may appear to be on abstract subjects, and however silly some of their customs may seem, they are neither childish nor silly in reality. They are almost always the result of "correct argument from a false premiss"—a mental process not unknown to civilised races. The student will also surely find that savages are not fools where their concrete interests are concerned, as they conceive those interests to be. For example, in commerce, beads do not appeal to savages merely because they are pretty things, except for purposes of adornment. They will only part with articles they value for particular sorts of beads which are to them money, in that they can procure in exchange for them, in their own country, something they much desire. They have no other reason for accepting any kind of bead in payment for goods. On few anthropological points can mistakes be made more readily than on this, and when they are made by merchants, financial disaster can well follow, so that what I have already said elsewhere as to this may bear repetition in part here. Savages in their bargains with civilised man never make one that does not, for reasons of their own, satisfy themselves. Each side, in such a case, views the bargain according to its own interest. On his side, the trader buys something of great value to him, when he has taken it elsewhere, with something of little value to him, which he has brought from elsewhere, and then, and only then, can he make what is to him a magnificent bargain. On the other hand, the savage is more than satisfied, because with what he has got from the trader he can procure from among his own people something he very much covets, which the article he parted with could not have procured for him. Both sides profit by the bargain from their respective points of view, and traders cannot, as a matter of fact, take undue advantage of savages, who, as a body, part with products of little or no value to themselves for others of vital importance, though these last may be of little or none to the civilised trader. The more one dives into recorded bargains, the more clearly one sees the truth of this view.

I have always advocated personal inquiry into the native currency and money, even of pre-British days, of the people amongst whom a Britisher's lot is cast, for the reason that the study of the mental processes that lead up to commercial relations, internal and external, the customs concerned with daily buying and selling, take one more deeply into aliens' habits of mind and their outlook on practical life than any other branch of research. The student will find himself involuntarily acquiring a knowledge of the whole life of a people, even of superstitions and local politics, matters that commercial men, as well as administrators, cannot, if they only knew it, ever afford to ignore. The study has also a great intellectual interest, and neither the man of commerce nor the man of affairs should disregard this side of it if he would attain success in every sense of that term.

Just let me give one instance from personal experience. A few years back a number of ingots of tin, in the form of birds and animals and imitations thereof, hollow tokens of tin ingots, together with a number of rough notes taken on the spot, were handed over to me for investigation and report. They came from the Federated Malay States, and were variously said to have been used as toys and as money in some form. A long and careful investigation unearthed the whole story. They turned out to be surviving specimens of an obsolete and forgotten Malay currency. Bit by bit, by researches into travellers' stories and old records, European and vernacular, it was ascertained that some of the specimens were currency and some money, and that they belonged to two separate series. Their relations to each other were ascertained, and also to the currencies of the European and Oriental nations with whom the Malays of the Peninsula had come in contact. The mint profit in some instances, and in other instances the actual profit European Governments and mercantile authorities, and even native traders, had made in recorded transactions of the past, was found out. The origin of the British, Dutch, and Portuguese money, evolved for trading with the Malays, was disclosed, and several interesting historical discoveries were made; as, for instance, the explanation of the coins still remaining in museums and issued in 1510 by the great Portuguese conqueror, Albuquerque, for the then new Malay possessions of his country, and the meaning of the numismatic plates of the great French traveller Tavernier in the next century. Perhaps the most interesting, and anthropologically the most important, discovery was the relation of the ideas that led up to the animal currency of the Malays to similar ideas in India, Central Asia, China, and Europe itself throughout all historical times. One wonders how many people in these isles grasp the fact that our own monetary scale of 960 farthings to the sovereign, and the native Malay scale of 1,280 cash to the dollar, are representatives of one and the same universal scale, with more than probably one and the same origin out of a simple method of counting seeds, peas, beans, shells, or other small natural constant weights. But the point for the present purpose is that not only will the student find that long practice in anthropological inquiry, and the learning resulting therefrom, will enable him to make similar discoveries, but also that the process of discovery is intensely interesting. Such discoveries, too, are of practical value. In this instance they have taught us much of native habits of thought and views of life in newly acquired possessions which no administrator there, mercantile or governmental, can set aside with safety.

I must not dwell too long on this aspect of my subject, and will only add the following remark. If any of my hearers will go to the Pitt-Rivers Museum at Oxford he will find many small collections record-

ing the historical evolution of various common objects. Among them is a series showing the history of the tobacco pipe, commonly known to literary students in this country as the nargileh and to Orientalists as the hukka. At one end of the series will be found a hollow coconut with an artificial hole in it, and then every step in evolution between that and an elaborate hukka with its long, flexible, drawing-tube at the other end. I give this instance as I contributed the series, and I well remember the eagerness of the hunt in the Indian bazaars and the satisfaction on proving every step in the evolution.

There is one aspect of life where the anthropological instinct would be more than useful, but to which, alas, it cannot be extended in practice. Politics, government, and administration are so interdependent throughout the world that it has always seemed to me to be a pity that the value to himself of following the principles of anthropology cannot be impressed on the average politician of any nationality. I fear it is hopeless to expect it. Were it only possible the extent of the consequent benefit to mankind is at present beyond human forecast, as then the politician could approach his work without that arrogance of ignorance of his fellow-countrymen on all points except their credulity that is the bane of the ordinary types of his kind wherever found, with which they have always poisoned and are still poisoning their minds, mistaking the satisfaction of the immediate temporary interests and prejudices of themselves and comrades for the permanent advantage of the whole people, whom, in consequence, they incontinently misgovern whenever and for so long as their country is so undiscerning as to place them in power.

Permit me, in conclusion, to enforce the main argument of this address by a personal note. It was my fortune to have been partly trained in youth at a university college, where the tendency was to produce men of affairs rather than men of the schools, and only the other day it was my privilege to hear the present master of the college, my own contemporary and fellow-undergraduate, expound the system of training still carried out there. "In the government of young men," he said, "intellect is all very well, but sympathy counts for very much more." Here we have the root principle of applied anthropology. Here we have in a nutshell the full import of its teaching. The sound administration of the affairs of men can only be based on cultured sympathy, that sympathy on sure knowledge, that knowledge on competent study, that study on accurate inquiry, that inquiry on right method, and that method on continuous experience.

SECTION I.

PHYSIOLOGY.

OPENING ADDRESS BY F. GOWLAND HOPKINS, F.R.S.,
PRESIDENT OF THE SECTION.

The Dynamic Side of Biochemistry.

IN the year 1837 Justus Liebig, whom we may rightly name the father of modern animal chemistry, presented a report to the Chemical Section of the British Association, then assembled at Liverpool. The technical side of this report dealt with the products of the decomposition of uric acid, with which I am not at the moment concerned, but it concluded with remarks which, to judge from other contemporary writings of Liebig, would have been more emphatic had the nature of his brief communication permitted. Liebig had a profound belief that in the then new science of organic chemistry, biology was to find its greatest aid to progress, and his enthusiastic mind was fretted by the cooler attitude of others. In the

report I have mentioned he called upon the chemists of this country to take note of what was in the wind, and while complimenting British physiologists and biologists upon their own work, urged upon them the immediate need of combining with the chemists. Ten years later, Liebig had still to write with reference to chemical studies: "Der Mann welcher in der *Thierphysiologie* wie Saussure in der *Pflanzenphysiologie* die ersten und wichtigsten Fragen zur Aufgabe "eines Lebens macht, fehlt noch in dieser Wissenschaft" (*Ann. Chem. Pharm.*, lxii., 257, 1847). Much later still, he was still making the same complaint. As a matter of fact, the combination of chemistry with biology, in the full and abundant sense that Liebig's earlier enthusiasm had pictured as so desirable, never happened in any country within the limits of his own century, while in this country, up to the end of that century, it can scarcely be said to have happened at all. But the regrettable divorce between these two aspects of science has been so often dwelt upon that you will feel no wish to hear it treated historically, and perhaps even any emphasis given to it now may seem out of place, since on the Continent, and notably in America, the subject of biochemistry (with its new and not very attractive name) has come with great suddenness into its kingdom. Even in this country the recent successful formation of a Biochemical Society gives sure evidence of a greatly increased interest in this borderland of science. Yet I am going to ask you to listen to some remarks which are a reiteration of Liebig's appeal, as heard by this association three-quarters of a century ago.

For one can, I think, honestly say that it is yet a rare thing in this country to meet a professed biologist, even among those unburdened either with years or traditions, who has taken the trouble so to equip himself in organic chemistry as to understand fully an important fact of metabolism stated in terms of structural formulæ. The newer science of physical chemistry has made a more direct appeal to the biological mind. Its results are expressed in more general terms and the bearing of its applications are perhaps more obvious, especially at the present moment. This fact increases the danger of a further neglect in biology of the organic structural side of chemistry, upon which, nevertheless, the whole modern science of intermediary metabolism depends. On the other hand, I think one may say that there are only a few among the present leaders of chemical thought in our midst who have set themselves to appraise with sympathy the drift of biological processes or the nature of the problems that biologists have before them. Anyone wishing to see the number of biochemical workers increased might therefore with equal justice appeal to the teachers of biology or to the teachers of chemistry for greater sympathy with the borderland. It is a moot point indeed as to which is the better side for that borderland to recruit its workers from.

But on the whole it is easier for the intelligent adult mind to grasp new problems than to learn a new technique. It is better that youth should be spent in acquiring the latter. That is why, though I admit that it would have been more obviously to the point if made some ten years ago, I feel justified in repeating to-day the appeal of Liebig to the leading chemists of this country, in the hope that they may see their way to direct the steps of more of their able students into the path of biochemistry. I have been specially tempted to do this, rather than to speak upon some of many subjects which would have interested this section more, for a very practical reason. I have been in a position to review the current demand of various institutions, home and Colonial, for the services of trained biochemists, and can say, I think

with authority, that the demand will rapidly prove to be in excess of the supply. It will be a pity if the generation of trained chemists now growing up in this country should not share in the restoration of this balance. You certainly have the right to tell me that I ought, in the circumstances, to be addressing another section; but it may be long before any member of my cloth will have the opportunity of appealing to that section from the position of advantage that I occupy here. I believe you will forgive the particular trajectory of my remarks, because I am sure you will sympathise with their aim. Moreover, I have some hope that the considerations upon which I shall chiefly base my appeal will have some interest for members of this section as well as for the chemist. My main thesis will be that in the study of the intermediate processes of metabolism we have to deal, not with complex substances which elude ordinary chemical methods, but with simple substances undergoing comprehensible reactions. By simple substances I mean such as are of easily ascertainable structure and of a molecular weight within a range to which the organic chemist is well accustomed. I intend also to emphasise the fact that it is not alone with the separation and identification of products from the animal that our present studies deal; but with their reactions in the body; with the dynamic side of biochemical phenomena.

I have made it my business during the last year or two to learn, by means of indirect and most diplomatic inquiries, the views held by a number of our leading organic chemists with respect to the claims of animal chemistry. I do not find any more the rather pitying patronage for an inferior discipline, and certainly not that actual antagonism, which fretted my own youth; but I do find still very widely spread a distrust of the present methods of the biochemist, a belief that much of the work done by him is amateurish and inexact. What is much more important, and what one should be much more concerned to deny (though but a very small modicum of truth is, or ever was, in the above indictment), is the view that such faults are due to something inherent in the subject.

My desire is to point out that continuous progress, yielding facts which, by whomsoever appraised, belong to exact science, has gone on in the domain of animal chemistry from the days of Liebig until now, and that if this progress was until recently slow, it was, in the main, due to a continuance of the circumstance which so troubled Liebig himself—the shortage of workers.

But we must also remember that the small band of investigators who concerned themselves with the chemistry of the animal in the latter half of the nineteenth century suffered very obviously from the fact that the channels in which chemistry as a whole was fated to progress left high and dry certain regions of the utmost importance to their subject. In three regions particularly the needs of biochemistry were insistent. The colloid state of matter dominates the milieu in which vital processes progress, but, notwithstanding the stimulating work of Graham, the pure chemist of the last century consistently left colloids on one side with a shudder of distaste. Again, we have come to recognise that the insidious influence of catalysts is responsible for all chemical change as it occurs in living matter, but for many years after Berzelius the organic chemist gave to the subject of catalysis very cursory attention, fundamental though it be. Lastly, every physiological chemist has to realise that among his basal needs is that of accurate methods for the estimation of organic substances when they are present in complex mixtures. But the organic chemist of the nineteenth century did not

develop the art of analysis on these lines. Of the myriad substances, natural or artificial, known to him at the most a few score could be separated quantitatively from mixtures, or estimated with any accuracy. It was a professional or commercial call rather than scientific need which evolved such processes as were available, so that this side of chemical activity developed only on limited and special lines.

All these circumstances were, of course, inevitable. Organic chemistry in Liebig's later years was concerned with laying its own foundations as a pure science, and for the rest of the century with building a giant, self-contained edifice upon them. The great business of developing the concepts of molecular structure and the wonderful art of synthesis were so absorbing as to leave neither leisure nor inclination for extraneous labours. But it is easy to recognise that, near the beginning of the present century, a sense of satiety had arisen in connection with synthetic studies carried out for their own sake. Workers came to feel that, so far as the fundamental theoretical aspects of chemistry were concerned, that particular side of organic work had played its part. In numerous centres, instead of only in a few, quite other aspects of the science were taken up: in particular, the study of the dynamic side of its phenomena. The historian will come to recognise that a considerable revolution in the chemical mind coincided roughly with the beginning of this century. Among the branches which are fated to benefit by this revolution—it is to be hoped in this country as well as others—is the chemistry of the animal.

But I would like to say that I do not find, on reading the contributions to science of those who, as professed physiological chemists, ploughed lonely furrows in the last century, any justification for the belief that the work done by them was amateurish or inexact; no suggestion that anything inherent in the subject is prone to lead to faults of the kind. Truly these workers had to share ignorance which was universal, and sometimes, compelled by the urgency of certain problems, had perforce to do their best in regions that were dark. But they knew their limitations here as well as their critics did, and relied for their justification upon the application of their results, which was often not understood at all by their critics.

There is little doubt, for instance, that it was the earlier attempts of various workers to fractionate complex colloid mixtures that led to the cynical statement that "*Thierchemie* is *Schmierchemie*." But the work thus done, even such work as Kühne's upon the albumoses and peptones, had important bearings, and led indirectly to the acquirement of facts of great importance to physiology and pathology.

In connection with enzyme catalysis the work done at this time by physiological chemists was in the main of a pioneer character, but it was urgently called for and had most useful applications. By the end of the century, indeed, it had become of great importance. I recall an incident which illustrates the need of suspended judgment before work done in new regions is assumed to be inexact. In 1885 E. Schütz published a study of the hydrolysis of protein by pepsin which showed that the rate of action of the ferment is proportionate to the square root of its concentration. When this paper was dealt with in Maly's "Jahresbericht" the abstractor (who from internal evidence, I believe, was Richard Maly himself) believed so little in such an apparent departure from the laws of mass action that he saw fit to deal with the paper in a ribald spirit, and to add, as a footnote to his abstract, the lines:—

"Musst mir meine Erde
Doch lassen steh'n
Und meine Hütte die du nicht gebaut!"

Yet it is now known that the relation brought to light by Schütz does hold for certain relative concentrations of ferment and substrate. That it had limitations was shown by Schütz himself. The fact, however, involves no such shaking of the foundations as the abstractor thought. We quite understand now how such relations may obtain in enzyme-substrate systems.

As for analytical work involving a separation of complex organic mixtures, the biochemist of the last century was in this ahead of the pure organic chemist, as the development of urinary analysis if considered alone will show.

In countless directions the acquirement of exact knowledge concerning animal chemistry has been, as I have already claimed, continuous from Liebig's days until now. I would like in a brief way to illustrate this, and if I choose for the purpose one aspect of things rather than another, it is because it will help me in a later discussion. I propose to remind you of certain of the steps by which we acquired knowledge concerning the synthetic powers of the animal body, apologising for the great familiarity of many of the facts which I shall put before you.

It seems that the well-known Glasgow chemist and physician, Andrew Ure, was the first actually to prove, from observations made upon a patient, that an increased excretion of hippuric acid follows upon the administration of benzoic acid. Wöhler had earlier fed a dog upon the latter substance, and decided at the time that it was excreted unchanged; but when, later, Liebig had made clear the distinction between the two acids, Wöhler recalled the properties of the substance excreted by his dog, and decided that it must have been hippuric acid and not benzoic acid itself. Excited by the novel idea that a substance thus extraneously introduced might be caught up in the machinery of metabolism, Wöhler, immediately after the publication of Dr. Ure's statement, initiated fresh experiments in his laboratory at Göttingen, where Keller, by observations made upon himself, showed unequivocally that benzoic acid is, and can be on a large scale, converted into hippuric acid in the body. Thus was established a fact which is now among the most familiar, but which at that time stirred the imagination of chemists and physiologists not a little. The discovery immediately led to a large number of observations dealing with various conditions which affect the synthesis, but we may pass to the acute observations of Bertagnini. This investigator wished to earmark, as it were, the benzoic acid administered to the animal, in order to make sure that it was the same molecule which reappeared in combination. He so marked it with a nitro-group, giving nitro-benzoic acid and observing the excretion of nitro-hippuric acid. Later on he continued this interesting line of research by giving other substituted benzoic acids, and showed that in each case a corresponding substituted hippuric acid was formed. Even so far back as the earlier 'fifties a clear understanding was thus established that the body was possessed of a special mechanism capable of bringing a particular class of substances into contact with the amino-acid glycine, and of converting them, by means of a synthetical condensation (which had not then been induced by any laboratory method), into conjugates which, as later experiments have shown, are invariably less noxious for the tissues than the substances introduced. Great is the number of compounds which are now known to suffer this fate. To the story begun by Ure and Wöhler, chapter after chapter has been added continuously up to the present day. In 1876 came the classical experiments of Bunge and Schmiedeberg. After laborious but successful efforts to obtain a good method for the estimation of

hippuric acid in animal fluids, these authors proved, by a method of exclusion, that, in the dog at least, the kidney is the seat of the hippuric synthesis. When, in their carefully controlled experiments, blood containing benzoic acid and glycine was circulated through that organ, after its isolation from the body, the production of hippuric acid followed. Schmiedeberg, a little later, convinced himself that the reaction in the kidney was a balanced one; the organ can not only synthesise hippuric acid, it can also hydrolyse it. As with reactions elsewhere, so in the kidney cell, the equilibrium of the reaction depends on the relative concentration of the products concerned. Schmiedeberg then separated from the tissues of the kidney what he believed to be an enzyme capable of inducing the hydrolysis. Mutch, with improved methods, has recently shown that a preparation from the kidney, wholly free from intact cells, can, beyond all doubt, hydrolyse hippuric acid under rigidly aseptic conditions, the reaction being one which comes to an equilibrium point when some 97 per cent. of the substance is broken down. The occurrence of this equilibrium, and the form of the reaction-velocity curve as obtained by Mutch, suggested that synthesis under the influence of the enzyme was to be expected, and, on submitting the mixture of benzoic acid and glycine to its influence, Mutch obtained a product which, though too small in amount for analysis, was almost certainly hippuric acid. I have myself obtained evidence which shows that the synthesis does certainly occur under these conditions.

The significance of this earliest known synthesis in the body is no limited one. The amide linkage established by it is one with which the body deals widely, and is, of course, of the type which is dominant in tissue complexes, since it is one which unites the amino-acids in the protein molecule.

Seeing, from the nature of the material supplied for the synthesis by the body itself, that the foreign substances administered must intrude themselves into the machinery of protein metabolism, it is not surprising that many have turned their minds to consider how far a detailed study of the phenomena might throw light upon this machinery. How far can the body extend its supply of glycine when stimulated by increasing doses of benzoic acid? What effects follow when administration is pushed to its limits? How is the fate in metabolism of the whole molecule of protein affected when one particular amino-acid is inharmoniously removed? Can the amino-acid be itself synthesised *de novo* in response to the call for it? These and similar questions clearly arise. I can only stop to remind you that there is evidence that, in connection with this particular chemical synthesis, the carnivore reacts differently to the herbivore. If the body of the former be flooded with benzoic acid, only a proportion undergoes condensation. Only so much glycine is supplied as would correspond, roughly, at any rate, with that rendered available by the normal contemporary breakdown of protein, whereas, in the herbivorous animal, pushing the administration of benzoic acid may lead to the excretion of so much conjugated glycine that it may contain more than half of the whole nitrogen excreted. This is, of course, much more than could come from the protein of the body, and it would seem that the amino-acid is prepared *de novo* for an express purpose, a significant thing. But I must not stop to consider questions which are still in course of study. Before the hippuric synthesis was first observed synthetic powers were thought to be absent from the animal. Since then we have been continuously learning of fresh instances of synthesis in the body, not only in connection with its treatment of foreign substances, with which I am

just now concerned, but in connection with all its normal processes.

Another most interesting group of syntheses in which substances are so dealt with in the body as to reappear in conjugation with protein derivatives are those in which the sulphur group plays its part. In 1876 Baumann first introduced us to the ethereal sulphates of the urine, and, from much subsequent work, we know how great a group of substances, chiefly those of phenolic character, are, after administration, excreted linked to sulphuric acid. We have evidence to show that, in all probability, the original condensation is not with sulphuric acid itself, but that oxidation of a previously formed sulphur containing conjugate has preceded excretion, and we know that another group of substances leave the body combined with unoxidised sulphur. Certain cyanides—the aliphatic nitriles, for example—reappear as sulphocyanides; but, above all in interest, is the case described by Baumann, in which the intact cystein complex of protein, after suffering acetylation of its amino group, is excreted as a conjugate. The administration of halogen-benzene compounds is followed by the appearance of the so-called mercapturic acids in which the cystein is linked by its sulphur atom to the ring of chlor-, bromo-, or iodo-benzene. That large amounts of these conjugates can be formed during the twenty-four hours is certain, but it would be interesting to know what limit is set to this loss of cystin from the body.

I will now recall to you syntheses in which the substance supplied by the body is derived, not from protein, but from carbohydrate. The study of the fate of camphor in the body, carried out by Schmiedeberg and Hans Meyer in 1878, if it stood by itself, would abundantly illustrate the significance of this type of experiment. As you are aware, these workers proved that, after the administration of camphor, the urine contains a conjugate formed between an oxidation product of the camphor and an oxidation product of glucose. Both substances were then new to chemistry, and the latter—glycuronic acid—has since proved itself of great physiological interest. After Schmiedeberg's and Hans Meyer's experiments it was realised for the first time that the sugar molecule might play a part in metabolism quite distinct from its function as fuel, a fact that has much of cogency at the present time. We have good reason to believe that though, as a matter of fact, glycuronic acid is a normal metabolite, the actual synthesis concerns sugar itself, the oxidation of the glucose molecule occurring later. The compound formed is of the glucoside type, and the analogy with the formation of glucosides in the plant is unmistakable. Already the number of substances known to suffer this particular synthesis is legion. Almost every organic group yields an example.

Lastly, in illustration of a quite different type of synthesis (I can only deal with a few of the many known cases) we may recall the methylation which certain compounds undergo. The mechanism of this process, as it occurs in the body, is obscure, and its explanation would be of the greatest chemical interest. I must mention only one particular instance investigated by Ackermann. When nicotinic acid is fed to animals, it is excreted as trigonellin, a known vegetable base. This conversion involves methylation, and is of striking character as an instance of the artificially induced production of a plant alkaloid in the animal body.

The full significance of all such happenings will not be understood unless it be remembered that a nice adjustment of molecular structure is in many cases necessary to prepare the foreign substance for syn-

thesis. Preliminary regulated oxidations or reductions may occur so as to secure, for example, the production of an alcoholic or phenolic hydroxyl group, which then gives the opportunity for condensation which was otherwise absent.

I have touched only on the fringes of this domain. The body of knowledge available concerning it has not been won systematically, and the fate of a multitude of other types of organic substances remains for investigation. The known facts have, one feels, an academic character in the view of the physiologist, and even in that of the pharmacologist, to whom we owe most of our knowledge about them. But, in my opinion, the chemical response of the tissues to the chemical stimulus of foreign substances of simple constitution is of profound biological significance. Apart from its biological bearings as the simplest type of immunity reaction, it throws vivid light, and its further study must throw fresh light on the potentialities of the tissue laboratories.

In a brilliant address delivered before the faculty of medicine of the University of Leeds, Lord Moulton likened the process of recovery in the tissues after bacterial invasion to the generation of forces which establish what is known to the naval architect as the "righting couple." This grows greater the greater the displacement of a ship, and finally may become sufficient to overpower the forces tending to make her heel over. It is surely striking to realise that the establishment of the "righting couple" which brings the tissue cell back to equilibrium after the disturbances due to the intrusion of simple molecules calls for such a complex of chemical events, events which ultimately result in the modification of the disturbing substance and its extrusion from the tissues concerned in a form less noxious to the body as a whole.

Oxidation, reduction, desaturation, alkylation, acylation, condensation; any or all of these processes may be brought *de novo* into play as the result of the intrusion of a new molecule into reactions which were in dynamic equilibrium. It is clear that chemical systems capable of so responding to what may be termed specific chemical stimuli must not be neglected by any student of chemical dynamics. The physiologist has for many years been engaged upon careful analyses of the mechanical and electric responses to stimulation. In the phenomena before us we find "responses" which are equally fundamental. If we do not study them exhaustively we shall miss an important opportunity for throwing light upon the nature of animal tissues as chemical systems.

One reason which has led the organic chemist to avert his mind from the problems of biochemistry is the obsession that the really significant happenings in the animal body are concerned in the main with substances of such high molecular weight and consequent vagueness of molecular structure as to make their reactions impossible of study by his available and accurate methods. There remains, I find, pretty widely spread, the feeling—due to earlier biological teaching—that, apart from substances which are obviously excreta, all the simpler products which can be found in cells or tissues are as a class mere dejecta, already too remote from the fundamental biochemical events to have much significance. So far from this being the case, recent progress points in the clearest way to the fact that the molecules with which a most important and significant part of the chemical dynamics of living tissues is concerned, are of a comparatively simple character. The synthetic reactions which we have already considered surely prepare us for this view; but it may be felt that, however important, they represent abnormal events, while the study of them has been largely confined to determin-

ing the end-products of change. Let me now turn to normal metabolic processes and to intermediary reactions.

We know first of all that the raw material of metabolism is so prepared as to secure that it shall be in the form of substances of small molecular weight; that the chief significance of digestion, indeed, lies in the fact that it protects the body from complexes foreign to itself. Abderhalden has ably summarised the evidence for this and has shown us also that, so far as the known constituents of our dietaries are concerned, the body is able to maintain itself when these are supplied to it wholly broken down into simple *bausteine*, any one of which could be artificially synthesised with the aid of our present knowledge. Dealing especially with the proteins, we have good reason to believe that the individual constituent amino-acids, and not elaborate complexes of these, leave the digestive tract, while Folin, Van Slyke, and Abel have recently supplied us with suggestive evidence for the fact that the individual amino-acids reach the tissues as such and there undergo change.

But still more important, when things are viewed from my present point of view, is the fact that recent work gives clear promise that we shall ultimately be able to follow, on definite chemical lines, the fate in metabolism of each amino-acid individually; to trace each phase in the series of reactions which are concerned in the gradual breakdown and oxidation of its molecule. Apart from the success to which it has already attained, the mere fact that the effort to do this has been made is significant. To those at least who are familiar with the average physiological thought of thirty years ago, it will appear significant enough. So long as there were any remains of the instinctive belief that the carbonic acid and urea which leave the body originate from oxidations occurring wholly in the vague complex of protoplasm, or at least that any intermediate products between the complex and the final excreta could only be looked for in the few substances that accumulate in considerable amount in the tissues (for instance, the creatin of muscle), the idea of seriously trying to trace within the body a series of processes which *begin* with such simple substances as tyrosin or leucin was as foreign to thought as was any conception that such processes could be of fundamental importance in metabolism. However vaguely held, such beliefs lasted long after there was justification for them; their belated survival was due, it seems to me, to a certain laziness exhibited by physiological thought when it trenched on matters chemical; they disappeared only when those accustomed to think in terms of molecular structure turned their attention to the subject. But it should be clearly understood that the progress made in these matters could only have come through the work and thought of those who combined with chemical knowledge trained instinct and feeling for biological possibilities. Our present knowledge of the fate of amino-acids, as of that of other substances in the body, has only been arrived at by the combination of many ingenious methods of study.

It is easy in the animal, as in the laboratory, to determine the end-products of change; but, when the end result is reached in stages, it is by no means easy to determine what are the stages, since the intermediate products may elude us. And yet the whole significance of the processes concerned is to be sought in the succession of these stages. In animal experiments directed to the end under consideration, investigators have relied first of all upon the fact that the body, though the seat of a myriad reactions, and capable perhaps of learning, to a limited extent

and under stress of circumstances, new chemical accomplishments, is in general able to deal only with what is customary to it. This circumstance has yielded two methods of determining the nature of intermediate products in metabolism. Considerations of molecular structure will, for instance, suggest several possible lines along which a given physiological substance may be expected to undergo change. We may test these possibilities by administering various derivatives of the substance in question. Only those which prove on experiment to be fully metabolised, or to yield derivatives in the body identical with those yielded by the parent substance, can be the normal intermediate products of its metabolism. All others may be rejected as not physiological. In a second method dependent upon this eclecticism of the body, substances are administered which so far differ from the normal that, instead of suffering a complete breakdown, they yield some residual derivative which can be identified in the excreta, and the nature of which will throw light upon the chemical mechanism which has produced it. For instance, a substance with a resistant (because abnormal) ring structure, but possessing a normal side chain, may be used to demonstrate how the side chain breaks down. Again, we may sometimes obtain useful information by administering a normal substance in excessive amounts, when certain intermediate products may appear in the excreta. Another most profitable method of experiment is that in which the substance to be studied is submitted to the influence of isolated organs instead of to that of the whole animal. Under these conditions, a series of normal reactions may go on, but with altered relative velocities, so that intermediate products accumulate; or again when, as may happen, the successive changes wrought upon a substance by metabolism occur in different organs of the body, this use of isolated organs enables us to dissect, as it were, the chain of events. Extraordinarily profitable have been the observations made upon individuals suffering from those errors of metabolism which Dr. Garrod calls "metabolic sports, the chemical analogues of structural malformations." In these individuals, nature has taken the first essential step in an experiment by omitting from their chemical structure a special catalyst which at one point in the procession of metabolic chemical events is essential to its continuance. At this point there is arrest, and intermediate products come to light.

As you know, most ingenious use of this ready-made experimental material has added greatly to our knowledge of intermediate metabolism. Admirable use, too, has been made of the somewhat similar conditions presented by diabetes, clinical and experimental. Every day our knowledge of the dynamics of the body grows upon these lines.

I know that the history of all these efforts is familiar to you, but I am concerned to advertise the fact that our problems call for ingenuity of a special sort, and to point out that an equipment in chemical technique alone would not have sufficed for the successful attack which has been made upon them. But I am even more concerned to point out that the direct method of attack has been too much neglected, or has been in the hands of too few; I mean the endeavour to separate from the tissues further examples of the simpler products of metabolic change, no matter how small the amount in which they may be present; an endeavour which ought not to stop at the separation and identification of such substances, but to continue until it has related each one of them to the dynamic series of reactions in which each one is surely playing a part. The earliest attempts at tracing the intermediate processes of metabolism looked for information to the products which accumulate in the tissues, but it seemed to be always tacitly assumed that only

those few which are quantitatively prominent could be of importance to the main issues of metabolism. It is obvious, however, upon consideration, that the degree to which a substance accumulates is by itself no measure of its metabolic importance; no proof as to whether it is on some main line of change, or a stage in a quantitatively unimportant chemical by-path. For, if one substance be changing into another through a series of intermediate products, then, as soon as dynamical equilibrium has been established in the series, and to such equilibrium tissue processes always tend, the rate of production of any one intermediate product must be equal to the rate at which it changes into the next, and so throughout the series. Else individual intermediate products would accumulate or disappear, and the equilibrium be upset. Now the rate of chemical change in a substance is the product of its efficient concentration and the velocity constant of the particular reaction it is undergoing. Thus the relative concentration of each intermediate substance sharing in the dynamic equilibrium, or, in other words, the amount in which we shall find it at any moment in the tissue, will be inversely proportional to the velocity of the reaction which alters it. But the successive velocity constants in a series of reactions may vary greatly, and the relative accumulation of the different intermediate products must vary in the same degree. It is certain that in the tissues very few of such products accumulate in any save very small amount, but the amount of a product found is only really of significance if we are concerned with any function¹ which it may possibly possess. It is of no significance as a measure of the quantitative importance of the dynamical events which give rise to it.

To take an instance. The substance creatin has always asserted itself in our conceptions concerning nitrogenous metabolism because of the large amount in which it is found in the muscle. It may be of importance *per se*, and abnormalities in its fate are certainly important as an indication of abnormalities in metabolism, but we must remember that the work of Gulewitsch, Krimberg, Kutscher, and others has shown us that a great number of nitrogenous basic bodies exist in muscle in minute amounts. Maybe we shall need to know about each of these all that we now know, or are laboriously trying to know, about creatin, before the dynamics of basic nitrogen in muscle become clear. Fortunately for the experimenter, most of the raw materials required for tissue analysis are easily obtainable; there is no reason save that of the labour involved why we should not work upon a ton of muscle or a ton of gland tissue.

I am certain that the search for tissue products of simple constitution has important rewards awaiting it in the future, so long as physiologists are alive to the dynamical significance of all of them. Such work is laborious and calls for special instincts in the choice of analytical method, but, as I mentioned in an earlier part of this address, I am sure that high qualifications as an analyst should be part of the equipment of a biological chemist.

I should like now to say a few words concerning the actual results of this modern work upon intermediate metabolism, and will return to the amino-acids. It is clear that what I can say must be very brief.

We know that the first change suffered by an α -amino-acid when it enters the metabolic laboratories is the loss of its amino group, and, thanks to the labours of Knoop, Neubauer, Embden, Dakin, and others, we have substantial information concerning the mechanism of this change. The process involved

¹ A product of metabolism can only be said to have a "function" in a cell or in the body when, being the end-product of one reaction, it initiates or modifies reactions in another milieu.

in the removal of the amino group is not a simple reduction, which would yield a fatty acid, or substituted fatty acid, nor a hydrolytic removal which would leave an α -hydroxy-acid; but the much less to be expected process of an oxidative removal, which results in the production of a keto-acid.² If the direct evidence for this chemically most interesting primary change were to be held insufficient (though there is no insufficiency about it), its physiological reality is strongly supported by the proof given us by Knoop and Embden that the liver can resynthesise the original amino-acid from ammonia and the corresponding keto-acid. This profoundly significant observation is part of the evidence which is continually accumulating to show that all normal chemical processes of the body can suffer reversal. The next step in the breakdown involves the oxidation of the keto-acid, with the production of a fatty acid containing one carbon less than the original amino-acid. This in turn is oxidised to its final products along the lines of the β -oxidation of Knoop, two carbon atoms being removed at each stage of the breakdown. All this is true of the aliphatic α -amino-acids, and, with limitations, of the side chains of their aromatic congeners. In the case of certain amino-acids the course of breakdown passes through the stage of aceto-acetic acid. This happens to those of which the molecule contains the benzene ring, and Dakin has enabled us to picture clearly the path of change which involves the opening of the ring. This particular stage does not seem to occur in the breakdown of the aliphatic amino-acids, save in the case of leucine; the rule and the exception here being alike easy of explanation by considerations of molecular structure.

But direct breakdown on the lines mentioned is far from being the only fate of individual amino-acids in the body. The work of Lusk, completed by that of Dakin, has shown us that of seventeen amino-acids derived from protein no less than nine may individually yield glucose in the diabetic organism, and there are excellent grounds for believing (indeed, there is no doubt) that they do the same to a duly regulated extent in the normal organism. The remaining seven have been shown not to yield sugar, and there is therefore a most interesting contrast in the fate of two groups of the protein *Bausteine*. Those which yield sugar do not yield aceto-acetic-acid, and those which yield the latter are not glycogenic. One set, after undergoing significant preliminary changes, seems to join the carbohydrate path of metabolism, the other set ultimately joins a penultimate stage in the path which is traversed by fats.

I will here venture to leave for one moment the firm ground of facts experimentally ascertained. Unexplored experimentally, but quite certain so far as their existence is concerned, are yet other metabolic paths of prime importance, along which individual amino-acids must travel and suffer change. We know now from the results of prolonged feeding experiments upon young growing animals, which I myself, as well as many others, have carried out, that all the nitrogenous tissue complexes, as well as the tissue proteins, can be duly constructed when the diet contains no other source of nitrogen beside the amino-acids of protein. The purin and pyrimidin bases, for instance, present in the nuclear material of cells certainly take origin from particular amino-acids, though we have no right to assume that groups derived from carbohydrates or fats play no part in the necessary syntheses. While recent years have given us a

wonderfully clear picture as to how the nucleic acids and the purin bases contained in them break down during metabolism, we have as yet no knowledge of stages in their synthesis. But it is clear that to discover these is a task fully open to modern experimental methods, and though a difficult problem, it is one ready to hand. Again, in specialised organs substances are made which are of great importance, not to the structure, but to the dynamics of the body. These have become familiar to us under the name of Hormones. We know the constitution of one of these only, adrenaline. The molecule of this exemplar has a simple structure of a kind which makes it almost certain to be derived from one of the aromatic amino-acids. It is clearly open to us to discover on what lines it takes origin. Facts of this kind, we may be sure, will form a special chapter of biochemistry in the future. I would like to make a point here quite important to my main contention that metabolism deals with simple molecules. As a pure assumption it is often taught, explicitly or implicitly, that although the bowel prepares free amino-acids for metabolism, only those which are individually in excess of the contemporary needs of the body for protein are directly diverted to specialised paths of metabolism, and these to the paths of destructive change. All others—all those which are to play a part in the intimacies of metabolism—are supposed to be first reconstructed into protein, and must therefore again be liberated from a complex before entering upon their special paths of change. But there is much more reason (and some experimental grounds) for the belief that the special paths (of which only one leads to the repair or formation of tissue protein) may be entered upon straightway. Mrs. Stanley Gardiner (then Miss Willcock) carried out some feeding experiments a few years ago, and in discussing these I pointed out that they offered evidence of the direct employment for special purposes of individual amino-acids derived as such from the bowel. It seemed at the time that the argument was misunderstood or felt to carry little weight, but later Prof. Kossel (*Johns Hopkins Hospital Bulletin*, March, 1912) quoted my remarks with approval and expressed agreement with the view that the *Bausteine* of the food protein must, in certain cases, be used individually and directly.

I wish I had time to illustrate my theme by some of the abundant facts available from quite other departments of metabolism; but I must pass on.

The chief thing to realise is that as a result of modern research the conception of metabolism in block is, as Garrod puts it, giving place to that of metabolism in compartments. It is from the behaviour of simple molecules we are learning our most significant lessons.

Now interest in the chemical events such as those we have been dealing with may still be damped by the feeling that, after all, when we go to the centre of things, to the bioplasm, where these processes are initiated and controlled, we shall find a milieu so complex that the happenings there, although they comprise the most significant links in the chain of events, must be wholly obscure when seen from the point of view of structural organic chemistry. I would like you to consider how far this is necessarily the case.

The highly complex substances which form the most obvious part of the material of the living cell are relatively stable. Their special characters, and in particular the colloidal condition in which they exist, determine, of course, many of the most fundamental characteristics of the cell: its definite yet mobile structure, its mechanical qualities, including the contractility of the protoplasm, and those other colloidal characters which the modern physical chemist is

² Dakin's recent work is giving us an insight into the mechanism of the keto-acid formation. Amino-acids in aqueous solution dissociate into ammonia and the corresponding keto-aldehyde. The oxidation involved is therefore concerned with the conversion of the aldehyde into the acid.

studying so closely. For the dynamic chemical events which happen within the cell, these colloid complexes yield a special milieu, providing, as it were, special apparatus, and an organised laboratory. But in the cell itself, I believe, simple molecules undergo reactions of the kind we have been considering. These reactions, being catalysed by colloidal enzymes, do not occur in a strictly homogeneous medium, but they occur, I would argue, in the aqueous fluids of the cell under just such conditions of solution as obtain when they progress under the influence of enzymes *in vitro*.

There is, I know, a view which, if old, is in one modification or another still current in many quarters. This conceives of the unit of living matter as a definite, if very large and very labile molecule, and conceives of a mass of living matter as consisting of a congregation of such molecules in that definite sense in which a mass of, say, sugar is a congregation of molecules, all like to one another. In my opinion, such a view is as inhibitory to productive thought as it is lacking in basis. It matters little whether in this connection we speak of a "molecule" or, in order to avoid the fairly obvious misuse of a word, we use the term "biogen," or any similar expression with the same connotation. Especially, I believe, is such a view unfortunate when, as sometimes, it is made to carry the corollary that simple molecules, such as those provided by foodstuffs, only suffer change after they have become in a vague sense a part of such a giant molecule or biogen. Such assumptions became unnecessary as soon as we learnt that a stable substance may exhibit instability after it enters the living cell, not because it loses its chemical identity, and the chemical properties inherent in its own molecular structure, by being built into an unstable complex, but because in the cell it meets with agents (the intracellular enzymes) which catalyse certain reactions of which its molecule is normally capable.

Exactly what sort of material might, in the course of cosmic evolution, have first come to exhibit the elementary characters of living stuff, a question raised in the presidential address which so stirred us last year, we do not, of course, know. But it is clear that the living cell as we now know it is not a mass of matter composed of a congregation of like molecules, but a highly differentiated system; the cell, in the modern phraseology of physical chemistry, is a system of coexisting phases of different constitutions.¹ Corresponding to the difference in their constitution, different chemical events may go on contemporaneously in the different phases, though every change in any phase affects the chemical and physico-chemical equilibrium of the whole system. Among these phases are to be reckoned not only the differentiated parts of the bioplasm strictly defined (if we can define it strictly) the macro- and micro-nuclei, nerve fibres, muscle fibres, &c., but the material which supports the cell structure, and what have been termed the "metaplasmic" constituents of the cell. These last comprise not only the fat droplets, glycogen, starch grains, aleurone grains, and the like, but other deposits not to be demonstrated histologically. They must be held, too—a point which has not been sufficiently insisted upon—to comprise the diverse substances of smaller molecular weight and greater solubility, which are present in the more fluid phases of the system—namely, in the cell juices. It is important to remember that change in any one of these constituent phases, including the metaplasmic phases, must affect the equilibrium of the whole cell system, and because of this necessary equilibrium-relation it is difficult to say that any one of the constituent

phases, such as we find *permanently* present in a living cell, even a metaplasmic phase, is less essential than any other to the "life" of the cell, at least when we view it from the point of view of metabolism. It is extremely difficult and probably impossible by any treatment of the animal completely to deprive the liver of its glycogen deposits, so long as the liver cells remain alive. Even an extreme variation in the quantity is in the present connection without significance because, as we know, the equilibrium of a polyphasic system is independent of the mass of any one of the phases; but I am inclined to the bold statement that the integrity of metabolic life of a liver cell is as much dependent on the coexistence of metaplasmic glycogen, however small in amount, as upon the coexistence of the nuclear material itself; so in other cells, if not upon glycogen, at least upon other metaplasmic constituents.

Now we should refuse to speak of the membrane of a cell, or of its glycogen store, as living material. We should not apply the term to the substances dissolved in the cell juice, and, indeed, would scarcely apply it to the highly differentiated parts of the bioplasm if we thought of each detail separately. We are probably no more justified in applying it, when we consider it by itself, to what, as the result of microscopic studies, we recognise as "undifferentiated" bioplasm. On ultimate analysis we can scarcely speak at all of living matter in the cell; at any rate, we cannot, without gross misuse of terms, speak of the cell life as being associated with any one particular type of molecule. Its life is the expression of a particular dynamic equilibrium which obtains in a polyphasic system. Certain of the phases may be separated, mechanically or otherwise, as when we squeeze out the cell juices, and find that chemical processes still go on in them; but "life," as we instinctively define it, is a property of the cell as a whole, because it depends upon the organisation of processes, upon the equilibrium displayed by the totality of the coexisting phases.

I return to my main point. The view I wish to impress upon you is that some of the most important phenomena in the cell, those involving simple reactions of the type which we have been discussing, occur in ordinary crystalloid solution. We are entitled to distinguish fluid (or more fluid) phases in the cell. I always think it helpful in this connection to think of the least differentiated of animal cells—to consider, for instance, the amoeba. In this creature a fluid phase comes definitely into view with the appearance of the food vacuole. In this vacuole digestion goes on, and there can be no doubt, from the suggestive experimental evidence available, that a digestive enzyme, and possibly two successive enzymes (a pepsin followed by a trypsin) appear in it. It is now generally admitted that digestion in the amoeba, though intracellular, is metaplasmic. The digestion products appear first of all in simple aqueous solution. Is it not unjustifiable to assume that the next step is a total "assimilation" of the products, a direct building up of all that is produced in the vacuole into the complexes of the cell? If there be any basis for our views concerning the specificity of, say, the tissue proteins, they must apply to the amoeba no less than to the higher animal, and we must picture the building-up of its specific complexes as a selective process. The mixture of amino-acids derived from the proteins of the bacteria or other food eaten by it may be inharmonious with their balance in the amoeba. Some have to be more directly dealt with, by oxidation or otherwise. If the digestive hydrolysis occur outside the complexes, we may most justifiably assume that other prepara-

¹ See in this connection the very able exposition of the views developed by Zwaardemaker and others, by Botazzi in Winterstein's "Handbuch," vol. i.

tive processes also occur outside them. We need not think of a visible vacuole as the only seat of such changes. Similar fluid phases in the cell may elude the microscope, and the phenomena would be just as significant if reactions occur in the water imbibed by the colloids of the cell or present in the intra-micellar spaces of the bioplasm. It is always important to remember that 75 per cent. of the cell substance consists of water.

All of these considerations we may apply to the tissue cells of the higher animal. To my mind, at least, the following considerations appeal. It is noteworthy that all the known complexes of the cell—the proteins, the phosphorous complexes, the nucleic acids, &c.—are susceptible to hydrolysis by catalytic agents, which are always present, or potentially present. If the available experimental evidence be honestly appraised, it points to the conclusion that only to hydrolytic processes are the complexes unstable. Under the conditions of the body they are, while intact, resistant to other types of change, their hydrolytic products being much more susceptible. Since hydroclastic agents are present in the cell we must suppose that there is, at any moment, equilibrium between the complexes and their water-soluble hydrolytic products, though the amount of the latter present at any moment may be very small. Now, I think we are entitled to look upon assimilation and dissimilation, while very strictly defined, as being dependent upon changes in this equilibrium alone. They are processes of condensation and hydrolysis respectively. Substances which are foreign to the normal constitution of the complexes—and these comprise not only strictly extraneous substances, but material for assimilation not yet ready for direct condensation, or metabolites which are no longer simple hydrolytic products—do not enter or re-enter the complexes. They suffer change within the cell, but not as part of the complexes. When, for instance, a supply of amino-acids transferred from the gut reaches the tissue cell, they may be in excess of the contemporary limits of assimilation; or, once more, individual acids may not be present in the harmonious proportion required to form the specific proteins in the cell. Are we to suppose that all nevertheless become an integral part of the complexes before the harmony is by some mysterious means adjusted? I think rather that the normality of the cell proteins is maintained by processes which precede actual condensation or assimilation. Conversely, when the cell balance sets towards dissimilation, the amino-acids liberated by hydrolysis suffer further changes outside the complexes. So when a foreign substance, say benzoic acid, enters the cell, we have no evidence, experimental or other, to suggest that such a body ever becomes an integral part of the complexes. Rather does it suffer its conjugation with glycine in the fluids of the cell. So also with cases of specific chemical manufacture in organs. When, for instance, adrenaline—a simple, definite crystalline body—appears in the cells of the gland which prepares it, are we to suppose that its molecule emerges in some way ready-made from the protein complexes of the gland, rather than that a precursor derived from a normal hydrolytic product of these proteins or from the food supply is converted into adrenaline by reactions of a comprehensible kind, occurring in aqueous solution, and involving simple molecules throughout? While referring to adrenaline, I may comment upon the fact that the extraordinarily wide influence now attributed to that substance is a striking illustration of the importance of simple molecules in the dynamics of the body.

It should be, of course, understood, though the

consideration does not affect the essential significance of the views I am advancing, that the isolation of reactions in particular phases of the cell is only relative. I have before emphasised the point that the equilibrium of the whole system must, to a greater or less degree, be affected by a change in any one phase. A happening of any kind in the fluid phases must affect the chemical equilibrium and, no less, the physico-chemical equilibrium, between them and the complexes or less fluid phases. A drug may have an "action" on a cell, even though it remain in solution, and it may have a specific action because its molecular constitution leads it to intrude into, and modify the course of, some one, rather than any other, of the numerous simple chemical reactions proceeding in the cells of different tissues.

But I must now turn from consideration of the reactions themselves to that of their direction and control. It is clear that a special feature of the living cell is the organisation of chemical events within it. So long as we are content to conceive of all happenings as occurring within a biogen or living molecule all directive power can be attributed in some vague sense to its quite special properties.

But the last fifteen years have seen grow up a doctrine of a quite different sort which, while it has difficulties of its own, has the supreme merit of possessing an experimental basis and of encouraging by its very nature further experimental work. I mean the conception that each chemical reaction within the cell is directed and controlled by a specific catalyst. I have already more than once implicitly assumed the existence of intracellular enzymes. I must now consider them more fully.

Considering the preparation made for it by the early teaching of individual biologists, prominent among whom was Moritz Traube, it is remarkable that belief in the endo-enzyme as a universal agent of the cell was so slow to establish itself, though in the absence of abundant experimental proof scepticism was doubtless justified. So long as the ferments demonstrated as being normally attached to the cell were only those with hydroclastic properties, such as were already familiar in the case of secreted digestive ferments, the imagination was not stirred. Only with Buchner's discovery of zymase and cell-free alcoholic fermentation did the faith begin to grow. Yet, a quarter of a century before, Hoppe-Seyler had written (when discussing the then vexed question of nomenclature, as between organised and unorganised "ferments"): "The only question to be determined is whether that hypothesis is too bold which assumes that in the organism of yeasts there is a *substance* [the italics are mine] that decomposes sugar into alcohol and CO₂. . . I hold the hypothesis to be *necessary* because fermentations are chemical events and must have chemical causes. . . ." If in the last sentence of this quotation we substitute for the word "fermentations" the words "the molecular reactions which occur within the cell," Hoppe-Seyler would, I think, have been equally justified.

Remembering, however, the great multiplicity of the reactions which occur in the animal body, and remembering the narrow specificity in the range of action of an individual enzyme, we may be tempted to pause on contemplating the myriad nature of the army of enzymes that seems called for. But before judging upon the matter the mind should be prepared by a full perusal of the experimental evidence. We must call to mind the phenomena of autolysis and all the details into which they have been followed; the specificity of the proteolytic ferments concerned, and especially the evidence obtained by Aberhalden and others, that tissues contain numerous enzymes, of

which some act upon only one type of polypeptide, and some specifically on other polypeptides. We must remember the intracellular enzymes that slit the phosphorous complexes of the cell; the lipases, the amylases, and the highly specific invert ferments, each adjusted to the hydrolysis of a particular sugar. We have also to think of a large group of enzymes acting specifically upon other substances of simple constitution, such as the arginase of Kossel and Dakin, the enzyme recently described by Dakin which acts with great potency in converting pyruvic aldehyde into lactic acid, and many others. Nothing could produce a firmer belief in the reality and importance of the specialised enzymes of the tissues than a personal repetition of the experiments of Walter Jones, Schittenhelm, Wiechowski, and others, upon the agents involved in the breakdown of nucleic acids; each step in the elaborate process involves a separate catalyst. In this region of metabolism alone a small army of independent enzymes is known to play a part, each individual being of proven specificity. The final stages of the process involve oxidations which stop short at the stage of uric acid in man, but proceed to that of allantoin in most animals. It is very instructive to observe the clean, complete oxidation of uric acid to allantoin, which can be induced *in vitro* under the influence of Wiechowski's preparations of the uric acid oxidase, especially if one recalls at the same time, in proof of its physiological significance, that this oxidase, though always present in the tissues of animals, which excrete allantoin, is absent from those of man, who does not.

I will not trouble you with further examples. We have arrived, indeed, at a stage when, with a huge array of examples before us, it is logical to conclude that all metabolic tissue reactions are catalysed by enzymes, and, knowing the general properties of these, we have every right to conclude that all reactions may be so catalysed in the synthetic as well as in the opposite sense. If we are astonished at the vast array of specific catalysts which must be present in the tissues, there are other facts which increase the complexity of things. Evidence continues to accumulate from the biological side to show that, as a matter of fact, the living cell can acquire *de novo* as the result of special stimulation new catalytic agents previously foreign to its organisation.

It is certain, from very numerous studies made upon the lower organisms, and especially upon bacteria, that the cell may acquire new chemical powers when made to depend upon an unaccustomed nutritive medium. I must be content to quote a single instance out of many. Twort has shown that certain bacteria of the *Coli-typhosus* group can be trained to split sugars and alcohols which originally they could not split at all. A strain of *B. typhosus* which after being grown upon a medium containing dulcitol had acquired the power of splitting this substance, retained it permanently, even after passage through the body of the guinea-pig, and cultivation upon a dulcitol-free medium. Similar observations have been made upon the Continent by Massini and Burri; the latter showed by ingenious experiments that all the individuals of a race which acquires such a new property have the same potency for acquiring it. No one, at the present time, will deny that the appearance of a new enzyme is involved in this adjustment of the cell to a new nutritive medium.

We have not, it is true, so much evidence for similar phenomena in the case of the higher animals. The milk-sugar splitting ferment may be absent from the gut epithelium before birth, and in some animals may disappear again after the period of suckling, but here we probably have to do with some simple alterna-

tion of latency and activation. But among the "protective" ferments studied by Abderholden we have, perhaps, cases in which specific individuals appear *de novo* as the result of injecting foreign proteins, &c., into the circulation. Consider, moreover, the case of the reactions called out by simpler substances. We have seen that an enzyme separable from the kidney tissue can catalyse the synthesis no less than the breakdown of hippuric acid. Now the cells of the mammalian kidney have always had to deal with benzoic acid or chemical precursors of benzoic acid, and the presence of a specific enzyme related to it is not surprising. But living cells are not likely to have ever been in contact with, say, bromo-benzol, until the substance was administered to animals experimentally. Yet a definite reaction at once proceeds when that substance is introduced into the body. It is linked up, as we have seen, with cystein. Now, this reaction is not one which would proceed in the body uncatalysed; if it be catalysed by an enzyme, all that we know about the specificity of such agents would suggest that a new one must appear for the purpose. I have allowed myself to go beyond ascertained facts in dealing with this last point. But once we have granted that specific enzymes are real agents in the cell, controlling a great number of reactions, I can see no logical reason for supposing that a different class of mechanism can be concerned with any particular reaction.

If we are entitled to conceive of so large a part of the chemical dynamics of the cell as comprising simple metaplastic reactions catalysed by independent specific enzymes, it is certain that our pure chemical studies of the happenings in tissue extracts, expressed cell juices, and the like, gain enormously in meaning and significance. We make a real step forward when we escape from the vagueness which attaches to the "bioplasmic molecule" considered as the seat of all change. But I am not so foolish as to urge that the step is one towards obvious simplicity in our views concerning the cell. For what indeed are we to think of a chemical system in which so great an array of distinct catalysing agents is present or potentially present; a system, I would add, which when disturbed by the entry of a foreign substance regains its equilibrium through the agency of new-born catalysts adjusted to entirely new reactions? Here seems justification enough for the vitalistic view that events in the living cell are determined by final as well as by proximate causes, that its constitution has reference to the future as well as the past. But how can we conceive that any event called forth in any system by the entry of a simple molecule, an event related qualitatively to the structure of that molecule, can be of other than a chemical nature? The very complexity, therefore, which is apparent in the catalytic phenomena of the cell to my mind indicates that we must have here a case of what Henri Poincaré has called *la simplicité cachée*. Underlying the extreme complexity we may discover a simplicity which now escapes us. If so, I have of course no idea along what lines we are to reach the discovery of that simplicity, but I am sure the subject should attract the contemplative chemist, and especially him who is interested and versed in the dynamical side of his subject. If he can arrive at any hypothesis sufficiently general to direct research he will have opened a new chapter of organic chemistry—almost will he have created a new chemistry.

It must not be supposed that I am blind to the fact that the phenomena of the cell present a side to which the considerations I have put before you do not apply. Paul Ehrlich, in his recent illuminating address to the International Congress of Medicine,

remarked that if, in chemistry, it be true that *Corpora non agunt nisi liquida*, then, in chemotherapy, it is no less true that *Corpora non agunt nisi fixata*. Whatever precisely may be involved in the important principle of "fixation" as applied to drug actions, it remains, I think, true that the older adage applies to the dynamic reactions which occur in the living cell. But there are doubtless dynamic phenomena in which the cell complexes play a prominent part. The whole of our doctrine concerning the reaction of the body to the toxins of disease is based upon the fact that when the cell is invaded by complexes other than those normal to it, its own complexes become involved. I must not attempt to deal with these phenomena, but rather proceed to my closing remarks. I would like, however, just to express the hope that the chemist will recognise their theoretical importance. He will not, indeed, be surprised at the oligo-dynamic aspects of the phenomena, startling as they are. When physico-chemical factors enter into a phenomenon the influence of an infinitely small amount of material may always be expected. It is a fact, for instance, as Dr. W. H. Mills reminds me, that when a substance crystallises in more than one form it may be quite impossible to obtain the less stable forms of its crystals in any laboratory which has been "infected" with the more stable form, even though this infection has been produced by quite ordinary manipulations dealing with the latter. Here, certainly, is a case in which the influence of the infinitesimal is before us. But what I feel should arrest the interest of the chemist is the remarkable mingling of the general with the particular which phenomena like those of immunity display. In the relations which obtain between toxin and anti-toxin, for example, we find that physico-chemical factors predominate, and yet they are associated to a high degree with the character of specificity. The colloid state of matter, as such, and the properties of surface determine many of the characteristics of such reactions, yet the chemical aspect is always to the front. Combinations are observed which do not seem to be chemical compounds, but rather associations by adsorption; yet the mutual relations between the interacting complexes are in the highest degree discriminative and specific. The chemical factor in adsorption phenomena has, of course, been recognised elsewhere; but in biology it is particularly striking. Theoretical chemistry must hasten to take account of it. The modern developments in the study of valency probably constitute a step in this direction.

It is clear to everyone that the physical chemist is playing, and will continue to play, a most important part in the investigation of biological phenomena. We need, I think, have no doubt that in this country he will turn to our problems, for the kind of work he has to do seems to suit our national tastes and talents, and the biologist just now is much alive to the value of his results. But I rather feel that the organic chemist needs more wooing and gets less, though I am sure that his aid is equally necessary. In connection with most biological problems, physical and organic chemists have clearly defined tasks. To take one instance. In muscle phenomena it is becoming every day clearer that the mechanico-motor properties of the tissue, its changes of tension, its contraction and relaxation, depend upon physico-chemical phenomena associated with its colloidal complexes and its intimate structure. Changes in hydrogen-ion concentration and in the concentration of electrolytes generally, by acting upon surfaces or by upsetting osmotic equilibria, seem to be the determining causes of muscular movement. Yet the energy of the muscle is continuously supplied by the progress of organic

reactions, and for a full understanding of events we need to know every detail of their course. Here then, as everywhere else, is the need for the organic chemist.

But I would urge upon any young chemist who thinks of occupying himself with biological problems the necessity for submitting for a year or two to a second discipline. If he merely migrate to a biological institute, prepared to determine the constitution of new products from the animal and study their reactions *in vitro*, he will be a very useful and acceptable person, but he will not become a bio-chemist. We want to learn how reactions run in the organism, and there is abundant evidence to show how little a mere knowledge of the constitution of substances, and a consideration of laboratory possibilities, can help on such knowledge. The animal body usually does the unexpected.

But if the organic chemist will get into touch with the animal, it is sure that the possession of his special knowledge will serve him well. Difficulties and peculiarities in connection with technique may lead the professor of pure chemistry to call his work amateurish, and certainly his results, unlike those of the physical chemist, will not straightway lend themselves to mathematical treatment. He may himself, too, meet from time to time the spectre of Vitalism, and be led quite unjustifiably to wonder whether all his work may not be wide of the mark. But if he will first obtain for us a further supply of valuable qualitative facts concerning the reactions in the body, we may then say to him, as Tranio said to his master:

"The mathematics and the metaphysics
Fall to them as you find your stomach serves you."

All of us who are engaged in applying chemistry and physics to the study of living phenomena are apt to be posed with questions as to our goal, although we have but just set out on our journey. It seems to me that we should be content to believe that we shall ultimately be able at least to describe the living animal in the sense that the morphologist has described the dead; if such descriptions do not amount to final explanations, it is not our fault. If in "life" there be some final residuum fated always to elude our methods, there is always the comforting truth to which Robert Louis Stevenson gave perhaps the finest expression, when he wrote:

"To travel hopefully is better than to arrive,
And the true success is labour."

UNIVERSITY AND EDUCATIONAL INTELLIGENCE.

LEEDS.—An anonymous donor has generously signified, through the Chancellor (the Duke of Devonshire), his intention of presenting to the University of Leeds the sum of 10,000*l.* for the erection of the much-needed building for the school of agriculture at the University. This gift will enable the University, in conjunction with the Yorkshire Council for Agricultural Education and with the help, it is hoped, of a grant from the Government, to provide without further delay the headquarters of agricultural education and research for the three Ridings of Yorkshire. The organisation of agricultural teaching in Yorkshire has been taken by the Board of Agriculture as the model for all other parts of England, and the rapid growth of the agricultural courses and the development of research in animal nutrition and other subjects have made it necessary to provide new buildings and laboratories on an extensive scale for the school