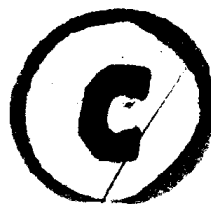


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SCIENCE NEWS

EDITED BY ARCHIE AND NAN CLOW

4I

PENGUIN BOOKS

FROM MAUVE TO MACROMOLECULES

PETER SYKES

THE celebration of centenaries has in recent times become something of an overworked cult; nothing has been too small to be overlooked; the year 1856, however, has a number of real claims. In this year Henry Bessemer invented his steel process which was to convert a comparatively rare metal into the staple of the then rapidly expanding railways and, no less important, William Henry Perkin prepared the first synthetic dyestuff, mauve. It can be said with some truth that the vast organic chemical industry of today stems from this beginning.

THE DISCOVERY OF MAUVE

In 1856, Perkin was an eighteen-year-old research assistant at the recently founded Royal College of Chemistry in London, working under its Director, A. W. Hofmann, who had himself been a pupil of the great Justus von Liebig. Perkin had fitted up a small laboratory at his home and during the Easter vacation of 1856 was attempting to synthesize the alkaloid quinine. The molecular composition of quinine was known, but nothing at all about its actual structure; in fact, at this time structure, implying the pattern in which the various atoms are arranged in a compound, had not been recognized in organic chemistry at all, so it is hardly surprising that Perkin was unsuccessful in his endeavour. Quinine was not, in fact, synthesized till 1945. Turning to the study of simple bases, however, he tried the oxidation of aniline sulphate with potassium dichromate and found that it resulted in the formation of a black precipitate. On further investigation of this rather unpromising material he was able to isolate from it the bright colouring matter since known as aniline

purple or more frequently by its French name mauve. Perkin soon discovered that mauve could be used as a dye, and the next year he established a small factory at Greenford Green, near Harrow in Middlesex, and began to make it on a commercial scale. During the next eighteen years Perkin had a highly successful career as a chemical industrialist, but in 1874 he retired to devote himself to fundamental research. During this period the majority of the important advances in dye chemistry were made in Britain; after 1874, however, the initiative in the dyestuffs industry, and indeed in the organic chemical industry in general, passed to Germany; Caro, the technical director of the great chemical firm, Badische Anilin und Soda Fabrik, being in no small measure responsible.

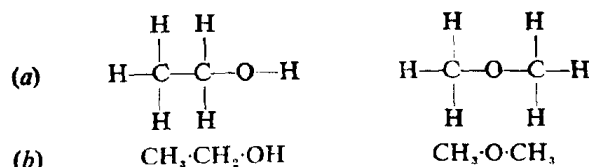
ORGANIC CHEMISTRY IN 1856

As a result of the work of great pioneers such as Wohler, Dumas, and Liebig, a number of organic compounds had been identified and the idea of a special 'life-force' attached to substances derived from animal and plant material had been abandoned. Organic chemistry, previously the chemistry of such naturally derived substances, was becoming rather more generalized as the chemistry of the compounds of carbon. There had been a number of attempts by chemists at arranging organic compounds into groups that reflected particular properties they had in common, but there remained the puzzling phenomenon that it was possible to have two compounds of the same molecular composition (i.e., giving the same analytical results) yet which differed widely in their observed properties – the phenomenon of isomerism. What was still lacking was the concept of structure or spatial arrangement of the atoms in a molecule, and the idea that it was this characteristic arrangement that was responsible for the observed chemical properties of a compound.

STRUCTURE IN ORGANIC CHEMISTRY

The first clue to this concept of molecular architecture was supplied by Frankland in 1852 with his idea of valency, or com-

binning power; this combining power of atoms of an element being limited in extent though not necessarily constant for each element. The twin foundations on which structural organic chemistry was built were the quadrivalency of carbon, and the highly developed ability that carbon atoms have of combining with themselves as well as with other atoms. It was then possible for Kekulé in 1858 (at that time a Professor at Ghent) to put forward suggestions for representing the actual structures of organic substances; these were simplified in 1861 by Professor Crum Brown of Edinburgh, and the same type of structural formulae are still used today, though in a slightly more simplified form.



Formulae of ethyl alcohol and dimethyl ether (a) according to Crum Brown, (b) as represented today.

Figure 1. Isomers of $\text{C}_2\text{H}_6\text{O}$.

The advantages of being able to write such structural formulae are numerous. It is possible to see at a glance that two different structures and no more, those of ethyl alcohol and dimethyl ether, can be written for compounds that contain two atoms of carbon, one of oxygen, and six of hydrogen; all that has to be remembered is that the valency of carbon is four, that of oxygen two, and of hydrogen one. In other words, the phenomenon of isomerism becomes readily understandable. Further, such formulae enable one to see readily the relation between different compounds and how they may be converted one into the other by the direct replacement of single atoms or small numbers of atoms arranged to form specific 'functional' groups, e.g., $-\text{OH}$, $-\text{CO}_2\text{H}$, and so on.

A special structural problem was raised by the so-called aromatic compounds related to benzene, C_6H_6 ; these were found

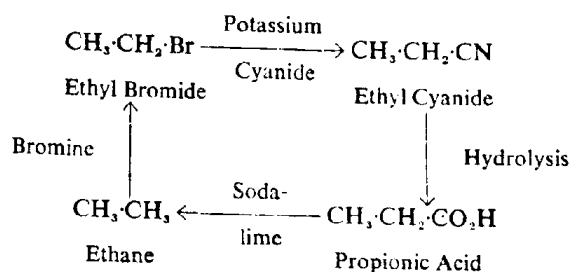
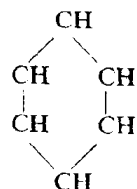


Figure 2. Structural formulae illustrating the interconversion of a series of compounds.

to have a peculiar stability and were noteworthy for the persistence of a group of six carbon atoms through reactions of the utmost vigour. Again Kekulé, in 1865, supplied the clue by suggesting that the six carbon atoms were joined together in a ring:



Original Kekulé formula for benzene

This was objected to, however, on the grounds that the carbon atoms were tri- instead of quadri-valent. Controversy over this particular point has continued into recent times and has only been satisfactorily settled by X-ray and other physical methods which have measured and charted the benzene molecule exactly; in essentials Kekulé's idea was perfectly correct.

The last vital principle of chemical structure was laid down in 1874 by Van't Hoff (of the veterinary school at Utrecht) and Le Bel, who together suggested that organic molecules are three-dimensional and that the four valencies of carbon atoms are distributed symmetrically in space or, in more concrete terms, that a carbon atom can be represented by a tetrahedron with its

valencies emerging from the four vertices. This contribution to chemical theory was ultimately recognized by the award to Van't Hoff in 1901 of the first Nobel prize for chemistry.

The fundamental theoretical principles of structural organic chemistry now being established, the next requirement was the development of general methods for converting one type of organic compound into another. The second half of the nineteenth century saw the development of a wide variety of such methods, the vast majority of which are still in use. These methods are the life-blood of synthesis, of the building up of larger molecules from smaller ones. The great source of raw materials upon which much of this synthetic organic chemistry depended was the coal gas industry which produced as a by-product to gas considerable quantities of coal tar. This dependence was particularly marked in the case of the synthetic dyestuffs industry.

SYNTHETIC DYESTUFFS AFTER MAUVE

Perkin's discovery of the first coal tar dye, mauve, rapidly led to great developments in the dye industry, because few of the natural colours then available were fast to light and wear. At first the search for new colours was largely a haphazard affair of reacting one substance with another to see what resulted; by the mid 1870's, however, largely owing to the work of Emil and Otto Fischer, the molecular structure of a number of now important synthetic dyestuffs had been worked out. It then became possible to proceed in a more systematic fashion by making known modifications in these structures in order to study the effect this had on the colour and dyeing properties of the new compounds. Wider ranges of colour and much brighter tints were thus produced, and it was also found possible to convert a number of attractive pigments into useful dyestuffs by making them soluble in water, this being achieved by the introduction into their molecules of sulphonic acid (SO_3H) groups.

Once the new industry had found its feet, attention was turned to the possibility of synthesizing some of the more important natural dyestuffs, in particular madder and indigo. Both these

had been in use continuously since ancient times and were important items in trade. Red madder was obtained from the root of the madder plant (*Rubia tinctoria*) and its coloured principle was called alizarin. The problem of the structure of alizarin was taken up by Graebe and Liebermann, then working in Baeyer's laboratory in Berlin, and in 1868 they were able to synthesize it; this being another landmark in synthetic chemistry – the first synthesis of a naturally occurring colouring matter. Their first method of synthesis involved the use of bromine, which was then still very expensive, and the method could not therefore be exploited commercially. The next year, however, both they and Perkin, working independently, devised alternative methods, and synthetic alizarin was on the market in 1871. In 1873 nearly 1,500 tons of synthetic alizarin were produced and by 1878 the price had dropped from £50 to £10 a ton; within a short time it supplanted the natural product entirely; a change not without its social consequences.

The next great triumph of the synthetic chemist was the production of indigo. Almost all the nitrogen-containing dyestuff indigo came from plantations of *Indigofera tinctoria* and *Polygonum tinctorium* in India and Java. It was greatly valued on account of its fastness. Its structure was established by Baeyer in 1883, but the problem was much more difficult than that of alizarin and it took in fact some eighteen years to solve. Baeyer developed two different syntheses, but neither was suitable for commercial exploitation. An economic process had to wait for supplies of cheap chlorine, ammonia, acetic acid, and other developments in the heavy chemical industry, and it was not until 1897 that synthetic indigo began to compete effectively with the natural product; the consequent decay of the indigo plantations was very rapid.

The most prized dyestuff of antiquity was the purple of Tyre that was used to colour the robes of the Roman emperors. This dye was derived from a small mollusc (*Murex brandaris*) found particularly on the coast of the Eastern Mediterranean. In 1911 Friedlander dissected over 12,000 molluscs and so collected 1.4 grammes of the dye; working with this sample he discovered

that it was a bromine-containing derivative of indigo, but he had to synthesize three of these before hitting on the right one. Tyrian purple is no longer of any commercial importance as superior dyes of the same colour are now available.

Another use found for the synthetic dyestuffs was in replacing natural colours used in the laboratory as biological stains. In the 1880's bacteriology was just becoming a science, largely owing to the work of Koch. Most of the difficulties experienced by the early workers were in matters of technique, not least in making micro-organisms readily visible under the microscope; they are quite large enough to be seen, but being transparent are very difficult to define. They will, however, readily soak up a number of dyestuffs and their different parts can then be delineated clearly in contrasting colours.

Up to the present day the search for new dyestuffs has hardly slackened, one of the main reasons being the introduction of new textile fibres. It is rare for a dyestuff to be fast on all fabrics, the division coming particularly between colours for animal fibres such as silk and wool on the one hand and vegetable fibres such as cotton on the other. The introduction of the artificial silk posed many new problems, and the more recent development of truly synthetic fibres such as nylon and terylene of very low chemical reactivity has involved the invention of entirely new techniques for dyeing them satisfactorily.

The more systematic approach to the production of new colouring matters prompted the theoretical study of the relationship between the colour of compounds and their chemical constitution; a problem that still excites a good deal of interest, though it has now become rather more general in its terms. Thus substances are coloured because they absorb light of certain wavelengths, the actual colour of the compound differing according to the wavelengths absorbed. All compounds, however, absorb radiation in this way, though with colourless substances the absorption is of wavelengths that lie outside the visual range. Thus the presence of colour or otherwise is seen to be only part of a larger problem, the relation between chemical constitution and the absorption of radiant energy. A study

of this relationship has proved of the utmost value in assigning tentative structures to compounds of unknown constitution on the basis of measuring their light absorption.

THE INVESTIGATION OF NATURAL PRODUCTS

Although in the second half of the nineteenth century the investigation of natural and synthetic dyestuffs absorbed a good deal of the time and skill of organic chemists, other lines of research were also developed. Attention was turned to products of natural origin in general, but especially to those believed to be involved in life processes. The fact that such a trend was even remotely possible gives some idea of the progress that had been made by the 1880's – the idea of chemical constitution, i.e., of the orderly pattern of molecular structure, was by then clearly established and a wide variety of degradative and synthetic methods of great power had been developed; the time was ripe for great advances.

The man of genius to appear was Emil Fischer, perhaps the greatest experimentalist in organic chemistry to date. In 1884, Fischer decided to investigate the carbohydrates. These had previously received very little attention largely owing to the great experimental difficulties encountered in working with them. Almost the only way of separating and purifying solid substances at this time was by repeated crystallization, a method that works admirably and is still much used, but many carbohydrates form uncrystallizable syrups, making their separation and purification by this means difficult if not impossible. Fischer entirely changed the position by the introduction of phenylhydrazine, $C_6H_5NHNH_2$, a substance which he had himself first prepared in 1875. Phenylhydrazine forms highly crystalline derivatives with most sugars, and it proved to be the keystone in Fischer's phenomenal work on the characterization and synthesis of the carbohydrates. Thus he laid an extremely firm foundation on which all subsequent work in this field has been squarely based.

As if this were not enough, in 1899 Fischer turned his attention to the other important group of substances of biological

importance, the proteins. The experimental difficulties here are even greater than with the carbohydrates, for many are non-crystalline and most of them undergo at any rate partial decomposition during the course of attempts to purify them.

When he started work some amino-acids (compounds containing $-CO_2H$ and $-NH_2$ groups) were already known to be constituents of proteins, but Fischer went very much further in breaking down proteins into their constituent amino-acids, and invented elegant ways for separating the extremely complicated mixtures that resulted. Having followed the analytical approach as far as he was able, he turned to synthesis, the recombination of the amino-acid residues once again. He demonstrated the significance of the peptide ($-NH-CO-$) linkage in protein structure and was able to synthesize a number of compounds containing several amino-acids joined together, which he named polypeptides. Since Fischer's time proteins have been investigated in very much greater detail and many experimental methods of great ingenuity and elegance have been invented for dealing with them; but, as with the carbohydrates, Fischer's classical work laid the foundation. For his work he was awarded the Nobel prize for chemistry in 1902.

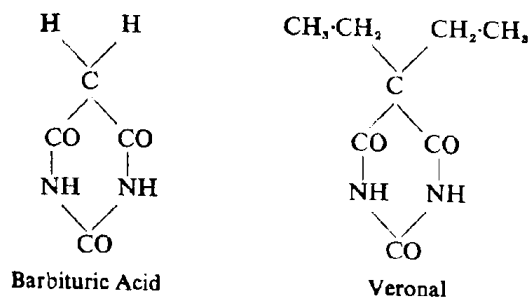
The ensuing years have seen the investigation of many diverse groups of natural products including the green colouring matter of plants, the chlorophylls (largely by Willstätter in Munich, for which he was awarded a Nobel prize in 1915), the essential oils and odoriferous principles of plants – the terpenes, not forgetting vitamins, hormones, and many others. Particular attention has also been devoted to the investigation of therapeutically active substances, both naturally occurring and synthetic compounds made in the laboratory.

CHEMOTHERAPEUTICS

Until very recent times most of the drugs used in medical practice were merely symptom relievers – analgesics, temperature-reducers, function-controllers, etc., which did not influence the actual causes of most diseases at all. Not surprisingly, therefore, attention was first turned to the synthesis of improved drugs of

this type. Early successes included the synthesis of the anti-pyretic, phenazone, by Knorr in 1883, phenacetin in 1887, and the introduction of aspirin in 1899. Attempts were next made to establish a relation between the chemical constitution of a group of compounds and their physiological activity, but though it has been possible to establish such a correlation in a number of relatively restricted fields, the main problem remains unsolved; there has been nothing like the same degree of success as that achieved in establishing the relation between colour and constitution. Thus a study of the structure and physiological effects of local anaesthetics led Einhorn and others to the synthesis of extremely effective drugs to replace the natural cocaine, which itself has a number of undesirable side-effects; but similar studies and the synthesis of many, many thousands of substances has only led to a partial solution of the problem of finding a substitute for morphine – a notorious drug of addiction – for use in the relief of deep-seated muscular pain.

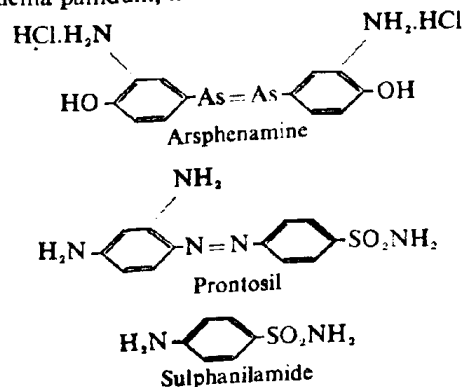
The group in which we know most about the correlation between structure and physiological activity is undoubtedly the Barbiturates, derivatives of barbituric acid, the first important example of which, veronal, was made by Emil Fischer in 1903:



By suitable modifications of structure it is possible to produce anything from the lightest of sleeping pills to the profoundest depression of consciousness, and also to vary considerably the rapidity of onset of action. Thus some soluble barbiturates,

administered by injection, produce immediate unconsciousness, while others may only begin to act after several hours.

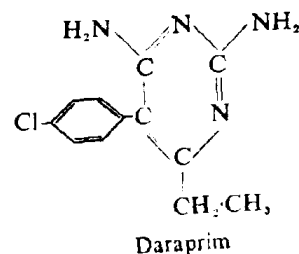
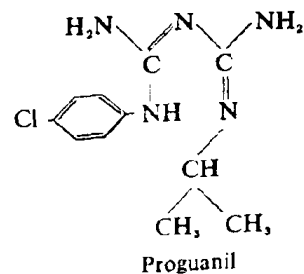
But a more important development was the production of remedies that cured diseases by acting directly on the micro-organisms responsible rather than acting merely by the relief of symptoms. The greatest figure in this field was Paul Ehrlich. Ehrlich did much of his work in Frankfurt, where a Paul Ehrlich Chair of Chemical Therapy was founded in his honour at the centenary celebrations of his birth in 1954. Ehrlich was impressed by the way that many bacteria would take up dyestuffs into their substance in the ordinary course of staining to render them visible under the microscope, and his aim was the production of toxic substances that would be taken up selectively by harmful bacterial cells while leaving human tissue cells unharmed. He was fortunate in having the opportunity of setting up a new type of scientific institution – the Georg Speyer Haus – in which chemical, biological, and medical work could be carried out side by side and in close collaboration. One of the most important results of this then novel approach was the production in 1911 of '606', or salvarsan (arsphenamine), the first substance discovered to have any real effect in the treatment of syphilis. The achievement lay in reducing the toxicity of arsenic to human tissue cells while at the same time retaining its toxicity to *Treponema pallidum*, the causal agent of the disease.



This first great success in chemotherapeutics has led to an ever intensified search for new specific remedies. Much of the earlier work was directed at tropical diseases and it was not until the 1930's that Domagk, working in the I.G. laboratories in Wuppertal-Elberfeld, showed the effect of Prontosil on streptococci, thus opening the way to the treatment of septic conditions produced by this group of bacteria. Trefouel of the Institut Pasteur showed that the antibacterial properties of Prontosil were due to its degradation in the tissues to sulphanilamide which was the physiologically active agent. Modifications of sulphanilamide have led to the extensive sulphonamide or sulpha group of drugs. For his part in the work Domagk was awarded the Nobel prize for Medicine in 1939.

In chemotherapy, however, perhaps most attention has been devoted to anti-malarial drugs. Malaria is unusual in that a natural specific remedy is available in the form of quinine; nevertheless this is by no means an ideal drug for the treatment of the disease. In consequence several hundred thousand substances have been produced and tested for anti-malarial activity, though only a handful of these have passed into clinical use. These include Pamaquin and Mepacrine (synthesized in Germany in 1926 and 1931 respectively), and the more satisfactory Proguanil produced in 1944 by Curd, Rose, and Davey of I.C.I. as the result of a prolonged investigation, in which, in a very long series of compounds, they tried to correlate chemical structure and anti-malarial activity. Investigations into the possible mode of action of Proguanil led in 1951 to the production in the Wellcome laboratories of another extremely effective anti-malarial, Daraprim.

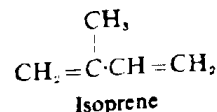
Further research has led to effective chemotherapeutic agents for the treatment of leprosy, tuberculosis, and many other diseases, but, following the discovery of Penicillin, perhaps the most rapid progress has been made in the field of therapeutically active substances produced by micro-organisms themselves, the so-called anti-biotic drugs. Here, however, synthesis has tended to lag behind and, though the chemical structure of many of these substances has been worked out, most of them have still



to be produced from their parent micro-organisms by fermentation processes. Thus it has not been possible in this field to make small controlled changes in the structure of the molecules in order to study the relation between structure and constitution, and most new discoveries have been restricted to screening vast numbers of micro-organisms to find out if they produce anything useful.

THE SEARCH FOR SUBSTITUTES

One of the most useful natural materials is rubber and as early as 1860 tentative experiments were being made to elucidate its composition; thus in that year the hydrocarbon isoprene was isolated by its destructive distillation.



It was soon discovered that rubber was a giant molecule, or polymer, made up by the joining together of many isoprene units in chains. It was also found that isoprene units could be made to join up comparatively readily to yield material with some resemblance to natural rubber. Further efforts were then made to polymerize isoprene and other similar small molecules to make synthetic rubbers that would be acceptable to commercial users. These efforts were intensified in Germany during the 1914-18 war, when supplies of the natural material from S.E. Asia were cut off, and also in the United States during the between-wars period. The raw materials tried were frequently derived from natural gas, or from the first fractions of oil refining, usually after these fractions had been 'cracked' into smaller molecules by the action of high temperature, pressure, and catalysts. This marks an important turning point, the change-over during the last twenty years or so from coal tar to petroleum as the great source of raw materials in industrial organic chemistry with the consequent founding of a great petrochemical industry. Today a very wide variety of synthetic rubbers is available, many of which are better than the natural material for doing specific jobs, though single substances with good all-round properties are still rare.

Much of the twentieth-century search for substitute materials has dealt with polymeric substances of a broadly similar nature. Thus a wide range of plastic materials are made from starting materials similar to those used for synthetic rubber, their actual properties being determined not only by the type of small molecules used to build them up but also by the length of the chain-like aggregates so built and the extent to which these chains remain free or are linked across from one to another in a more or less rigid three-dimensional aggregate or lattice. Perhaps the most interesting development in plastics to date is the production of transparent materials, some of them with interesting optical properties.

Also closely related is the field of artificial fibres. In the 1880's work began on the production of a cheap substitute for silk by dissolving a suitable natural polymer such as cellulose and

extruding the solution through a small hole to form a fibre. Artificial silk processes are still variants on this theme, the cellulose generally being obtained from wood pulp. There have also been a number of endeavours to make artificial wools, the latest utilizing the protein from ground-nuts as a polymeric raw material for the production of Ardil.

Most progress, however, has been made in the production of truly synthetic fibres in which a polymerization progress is carried out, starting with small molecules as raw materials. There are many examples of these, the best known being Nylon and Terylene. The former was produced after many years' work by the American chemist Carothers on the protein of natural silk. It is made from adipic acid and hexamethylene diamine (both derived from phenol obtained from coal tar) and resembles a protein in that it contains the characteristic peptide ($\text{CO}\cdot\text{NH}$) linkage. Terylene was obtained from terephthalic acid and ethylene glycol by the British chemist Whinfield in 1946. As textile fibres, both possess extremely good all-round properties.

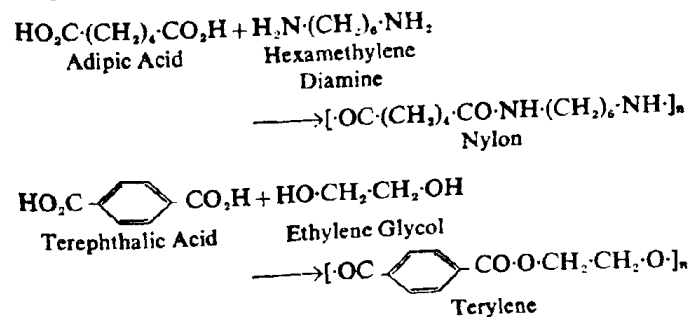
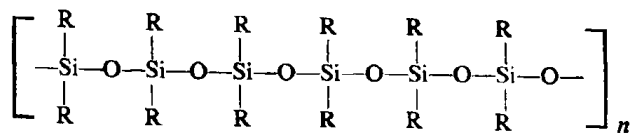


Figure 3. Two synthetic fibres.

By far the most interesting recent development in synthetic polymeric materials, however, has been the production of the silicones. These differ from all the materials mentioned so far in that they do not contain chains of carbon atoms, but chains of

alternate silicon and oxygen atoms with short branches of carbon atoms attached.



A Silicone ($\text{R} = \text{A small group of carbon atoms}$)

Owing to the presence of the $\text{O}-\text{Si}-\text{O}$ linkage these substances have much greater heat stability than carbon compounds and they can be obtained in a wide variety of physical forms, e.g., oils, resins, rubbers, etc., with an almost infinite variety of properties. They are without doubt the most versatile family of synthetic polymers made to date.

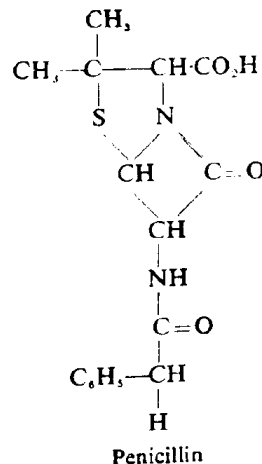
AIDS TO THE STUDY OF ORGANIC CHEMISTRY

One of the most important general advances in organic chemistry this century has been the development of micro-methods of elementary analysis by Fritz Pregl of Graz, for which he was awarded the Nobel prize for chemistry in 1923. These were combustion methods following the lines that had been laid down by Liebig in which the carbon content of the compound is converted to carbon dioxide, the hydrogen to water, and both are weighed. Pregl's contribution was to adapt the method so that it could be used on a sample of only a milligramme or two, thus making possible analyses of many substances obtainable only in traces from biological material. Today these methods are used as routine practice in laboratories all over the world, and are indeed the very foundation of all research work.

The last few years have also seen a revolution in the methods available for that salient operation in organic chemistry, the separation and purification of substances. These methods, which include selective adsorption on, and elution from, alumina, paper, and ion-exchange resins, and also much refined, and mechanized, techniques for the partition of substances between solvents, have led to feats of separation and isolation of minute

traces of material, for example, minor constituents of exceedingly complicated mixtures, that were quite outside the range of credibility only a few years ago.

Another valuable aid in the elucidation of the structure of organic compounds has been the study of spectra. Thus X-ray photographs can lead to the assignment of definite positions to each and every atom in crystals of a substance, as has in fact been achieved in the case of Penicillin in 1945 and Vitamin B_{12} in 1955, but the labour of calculating the results can be extremely tedious, and this method is not as yet suitable as a day-to-day laboratory aid to structure determination.



Ultra-violet spectroscopy gives an absorption pattern that is characteristic of the molecule as a whole, similar types of compound showing similar patterns of light absorption. Infra-red spectroscopy gives a very much more complicated pattern of absorption in which individual 'peaks' in the pattern correspond to the presence in the compound of particular linkages between atoms, thus the carbonyl group ($>\text{C}=\text{O}$) shows absorption at very much the same point in the spectrum irrespective of the nature of the compound in which it is contained, while the

azo linkage ($-\text{N}=\text{N}-$) also shows absorption at a constant though different place in the spectrum.

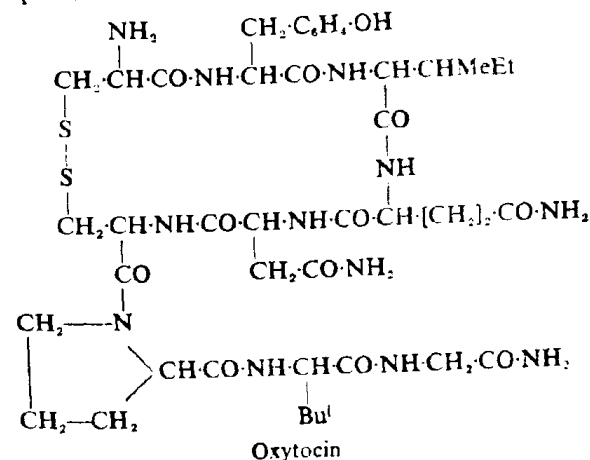
This means that when a new natural product has been isolated, instead of having to start on the elucidation of its structure entirely 'in the dark', a study of its spectra will often indicate not only the class of organic compounds to which it belongs but also suggest some of the characteristic functional groups that are present. The elucidation of structure may thus be accomplished in part before actual degradative and analytical chemical reactions are begun, and when these reactions are started those most suitable for the particular problem can be selected without their having to be found out first by a laborious process of trial and error. Another very useful technique has been the application of radio-active tracers in which radio-active 'labelled' atoms are introduced into molecules. In this way information has been obtained about the actual mechanism by which reactions between compounds take place and also about biological problems such as the pathways of metabolism in organisms and the effect of drug molecules on cells.

RECENT ACHIEVEMENTS

The application of such aids to organic chemistry, coupled with the devising of ever more delicate methods of synthesis, has led to some remarkable achievements, not only in elucidating the structure of naturally occurring compounds and subsequently synthesizing them, but also in making very many compounds that are unknown in nature, sometimes on account of interest in their utility, but more often in order to investigate the particular reactivity exhibited by their 'unnatural' structures. One of the most important developments this century has been the movement towards establishing the relationship between the chemical structure of a substance and the properties it exhibits; much remains to be done but no little progress has been made towards forecasting the properties of a compound before it has actually been prepared.

This conjunction between refined experimental methods and a rapidly developing theoretical interpretation of the reactions

of organic compounds has led to some very notable feats in the last few years; as, for instance, the total synthesis of strychnine by Woodward at Harvard and the establishment of the structure, followed by the synthesis, of the pituitary hormone, oxytocin, by Du Vigneaud of Cornell, for which he was awarded the Nobel prize.



This last century has seen the establishment of a set of working rules in the light of which organic chemistry is at present carried on; it is probably true to say that the majority of the main guiding principles in this branch of science have by now been laid down. Not a few of these guiding principles remain somewhat empirical, however, and there still remains the need for a more fundamental background to organic chemistry. This is, in part, being supplied by modern theoretical work on the combination of atoms, and groups of atoms, to form compounds. It is becoming ever more possible to postulate, on theoretical grounds, which molecules, because of their inherent instability, chemists will be wasting their time in trying to make; this will be a refreshing change from only finding it out in the laboratory after long and arduous endeavour ending in failure.

There has been recently a turning more and more to the

chemistry of biological systems, and notable successes have been achieved. There is, however, a change of attitude from the old days; chemists are certainly going on isolating new substances from natural sources, and many of them have proved of the utmost value in medicine and in other fields, but there is an increasing tendency to study chemical process *in situ* in living material, and to try to find out just how living cells accomplish their staggeringly complex chemical reactions. The fact that such a course can even be contemplated is some indication of the progress that has been made in the last decade or so. With the present signalized by such achievements it will be more than interesting to see what the next century will bring.

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WHY ARE CHILDREN BORN DEFORMED?

DAVID H. M. WOOLLAM and JAMES W. MILLEN

CHEMO-THERAPEUTIC drugs and modern methods of infant management have greatly reduced the number of deaths in infancy from infectious disease. In consequence, an increasingly large proportion of deaths occurring in infancy and early childhood are to be attributed to the more severe congenital defects of the infant heart and brain which allow only of a brief and precarious existence. Moreover, with each improvement in infant welfare the expectation of life of the physically deformed or mentally handicapped child has increased, so that today research into the cause of congenital malformations is a peculiarly pressing necessity.

In the sixteenth century families were large, but only one in three children survived infancy. Today there is a general expectation that a child will be born in a normal state and will survive to reach a healthy maturity. For social and economic reasons families tend to be limited to one, two, or three children, and, in these circumstances, the birth of a deformed child is a calamity that creates repercussions far beyond the immediate event. Even if the child is still-born, its birth tends to deter the parents from having further children lest they too be deformed. Although this fear is generally groundless, it does have some effect in reducing the size of families and increasing the number of only children. Should the child survive, the parents are frequently burdened with problems of finance and maintenance which can only be eased in a tragic fashion by the loss of the child. The community also has to make considerable financial provision for the rearing and education of congenitally handicapped children. Perhaps the most unfortunate of all the results

of the birth of such a child is, however, the assumption, frequently made but not proved scientifically, that its appearance must be due to the presence of a hereditary taint in the family of one or other parent or in both. It is true that genetic considerations can never be ignored when any biological process is under consideration; their significance can, however, be overstressed, and it is the purpose of this article to marshal the known facts which suggest that factors in addition to genetic ones are at work in the production of congenital malformations.

GENETICS AND MALFORMATION

The belief that congenital malformations always depend upon hereditary factors comes naturally to the lay mind, which observes the occasional appearance of several cases in one family and draws what appears to be the obvious conclusion. That Mendel's laws of inheritance applied to man became evident as long ago as 1905, when Farabee in America studied the occurrence of *brachydactyly* (congenital shortening of the fingers) in three families and found the condition in half the members, a clear suggestion of a dominant inheritance. At one time, in the absence of knowledge of any other factors that might produce congenital malformations, it was confidently expected that all deformities of the new-born would eventually be explained on a genetic basis. It does not, however, necessarily follow that, because more than one member of a family shows a congenital deformity, only hereditary factors are at work. Members of a family share more in common than their heredity: they tend to live in a similar environment and to eat the same food. In mountainous districts far from the sea, such as the Swiss Alps, a considerable number of children are born with *goitre* (swelling of the thyroid gland) or with the combination of severe mental and physical defects that together constitute the condition of *cretinism*. At first sight it might appear that the birth of these children in isolated families living in remote regions of the world was the result of a hereditary taint whose effect was enhanced by the close inbreeding invariably found in such enclosed societies. It has been conclusively shown, however, that the occurrence of

these diseases results from the very low iodine content of the soil in mountainous areas, and that the children are the victims of a deficiency of iodine in the diet.

It is of some significance to note that nearly all the conditions affecting human beings in which a strong hereditary basis for the deformity has been firmly established are those in which the deformity, however disabling or unsightly, does not produce death in infancy or childhood. This would be expected on the theory of Natural Selection, because families in which large numbers of handicapped children were born would tend to die out through failure of the young to survive to the age when they could reproduce their kind. This fact and the possible significance of environment must be borne in mind when we consider the information that is available about the family background of the congenitally deformed.

Statistics of congenital malformations, scanty as they are, do show certain trends which are inexplicable on grounds of heredity alone. Thus there is a tendency for malformed children to be born to mothers who are older than average, and, moreover, the later-born children of a family are more likely to be deformed than earlier ones. In addition, deformed children tend to appear after a period of relative sterility of the mother, and women who give birth to such children tend to have more miscarriages, still-births, and premature births than would be expected by mere chance. It has also been suggested that there is a higher incidence of congenital malformations in the lower social and economic strata of the community. All these findings suggest that some factor other than heredity must be at work in determining the birth of a deformed infant.

What can this factor be? If it is not present in the male and female germ cells, which combine to produce the fertilized egg from which the child develops, it must obviously be operating in the environment of the developing embryo. What then does the embryo require to ensure that it develops in the normal manner? It needs security of tenure in the uterus for nine months, an adequate supply of nutriment and oxygen, and freedom from injury by any disease process or other noxious agent

to which the human body is vulnerable. If any of these requirements is lacking, the development of the embryo will be interfered with, and, if the interference is sufficiently severe, it will die.

It is perhaps difficult to grasp that, from the reproductive point of view, the birth of a congenitally deformed child represents not a disastrous failure, but something that can best be described as a near success. If conditions are for some reason totally unfavourable the mother will not conceive at all. If they are slightly less unsuitable, she will conceive but will then proceed to abort or cast out the foetus early in pregnancy. It is interesting to note in this connexion that it has been suggested more than once that most aborted embryos are congenitally deformed. With still less unfavourable conditions the embryo will continue to develop in its mother's womb for nine months, but will then either be still-born, born congenitally deformed, or will thrive but poorly after a normal birth. It is only when conditions are entirely favourable that the birth of a normal healthy child results.

DIETARY INFLUENCES

The sequence of such a process is perfectly illustrated by what happens when a female animal is exposed to starvation. A starving female will not conceive. When a female rat is subject to starvation in early pregnancy, the young are either aborted or reabsorbed into the mother's body. If the starvation occurs later in pregnancy, the young are either still-born or, if born alive, are weak and puny and survive only with difficulty. This suggests that a most important prerequisite for the development of a normal healthy child is that the mother should receive throughout her life an ample diet containing adequate quantities of all essential foodstuffs, so that there can be no question of her suffering during pregnancy from any dietary deficiency. There is now a large volume of evidence that nutritional deficiencies in the mother can, in animals other than man, bring about the birth of congenitally malformed offspring. In an investigation in Philadelphia there was some evidence of an inadequate diet in

forty per cent of the families in which deformed children were born. If a deficient diet does operate in this way in the human, it is doubtful whether the fact that it does can ever be established scientifically. A laboratory animal like the rat starts to breed when it is a few months old, has several litters of five to nine a year, and can be fed throughout life on an artificial diet of known constitution designed to contain every essential ingredient except the one under investigation. The nutritional study of a human female who has had twenty years or more on a self-chosen diet before producing a small family singly at relatively long intervals is virtually impossible. Again human diet is so varied that single dietary deficiencies rarely occur, and, since we know from animal experimentation that it is relatively minor degrees of deficiency of a single vital element that are liable to result in the birth of deformed young, it is unlikely that clinical cases in the human being will ever be encountered which fulfil the criteria of a scientific experiment.

It must not be concluded, however, that the study of nutritional deficiencies in other animals has no importance in relation to the problem of congenital malformations in man. Although it may be impossible to detect these minor degrees of deficiency in the human being, if they do in fact occur, much information might be obtained from studying human social groups in which everything possible has been done to ensure their absence, and by comparing the incidence of congenital malformations with that in less favoured groups. In view of this, the results of nutritional experiments in animals have, as well as an intrinsic scientific value of their own and a considerable importance to animal husbandry, a positive significance in relation to the problem of congenital malformations in man.

It has been found that, if the birth of deformed young is to be avoided, the presence of a wide variety of substances in the diet is essential. Mineral deficiencies, notably those of copper and iodine, have been thought to be of much importance, but at the present moment it is deficiencies of vitamins that appear to be of the greatest significance. Of the vitamins, vitamin A and the various members of the B group seem to be most essential, and

the most unequivocal and dramatic proof of the importance of adequate nutrition in preventing the birth of abnormal young has come from experiments in which the mother has been deprived of vitamin A. What is perhaps even more significant is that in experimental vitamin A deficiency most of the congenital abnormalities commonly occurring in man have been faithfully reproduced in the experimental animal. Thus the young of laboratory animals fed on a diet deficiency in vitamin A exhibit congenital defects of the heart, cleft palates, maldeveloped limbs, and hydrocephalus or 'water on the brain'. These are among the commonest congenital deformities in man, and at one time or another have all been explained on a hereditary basis.

EXPERIMENTAL MALFORMATION

One of the main difficulties in nutritional experiments is that the number of deformed young born, although highly significant, generally represents such a small proportion of the young born to the deficient mothers that large colonies of animals have to be kept to obtain a relatively small number of young for study. Again, since these conditions are produced by a slight rather than a severe degree of maternal deficiency, it has long been difficult to reproduce a congenital defect by nutritional experiments, and the whole process has been tedious and costly. A striking example of the difficulties inseparable from work of this kind has been provided by Warkany. He found that he could increase the yield of abnormal young by adding fresh meat to the diet. Thus the apparently paradoxical situation arose that it was possible to increase the yield of abnormal young by improving the diet. The explanation is quite simple. The rats on the richer diet have a better reproductive performance; they do not abort abnormal young; they have bigger litters and so give a higher yield of deformed young. This is another illustration of the point previously made that the birth of a congenitally deformed offspring is to be regarded, not so much as a failure, but as a reproductive near-success.

Two years ago we found that hydrocephalus or 'water on the brain', one of the commonest congenital abnormalities in man,

occurred frequently in the young of female rabbits living on a vitamin A deficient diet. In order to study this condition we set up a colony of 50 unrelated female rabbits and fed them for varying periods before mating on a diet deficient in vitamin A. During the period of two years 180 young, representing seventy per cent of those born in the colony, have been found to have 'water on the brain'. The occurrence of this deformity in the rabbit provides, by virtue of its constant and relatively easy reproducibility, a very satisfactory method of investigating the mechanisms by which dietary deficiencies produce congenital malformations.

From the study of this colony over a period, during which some of the mothers have had up to four litters, it has been possible to formulate certain general principles. The incidence of hydrocephalic young in a litter depends on the length of time the mother has been on a deficient diet before mating, so that if she has been only ten weeks on the diet she is most unlikely to produce any deformed young, whereas after twenty weeks of the deficient diet it is highly likely that her young will suffer from hydrocephalus. Similarly, if the mother receives no vitamin A between litters, there are progressively more abnormal young in each succeeding litter. Subsequent addition of vitamin A results in the mother giving birth to normal young although she has previously given birth to hydrocephalics. The young born to those mothers with a severe degree of deficiency were most often still-born; with less severe deficiency the young were born alive and apparently normal, but showed signs of 'water on the brain' at varying periods after birth.

It is interesting to note how closely these findings parallel statistical studies on the incidence of congenital malformations in human communities. Congenitally abnormal children appear in older mothers and towards the younger end of a family, and the mother often gives a history of a miscarriage or other previous reproductive mishap. It is perhaps not too fanciful to compare this with the rabbit on a diet deficient in vitamin A producing an increasing number of hydrocephalic young in successive litters as she gets progressively shorter of the vitamin, and so

producing still-born rather than live young as her degree of deficiency increases.

A maternal dietary deficiency produces an environment for the growth of the embryo that differs from the normal by virtue of the absence of a specific important chemical substance. Experimental embryologists have performed an enormous number of experiments in which the environment of the embryo has been altered by adding to it one of a variety of injurious substances. For technical reasons this work is not performed on mammals, but utilizes the eggs of fishes, amphibians, and birds, which develop outside the mother's body. Modification of environment has been produced by a variety of methods of which well-known examples are the addition of magnesium salts to the fluid in which fish eggs are suspended, and the exposure of the egg of the sea-urchin to the effects of lithium chloride. In many experiments of this type developmental abnormalities have been reproduced with great regularity. Experimental embryology is therefore adding to the body of evidence which suggests that factors other than those of genetic origin are at work in the production of the congenital malformations.

The young of marsupials are born after a very short gestation period, subsequent development taking place in the mother's pouch. Burns, working in the Carnegie Institute at Washington, has utilized this characteristic of marsupials in a series of highly ingenious experiments on the Virginian opossum. By injecting male hormones into new-born females and female hormones into new-born males, he has been able to produce young in which the reproductive organs have changed their appearance to that of the opposite sex. This important study suggests a possible mechanism by which congenital deformities of the generative organs may be produced in the human.

INTRA-UTERINE HAZARDS

Even if the embryo has an untainted heredity and the mother receives an entirely adequate diet, there are other hazards that may prevent its normal development. It may be exposed to a variety of agents from the external world which penetrate its

mother's body and damage the embryonic tissues. In experimental work the dye trypan blue and the nitrogen mustards have been found to produce abnormal young when administered to the mother during pregnancy. The most important noxious agent that is known to act in this way is, however, X-radiation.

By the exposure of female rats and mice to the effects of X-rays during pregnancy most of the congenital abnormalities commonly occurring in man have been reproduced with great fidelity. The manner in which this effect expresses itself has been worked out by a number of experiments. For example, in order to show that the deformity was due to a direct effect of the radiation on the developing embryo, Wilson shielded one half of the uterus of a pregnant rat with a lead screen during the exposure to X-rays. It was subsequently found that young lying on the exposed side showed abnormalities at birth, those on the other side remaining perfectly healthy. Again developing young were removed from a rat's uterus before radiation and the uterus sewn up and returned to the abdominal cavity. After the rat was exposed to radiation, abnormal young were born, while the young removed before the radiation were found to be completely normal. It has been shown also that the type of deformity to be expected depends on the time in pregnancy when the radiation is administered. Wilson has shown that when pregnant rats are irradiated on the ninth day of pregnancy the brain and spinal cord are affected more than the kidneys and urinary system, but this distribution of abnormalities is reversed when the rat is irradiated on the eleventh day.

The question naturally arises: how does irradiation produce these abnormalities? As yet this question has not been satisfactorily answered. It has been suggested that its effect is simply to kill cells in certain areas. If these cells have a vital role to fulfill in the building up of an organ, that organ will be formed in an abnormal way. This explanation leaves certain important questions unanswered. How is it that only certain cells are affected? Why is the whole cellular structure of the organ not destroyed? Weiss has suggested that what may happen is that a single cell is

first affected, possibly because it is in a vulnerable phase of its cycle, and this cell in turn affects its immediate neighbours, so that a local nest of cell destruction is produced. Sometimes more than one cell may be primarily affected, so that multiple congenital abnormalities are produced.

At the present time the whole question whether X-rays can produce congenital malformations in the human being is constantly under debate. Many hold that the risk to a pregnant woman of an X-ray examination is negligible. On the other hand at a recent conference at Oak Ridge, Tennessee, on the effects of radiation on development, Rugh said: '... it was estimated that last year over 2,500,000 women in this country [the U.S.A.] were exposed to X-rays from 5 to 80 r in clinical diagnoses; and it is anybody's guess as to how many thousands of those women were pregnant within the first 3 or 4 weeks. Dr. Hicks has made the statement to me that a dose of as little as 40 r to the rat embryo at a time comparable to the 20-day stage in the human is extremely damaging to the central nervous system. . . . While mouse and rat experiments cannot be extrapolated to the human, the results are suggestive.' While it is never advisable to assume that the results of animal experimentation necessarily parallel those of human pathology, Rugh poses a question that urgently demands an answer, and it is to be hoped that large-scale statistical studies of the incidence of congenital malformations in children of mothers exposed to X-radiation in early pregnancy will be undertaken in the near future.

One of the most striking advances in our understanding of the way in which congenital malformations arise came from a brilliant deduction made by an Australian ophthalmologist, Gregg. In 1941 he noted a sudden increase in the number of children attending his clinic with cataract of the lens of the eye. He calculated from their ages that the early stages of intra-uterine development of each of these children coincided with the occurrence in Australia of a particularly severe and widespread epidemic of *rubella* or German measles. He saw an association between congenital defects in the child and an attack of rubella in the mother. This observation was quickly confirmed by other

doctors in various parts of the world, and it was noted that congenital disease of the heart, deaf-mutism, and mental deficiency of certain types also occurred when the mother suffered from German measles in the early months of pregnancy.

It has never been proved that any virus other than that of German measles produces a comparable effect. The reason for this is probably revealed by studying the effects of two other virus diseases, measles and the common cold. If the mother has measles during the critical period of pregnancy the embryo dies and is aborted. Other viruses like that of the common cold have no deleterious effects on the embryo and it survives to be born in a normal healthy state. German measles appears to be the only virus disease that causes just sufficient damage to produce a congenital defect in the embryo without killing it. It is interesting to note how closely this situation corresponds with the conditions encountered in nutritional experiments described earlier.

The study of the causes whereby children are born deformed is as yet in its infancy. One of the most hopeful developments of recent years has been the widening of the scope of the study so that not only geneticists, but clinicians, nutrition experts, experimental embryologists, biochemists, and many other specialists are finding, sometimes almost accidentally, that they are directly concerned with this important problem. As Professor Crew has aptly put it: 'Children yet unconceived are as much the patients of the physician as are the moribund senescents on whom he is prepared to lavish his care.' It is satisfactory to note that this responsibility to the unborn is becoming more and more appreciated, and that for this reason, as well as for the fascinating implications of the subject, there is today an ever increasing interest in the study of the congenital malformations.

THE GREYWACKÉ PROBLEM

J. E. PRENTICE

OVER three-quarters of the earth's land-surface consists of the rocks we call sedimentary. The processes that led to the formation of most of these rocks are perfectly well understood, because we can see such processes at work today. The sands at present on the seashore will one day become hardened into sandstones; estuary and delta muds will form the shales of a million years hence. Today geologists can study shoreline sands and deltaic muds that were formed millions of years ago; as rocks they have often been lifted thousands of feet above the present level of the sea and tilted through large angles; they may form the substance of vast mountain chains. But there is one group of rocks whose origin has always been in doubt. These are the *greywackés*. A greywacké is a hard gritty rock whose constituent particles range in size from the coarsest sand,

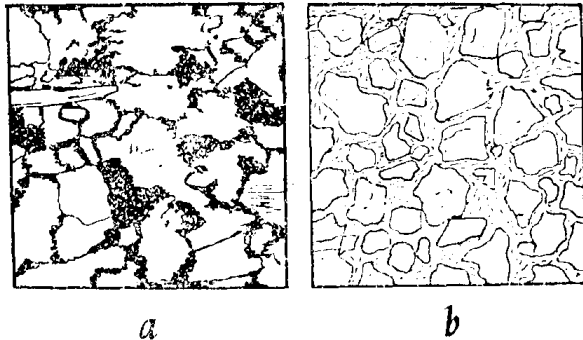


Figure 1. Thin section, by transmitted light, $\times 30$ magnification, of (a) a greywacké, with angular grains of quartz and mica set in a matrix of clay, and (b) a normal sandstone, with rounded grains of quartz cemented by calcite.

or even pebbles, down to the finest clay. It is this mixture of coarse and fine particles that is so difficult to explain. Most normal sandstones are in some degree sorted or 'clean'; that is, they consist of fragments of more or less uniform size: a greywacké is characteristically unsorted or 'dirty' (Figure 1). Greywackés are found in beds ranging from a few inches to several feet in thickness, and they are commonly interleaved by thin layers of black shale (Inset 3). In some beds of greywacké the coarse and fine particles are evenly distributed throughout their thickness; in others, the coarsest particles are confined to the base of the bed, and there is a gradual upward grading into finer material towards the summit.

DEPOSITION IN THE SEA

The normal processes of marine deposition would seem to be quite unable to produce a graded sediment of this kind. Deposition from the sea, as observed near the shore today, is the result of the action of waves and currents. Material supplied by rivers and by the breaking down of the shoreline is gradually drifted out to sea by their activity. Now the size of particle deposited by moving water depends directly upon the rate of movement. Water moving at a high velocity will carry along sand but drop pebbles; at slower speeds sand will be deposited and only finer particles of silt and clay will be held in suspension. It follows that the sediments of the nearshore regions are generally well sorted. In the shallowest water, where waves and currents are most active, pebbles and sand will be deposited; the fine silt and clay will be washed out to settle in the quieter regions offshore. It is thus difficult to see how normal moving water could deposit a mixed sediment of greywacké type. Graded bedding could be produced by settling from stagnant water; if a sediment is suddenly poured into still water, the coarser particles will naturally settle first, to be covered in turn by finer and finer material. But fine particles can only be carried down at the same time as coarse if the suspension is very dense, i.e., if the amount of sediment is great in relation to the amount of water. In short, the only known mechanism by which a graded greywacké could be

deposited is settling under conditions of comparative calm, from a dense muddy suspension.

Shallow water

The essential calm conditions could only be realized in two ways, one in sheltered land-locked bays, the other in the depths of the ocean. But greywacké sediments are far too widespread for us to suppose that they were all laid down in land-locked bays: moreover, the features normally regarded as evidence of shallow-water deposition are conspicuously absent from greywackés. For instance, practically all fossil remains of sea-floor organisms are missing, and none of the normal inhabitants of the shallow-seas are found fossilized in these strata. In fact the only organisms normally found in beds of greywacké are those whose body-form is appropriate to a floating existence, and which one might expect to find in the deposits of an ocean deep. Philip Kuenen, in the course of world-wide travels in the study of greywackés, has, in co-operation with V. Natland, obtained striking confirmation of this from the Pliocene greywackés of California. These are some of the most recently-formed greywackés in existence, and the shales associated with them contain minute animals whose living relatives are today the inhabitants of the deeper parts of the oceans. It is surely unlikely that such creatures would have changed their habitat in the few million years since these rocks were formed.

Other evidence that might suggest shallow-water deposition is equally lacking. Notable in this respect is the absence of any indication of temporary breaks in sedimentation, or surfaces of erosion, which by contrast are frequently found in the rocks known to have been formed under shallow water. It is, however, virtually undisputed that rises and falls of sea-level amounting to hundreds of feet are, geologically speaking, frequent occurrences. For instance, it is known that a fall in sea-level of 600 feet or more has occurred during the last million years, although geologists regard this millennium as a time of comparative stability in the earth's crust. So during the millions of years required to deposit thick beds of greywacké, which

include times of great crustal mobility, we must suppose that large oscillations of the sea-level must have taken place many times. If, therefore, the greywackés were deposited in less than a thousand feet of water we might expect to find some evidence that they had at some time been lifted above the sea. No such evidence exists, an absence that indicates a greater depth of water for their site of deposition. But the beds of greywacké are themselves thousands of feet thick, yet the troughs in which they were deposited never become any shallower. One can only suppose that subsidence of the sea-floor kept pace with the deposition, thus maintaining an approximately constant depth of water. Such subsiding areas of deposition were in fact postulated by geologists long ago to explain the accumulation of great thicknesses of sediment. They are known as *geosynclines*. These were relatively narrow troughs of water beneath which the floor was unstable. Sediment appears to have poured into them from land masses on either side, while the floor sank continuously. Today no geosyncline exists, though relics of them exist in the Java trough and the Pacific Coast trench of North America.

It appears that the sediments in the geosynclines were later folded and elevated into mountain chains. In fact almost all mountain ranges had their origin in geosynclines, the Alpine, Himalayan, and Rocky Mountain chains originating in this way in the most recent mountain-building period. Greywacké sediments are typical of mountain-belts and may be regarded as essentially sediments formed in what were once geosynclines. As the outcome of this conclusion, two questions pose themselves. First, are there similar sediments in deep waters in the oceans today: secondly, if there are, what brought them there?

Deep sea studies

The pioneer deep-sea investigations gave the impression that all deposits on the ocean floors were fine-grained oozes and clays, which might have been carried there by simple suspension, involving no great movement of water. Recent research has shown that this is not a true picture. Coarse sediment has been reported from a large number of localities at depths greater

than 3,000 feet, and while many of these finds have been at the foot of the continental slope, a number have been reported from flat ocean floors miles from any appreciable slope. Some of these deep-sea sands contain the rolled skeletons of foraminifera which live in shallow water. This sediment must have come from the land in the first place and there can thus be no doubt that some mechanism exists which is able to transport shallow-water sediment into the ocean depths. Close examination of the samples from the deep-sea shows that some of the sands are well-sorted, while others contain muddy material, i.e., they are incipient greywackés. The resemblance between these sediments and the greywackés is thus quite close, and we may reasonably regard the greywackés as the deep-sea sands of the past.

CHARACTERISTICS OF GREYWACKÉ DEPOSITS

If this connexion can be maintained, the structures observed in greywackés can be used to study sedimentation in the depths of the ocean, both today and in the past. This approach is very valuable, because structures may be so readily studied in the 'fossil' examples. The examination of a rock on a wave-washed foreshore is so much simpler than studying a wet sludge dredged from below a thousand feet of water. It has been observed that greywackés almost invariably contain small-scale *current-bedding* (Figure 2). This is an indication of rapid movement of water and has for that reason often been thought to be the outcome of shallow-water deposition. While it is probably true that current-bedding on a large scale is typical of inshore deposition, it can be shown that the current-bedding of greywackés is the product of ripple-marking; and underwater photographs have shown that today ripple-marking may be found at depths exceeding 600 feet. The implication is that at these depths, both today and in the past, current movement along the sea-floor was rapid. Laboratory experiments suggest that a velocity of between 25 and 60 centimetres per second is essential for the formation of ripple-marks, a much greater movement than has generally been believed to be possible on the ocean-floor.

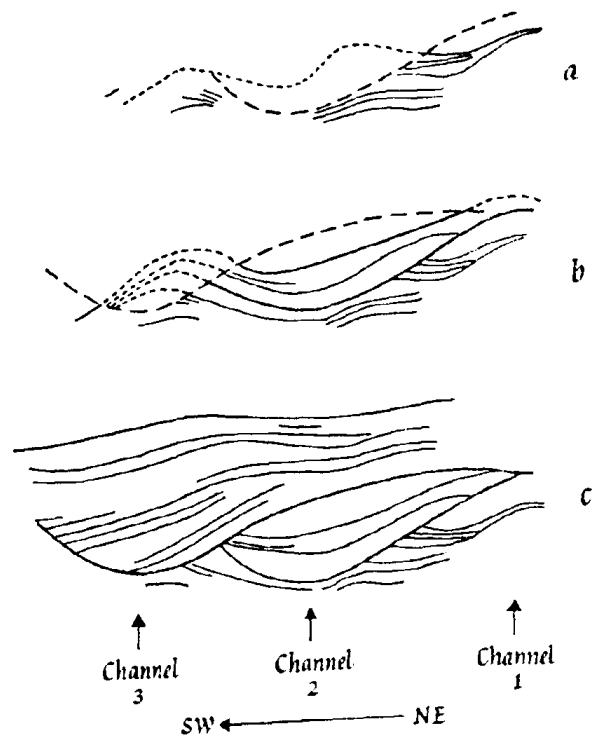


Figure 2. Diagram to show three stages in the development of current bedding by the progressive movement of ripple-marks. In *a* the two ripples (outlined ---) are eroded by channel 2 (—); in *b* sand is deposited in this channel and erosion moves forward to channel 3, which becomes filled in *c*. Drawn from actual specimen.

The bases of individual greywacké beds often show lines of markings known as *groove-casts*, *flute-casts*, and *flow-casts*. The *groove-casts* (Inset 4) are the infillings of parallel striations, which appear to have been cut into the surface of the mud below by sharply pointed fragments dragged along by a moving

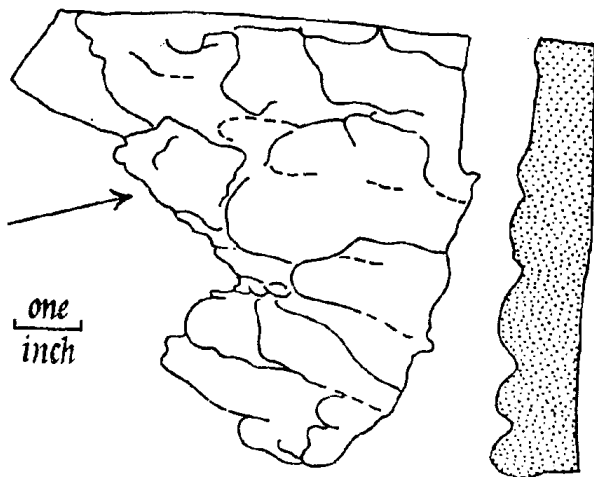


Figure 3. *Flute-casts* in plan (left), and section (right). These occur on the base of the bed of greywacké, and represent the infillings of scour-marks made in the underlying mud by a current moving in the direction indicated by the arrow.

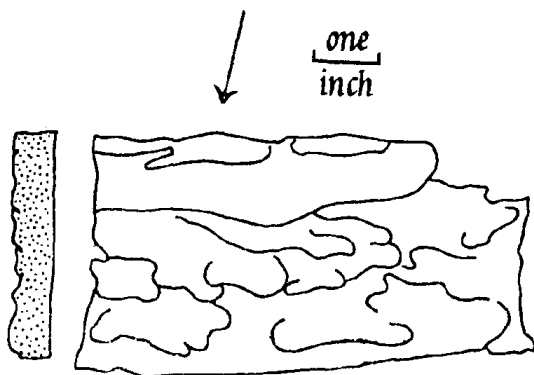


Figure 4. *Flow-casts* in plan (right), and section (left). These were formed by a thick sludge of sediment moving in the direction of the arrow.

current. The *flute-casts* (Figure 3 and Inset 5) fill in elongate hollows that have been scoured out from the mud below by the erosive activity of swift, sediment-laden water. By contrast, the *flow-casts* seem to have been formed during or after the deposition of the greywacké itself, and represent the structures formed by the greywacké material sinking and sliding into the soft mud below (Figure 4). Certain internal contortions, known as *convolute bedding* (Inset 6), also appear to be the result of internal adjustments during the deposition of the greywacké bed.

Turbidity currents

To bring the threads of the argument together, then, the current that emplaced the greywackés must have been dense, so as to produce grading and the groove-casts; it must have been swift, in order to cause ripple-marking, to transport the coarse sand, and to scour out the flutes; settling must have been rapid so that coarse and fine material settled together and so that movement of the lower parts of the bed was possible during the deposition of the upper. There must therefore have been a dense and rapid flow entering a region which was normally still. To this flow the name *turbidity current* has been given; it is pictured as a mass of swiftly moving sediment, held down on the sea-floor by its own weight, rolling rapidly down the continental slopes and out on to the ocean-floor. As it slows down, it deposits its load; each individual greywacké bed is pictured as being the deposit of a single flow, while the shales between the greywackés represent finer products carried in the ocean waters in suspension. This is the only mechanism that comes near to explaining the presence of sands on the floors of the deep-sea, though it is true that no one has ever observed a turbidity current in the ocean. Turbidity currents may however be seen in lakes and reservoirs; in Lake Mead, California, their activities have covered the floor of the basin to a mean depth of one foot since 1935, while in some places over 100 feet of sediment has been deposited in that time. They can be reproduced experimentally in sedimentation tanks and the hydraulic principles determining their movement can be calculated. Nevertheless,

in the ocean their existence remains a matter of inference, because the highest velocity recorded directly on the sea-floor is only just over 25 centimetres per second, which would be adequate to transport coarse silt but not sand.

The only convincing demonstration of water movement of greater velocity is a somewhat oblique one. After an earthquake on the Grand Banks, Newfoundland, in 1929, a number of submarine cables broke on the downslope side; the time of breakage of each successive cable was of course recorded and the extent of the broken cables was determined afterwards. The only mechanism that satisfactorily explains the timing and extent of the breakages is a turbidity current. Calculations show that this would have had a course of more than 400 miles along a 150-mile front, and a velocity (at 250 miles from its origin) of 15 knots, i.e., over 300 centimetres per second. At this latter point the slope was less than one degree, so that the current must surely have been moving under its own momentum. Seaward of this, sampling has revealed more than a metre of unconsolidated sediments, consisting of graded sand and muddy silt, which is attributed to this current. An important fact is that this current was generated by an earthquake of considerable magnitude, and as attempts by American scientists to 'trigger-off' these movements by submarine explosions have met with little success, it seems likely that the severest storms would be quite unable to initiate them. It follows that the generation of a major turbidity current must be an exceedingly rare event. Now it is suggested that each bed of greywacké represents a single turbidity flow, and it is possible to estimate the number of greywacké beds in the geological period they represent. Thus we can calculate the average length of time that in the past elapsed between each turbidity current. In Wales this works out at 100,000 years for the Cambrian period, and between 1,500 and 2,000 years for the Ordovician-Silurian periods. Since it is well known that mountain-building and earth-movement were slight in the Cambrian, and reached their climax at the end of the Silurian, these figures support the suggestion that there is a connexion between earthquake activity and greywacké

formation. We may picture the process somewhat as follows. For several thousand years sands and silts and muds accumulate on the higher parts of the continental shelf, brought there by the rivers and deposited by the sea. As they build up in thickness they become more and more unstable, until an earthquake shock starts them moving. Rapidly increasing in momentum, they roll down the continental shelf, down the steeper continental slope, and spread out over the ocean-floor.

Ocean-floor topography

The turbidity current hypothesis also provides a reasonable explanation of some of the more puzzling features of ocean-floor topography. At frequent intervals along the continental shelves of the world there are deep channels, whose steep sides have earned them the name of *submarine canyons*. These often begin near the mouths of large rivers, and trench deeply into the continental shelf, debouching at depths of between 4,000 and 6,000 feet below sea-level on to the ocean-floor. Their form is similar to that of normal river valleys, and this has led some authorities to suggest that they are really valleys formed originally on land, and since sunk below sea-level. The sediments into which they are cut are, however, fairly recent in origin and the acceptance of this theory would involve a world-wide uplift of 6,000 feet followed by subsidence within the last 20 million years. This would in turn imply a withdrawal of water of quite phenomenal dimensions from the oceans, so that this postulate is by no means easy to accept. To suppose that there has been no such movement, in other words that the shelf has remained relatively stable since that time, means that some powerful agent of erosion must have been in operation. It is possible that the turbidity current may fill this role; since its erosive activities would be most powerful where sediment supply was greatest, it would tend to erode most deeply offshore from the larger rivers. A further point of great significance is the occurrence at the foot of many of these canyons of a fan-shaped structure, such as might be expected if a great body of sediment flowed down the canyon and suddenly spread out on the sea-floor.

In other ways the form of the ocean-floor may prove to be a fruitful field of study. If the sediment was deposited from 'volume suspension' then the cover ought to form an even blanket over all irregularities. But if turbidity currents flowing across the ocean-floor were the major depositing agent, disposition should be directly related to the topography. In the Eastern Pacific, H. W. Menard has shown that irregular topography is only found where a region is cut off from the submarine canyons by barriers to turbidity flows; in regions to which turbidity currents could have direct access the sea-floor is smooth except on the 'lee' side of high ridges. In short, the form of the ocean-floor is more readily explained by the turbidity current hypothesis than by deposition from volume suspension.

That 'the present is the key to the past' has long been the fundamental tenet of geologists. In the study of greywackés, the converse has shown its value; and by a nice combination of evidence derived from both sources, a satisfactory working hypothesis has been built up. The tangible evidence for turbidity currents is slight, but by their nature that must be so. Geological processes are so slow that the lifetime of man is inadequate for their existence to be proved by observation. Nevertheless, no other hypothesis fits so many facts so neatly; that in itself should be persuasive, if not conclusive.

REFERENCES

Many useful papers, with full references to earlier work, are to be found in:

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SCIENCE AND TECHNOLOGY OF METAL ADHESIVES

N. A. DE BRUYNE

FUNDAMENTALLY adhesion is the result of forces due to molecular or atomic electric fields acting across the interface between adhesive and what may be called the adherends; it is not in essentials an effect produced by mechanical interlocking between adjacent surfaces. There is, however, still much uncertainty about the nature of these forces and it is probably best to content oneself by saying that experience shows that for a good joint two conditions must be satisfied, (a) the adhesive must wet the adherends, and (b) the internal stress produced when the adhesive solidifies must not be high. It will be profitable first to look a little more closely at these two rules.

TWO RULES OF ADHESION

The first rule

Reference should be made to Insets 7 and 8 which serve to illustrate the first of the rules. Both illustrations show a polyethylene sheet under a stream of water, but, while the first sheet is untreated polyethylene (note how the water is repelled by the surface), the second sheet had been previously 'flamed' with a bunsen burner, with the result that the water spreads out over the surface. Infra-red absorption measurements suggest that this flaming produces carbonyl groups ($>C=O$) on the surface of the polyethylene.

Now according to the first rule given above we should expect that if we use adhesives of a hydrophilic character, i.e., with setting properties similar to those of water, the adhesion to flamed polyethylene should be much better than to unflamed. This is in fact so. Table I gives some results of tests on lap joints,

one inch wide with one inch overlap, made from aluminium-coated duralumin strip. The adhesive was a polyethylene sheet coated on both sides with an epoxy type* adhesive.

TABLE I

Tests on lap joints made with:	
Untreated Polyethylene	Flamed Polyethylene
150	920
150	600
190	650
150	780
150	800
200	750
Mean 165 pounds	Mean 750 pounds

The second rule

To give an example of the second rule, i.e., that the internal stress produced on solidification must not be high, we can try to use polyethylene itself as an adhesive by melting it between two pieces of metal. If we simply use polyethylene by itself the adhesion obtained when the polyethylene has cooled down is insignificant. If, however, we reduce the interfacial stress caused by the difference in the shrinkage of the polyethylene and the metal, then we do in fact get surprisingly good adhesion. What is done to reduce the shrinkage stress is either (a) to pack the polyethylene with glass fabric, or (b) to use a very thin layer of polyethylene. With either modification good adhesion is obtained.

Significance of rules of adhesion

The fact that polyethylene sheet will stick to metals if its contraction is reduced is an example of what may be a general truth, that in themselves the interfacial molecular forces are probably always adequate to produce good adhesion, and that weak

*An adhesive produced by condensing epichlorhydrin with a polyhydric phenol.

joints result only when there are some disturbing factors present, such as stress concentration or inadequate contact between adhesive and adherend, or both.

It is not quite certain whether this is so, but support for the belief comes from physical chemistry. The heat produced when a surface is covered with a liquid can be measured. This heat of wetting can be converted into its equivalent in mechanical work, and if we divide this work by the range of molecular action (say 3×10^{-8} cm.) we can deduce what the force of adhesion should be. Even where a liquid makes a large contact angle with a surface, i.e., when we get poor wetting, the theoretical adhesive strength deduced from the heat of wetting is considerable and in fact much greater than anything observed in practice.

Why then does the first rule insist on good wetting of the adherends by the adhesive? Photoelastic investigations show that wherever the adhesive sets with a large contact angle, there will be a concentration of stress when an external load is applied. This may be one reason for the need for good wetting. Another reason is that an adhesive that tends to gather up into drops similar to the water on the polyethylene in Inset 7 will not produce an even film. Poor wetting may also be an indication of contamination, i.e., an oil film on the surface of the adherend.

The electrical properties of organic materials are critically influenced by whether or not they contain permanent molecular dipoles. Materials such as wood, which contain such permanent dipoles, are said to be 'polar', and materials such as polyethylene and natural rubber which do not are called 'non-polar'. One of the strongest permanent dipole groups is the hydroxyl group ($-O-H$) present in water ($H-O-H$). Now polar liquids do not wet smooth non-polar solids, with the result that, as a broad generalization, one can say in terms of the first rule that polar adhesives cannot be used to make strong joints between non-polar adherends. But our strong adhesives are polar, and both epoxy and polyvinyl formal* adhesives are full of hydroxyl groups.

*Adhesives made by reacting polyvinyl alcohol with aldehydes, e.g., formaldehyde.

Thus one cannot make strong joints with such adhesives to rubber, polyethylene, or polystyrene until one has changed the surface properties of the latter, for example by treatment with strong acid or direct oxidation. Another way of improving wetting is by roughening the surface as by sand blasting or abrading.

As to the real nature of the molecular forces that are primarily responsible for adhesion, there is as yet no clear evidence whether they are mainly physical forces, such as are responsible for surface tension in a liquid, or whether they are due to a stronger type of bond of the kind that we find when chemisorption takes place.

THE DISTRIBUTION OF STRESS IN A JOINT

When a lap joint is pulled, the applied force is not distributed uniformly over the glued area, with the result that the adhesive is subjected to a shearing strain which is least at the middle of the joint and greatest at each end. But in addition to the shearing stress, there is also a tearing stress. The extent of this concentration of stress at each end will depend upon the relative dimensions and elastic properties of the adhesive and the adherends. As a result, the strength of a lap joint, even when rupture takes place in the adhesive, depends on the nature and dimensions of the adherend. For instance, the rupture load with a given adhesive and overlap increases as the thickness of the adherend is increased. Figure 1 shows how complicated the stress distribution is in a lap joint. Yet for all its complexity it is in fact susceptible to mathematical analysis.

In a butt joint under tension similar effects occur; the strength of the joint rises as the thickness of the adhesive is reduced and the rupture strengths can far exceed that of the adhesive in bulk. Thus a tinned joint may show a strength of eight tons per square inch, which is about five times that of tin in bulk. This is because the adhesive is in a state of three-dimensional stress and its deformation is restricted by the presence of the comparatively rigid adherends which are being held together. In addition to non-uniformity of stress from an external load due to differences in the elastic and mechanical properties of adhesive and

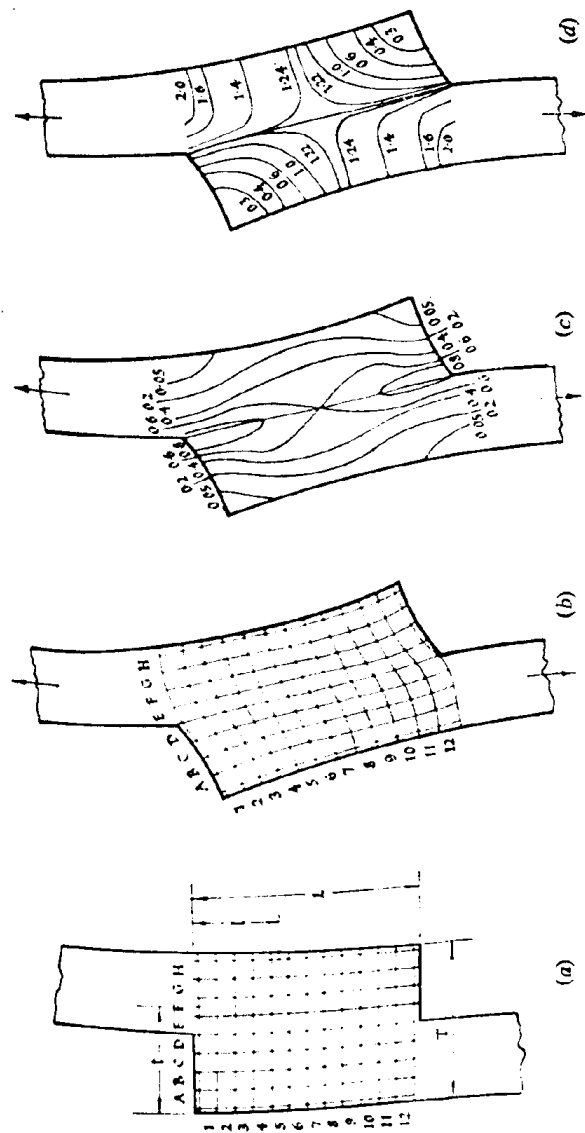


Figure 1. The stress distribution in the adherends of a simple lap joint under load can be demonstrated by using a rubber analogue as was shown by L. F. Demarkles and the late Prof. J. S. Newell: (a) is the side view of a joint without load on which a rectangular reference grid has been drawn; (b) shows how the grid is distorted under a load of 16 lb; (c) and (d) show the resulting shear and tensile load contours.

adherend, we must also take into account the effects of residual stress due to shrinkage of the adhesive as it sets. The magnitude of this residual stress will increase as the thickness of the adhesive increases. Thus great care must be taken in drawing conclusions from mechanical tests.

Monomolecular adhesion

When we pass from mechanical tests to attempts to explain the relation between molecular constitution and adhesion we find that much still waits to be done, since any change in the chemical structure of an adhesive is accompanied by a change in its mechanical properties, with the result that it is very difficult, for the reasons given above, to make deductions from breaking tests. Thus it is possible both with epoxy and with polyformal adhesives to find a close correlation of high statistical significance between the rupture strength of the joint and the concentration of hydroxyl groups in the adhesive, but is this owing to an increase in the molecular forces at the interface or is it just that the adhesive shrinks less or produces a more favourable stress distribution at rupture or both? The truth is we do not yet know.

Because of this difficulty of interpretation it is interesting to see what happens to an adhesive when it is in the form of a monomolecular layer on a water surface which under the conditions of the experiments acts as an adherend. If such a monomolecular film is compressed laterally it shows a steadily increasing pressure which finally reaches a maximum value at which it stays constant. This is the so-called 'collapse' pressure at which the film is a fully condensed monomolecular layer. When further compression is applied the layer begins to break up and slide over itself. The pressure-area curve is an isothermal, equivalent to that of a gas, and from the numerical values and a knowledge of the size of the molecules one can work out what portions of the molecule are turned towards the water. If, for instance, one examines an epoxy resin and compares its isothermal with those of partly and wholly acetylated derivatives, it is found that any reduction in the concentration of hydroxyl

groups greatly reduces the collapse pressure. So here again the influence of the hydroxyl groups seems to be decisive in determining the strength of the joint.

Another method of studying interfacial forces between an adhesive and an adherend is to examine the way in which a metal surface selectively adsorbs adhesives from solutions. The evidence here is again that hydroxyl bonds play a decisive role.

METAL ADHESIVES

Adhesives for metals, developed in the first place for the aircraft industry, are an interesting recent technological advance. A practical adhesive for metals in addition to fulfilling the two fundamental requirements of good wetting and small shrinkage must also be free from volatiles and must in addition not produce volatiles during solidification. It must also be resistant to prolonged immersion in various liquids and be unaffected by wide variations of temperature. It must have good cohesion as well as adhesion. In addition, it must not be too difficult to use. These are stringent requirements and not many materials are able to meet them all satisfactorily. Probably the most successful have been plastics with epoxy groups in them and mixtures of polyvinyl formal and phenol formaldehyde resins.* Adhesives of both these types are hot setting and require temperatures of from 145° C upwards to cause them to set: the heat can be applied by a heated press, an autoclave, or an oven.

Whatever adhesive is chosen, it is important that the metal surface be adequately cleaned. Aluminium and its alloys are best 'pickled' in a dilute solution of chromic acid, or they can be 'anodized' in chromic acid, after which they must be washed in cold or tepid water, because hot water causes the surface oxide layer to change from a 'Bayerite' type of structure to a much less strongly held 'Boehmite' oxide. The cleaned surface is in a very adsorptive state. Indeed, the electrical capacity of anodized aluminium varies greatly with the humidity of the atmosphere.

*These appear on the market as 'Araldite' and 'Redux' respectively.

Metal adhesives in aircraft construction

Over the years aircraft designers, to keep down structure weights, have improved the efficiency of their structures and used materials with higher and higher static strengths. Figure 2

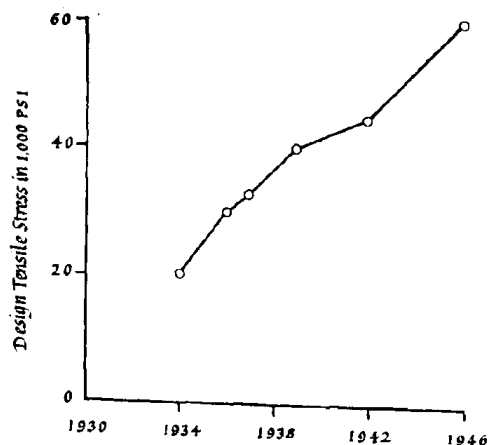


Figure 2. Graph showing how the trend of design stress rose steadily over the period 1934-46.

shows how design stresses have risen steadily, and this rise has brought serious difficulties in train. For example, the result of this tendency has been a growth in fatigue failures such that metal 'fatigue' is today the major worry of the aircraft designer. In Figure 3, curve A shows the probable trend of fatigue life in recent years, due to the use of higher design stresses and to stronger materials; and B shows the fatigue life of the materials themselves has become shorter as the static strength has risen. Curves B and C show the relative fatigue lives of aluminium alloys (17 ST, 24 ST, and 75 ST) under stress concentrations of 4 and 5 respectively. It will be seen that a reduction in stress concentration from 5 to 4 has a material effect on fatigue life.

It is because adhesive bonding of structures can do so much to help in the reduction of structure weight, in the removal of

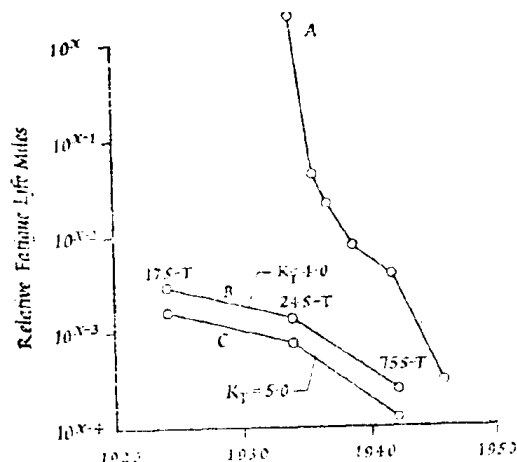


Figure 3. Curve A shows how fatigue life has suffered as design stress has increased. Curves B and C show how the change from 17 ST aluminium alloy to 24 ST and 75 ST has decreased fatigue life at stress concentrations of 4 and 5 respectively. (Figures 2 and 3 are from the *Proceedings of the Fourth Anglo-American Aeronautical Congress* published by the Royal Aeronautical Society, London.)

stress concentrations, and in the attainment of smooth surfaces and high torsional stiffness, that it is being so widely adopted in new aircraft at the present time. It is now over twelve years since the first flight of the de Havilland Hornet in which an adhesive was used in gluing the main spar tensions boom to the web. This machine was probably the fastest propeller-drawn fighter made. Since then adhesives have been used in fifty types of aircraft ranging from the Chance Vought 'Regulus' guided missile, and Cutlass fighter, to civil machines like the Comet, Britannia, and Fokker Friendship (Insets 9 and 12).

RIVETED VERSUS BONDED STRUCTURES

A lap joint made from two duralumin sheets a millimetre thick with a 13 mm. overlap and a spacing between rivets of 15 mm.

has an average shear strength of 1.44 kg. per sq. mm. of joint area when rivets of 4 mm. diameter are used. A lap joint with rivets, sheets, and spacing of the same dimensions, but with a 32 mm. overlap and three rows of rivets, has an average strength of 1.76 kg. per sq. mm. In joints of the same dimensions, but with rivets replaced by spotwelds, shear strengths of 0.77 kg. per sq. mm. and 0.88 kg. per sq. mm. can be obtained. If, however, the same duralumin sheets with 13 mm. overlap are glued together by means of hot setting adhesives, shear strengths of the order of 2.8 kg. per sq. mm. are obtained. Thus the static strength of joints made with adhesives exceeds that of similar riveted or spotwelded joints when tested under tensile shear.

The results of similar comparative tests on structures under compression are equally striking. Inset 13 shows the top surface of a 'Dove' wing under test. The skin is made of thin sheet with longitudinal stiffeners and it is under a compression load slightly lower than the failing load. The stiffeners are attached to the skin by means of a metal glue and it will be seen that, although between the stiffeners pronounced buckling can be observed, along the stiffeners the skin is fully stabilized. When a riveted wing is loaded in a similar way, this absence of buckling along the stringers does not occur. Compression buckles run chord-wise right across the surface between the rivets, and the difference in the distribution of buckling is a clear indication of the greater stability of the bonded joint, which is thus able to tolerate a higher compression loading before failure. Test figures confirmed this result. In panel-lengths of 60 cm., adhesive bonding showed a 23 per cent improvement in failing load over the riveting method. Tests of a similar kind made by the Gloster Aircraft Company and the English Electric Ltd have indicated the superiority of the bonding technique to the extent of 25 per cent and 22 per cent respectively.

Comparison of fatigue strength

A series of fatigue tests on bonded panels has been made in Holland. Several panels with 'top-hat' stringers were tested under pulsating compression loads on the large pulsator of the

National Luchtvaart Laboratorium at Amsterdam. In half the specimens stringers were riveted and in the other half they were bonded to the panels. Compression loading alternated between 1,000 kg. and 45, 60, and 75 per cent respectively of the static failing load. The results are given in Figure 4. Absence of stress

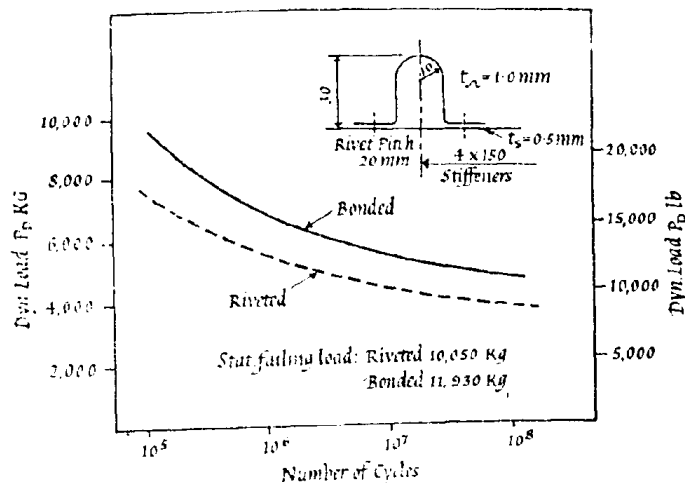


Figure 4. Comparison of the fatigue strength of similar 'Redux-bonded' and riveted panels.

concentration in this test again proved advantageous. The fatigue curve for the bonded panels is considerably higher than that for the riveted specimens. At a load of about 45 per cent of the static failing load, the life of bonded panels is 15.4 times as long as that of riveted panels.

In the bonded test-pieces, fracture of the sheet occurred near the stiffeners and thus gave rise to cracks in the stiffener flanges, and in the adhesive layers. Local failures in the adhesive layer, which occurred in certain of the specimens, caused no appreciable reduction in the load-bearing strength of the structure and did not result in immediate general failure. With each subsequent cycle the cracks increased very slowly and stopped at

the points of zero displacement in the areas of buckling. Cracks in the adhesive bond and cracks in the metal components occurred after roughly the same numbers of cycles.

FURTHER APPLICATIONS

Advantages of lamination

In all the above examples the structures were precisely similar, whether bonded or riveted. This, however, neglects one of the advantages of gluing which makes it possible to laminate thin sheets together so as to follow the load contours and so maintain uniform stress throughout a structure. This is one of the most important features of adhesive bonding because it makes it possible to achieve what are, in effect, integral structures without the enormous complication and expense of machining from the solid (Inset 15).

Moreover, where riveting is unavoidable strength can be considerably increased by previously gluing on a reinforcing patch. A substantial economy in production also results because the additional local thickening permits the use of simple 'cut countersunk' rivets, instead of expensive spin dimpling. Spar flanges in which the cross section varies along the length can be made without a milling machine. Even more remarkable, it is possible to glue laminations in the flat and then bend them in a rubber press into an angle section. One further point: in general, bonded structures become cheaper than riveted structures as soon as a component exceeds a certain size. This is because the time to set the adhesive is constant, whereas the time for riveting is proportional to the area.

Honeycomb construction

In a strut, i.e., a structure under compression, we can think of any applied load as consisting (a) of a uniform compression stress acting equally everywhere over the cross section, and (b) a couple tending to produce bending, buckling, twisting, or other forms of 'load dodging'. For a strut of given weight and length, therefore, it is a necessary consequence that it pays to

'expand' the material, provided that in doing so its elastic modulus and proof stress do not fall off more rapidly than the density. The reason for this is that while such expansion in no way reduces resistance to the uniform compressive stress, it gives stability to the structure to resist bending, buckling, and so on. In this context we mean by expansion a growth in the dimensions of the material without increase in weight. One thus arrives at the utility of the idea of putting small holes into metals, but a more practical idea is that of a honeycomb structure as shown in Inset 16.

A honeycomb panel consists of two skins enclosing the honeycomb core; it is an 'I' beam in which the web has been expanded to fill all the space between the flanges. Of course, there is no point in using a honeycomb girder or strut in applications where an engineer would use a rolled steel joist, or where only tensile loads are involved. But when the loads are so small and the need to reduce weight is so great that the flanges must be thin (say one-sixteenth of an inch or less), the honeycomb structure is well worth while. Such circumstances arise in a fuselage shell or the floor of an aeroplane or car, in boats, doors, and tables; in all such applications honeycomb can give a strength-to-strength weight ratio much superior to conventional structures.

The core of the structure is usually made of aluminium foil, corrugated and glued together to form a honeycomb, to which the skins are then glued at the open ends of the honeycomb cells. The honeycomb panel has been made possible as an efficient economic engineering structure by the development of strong metal adhesives.

One of the attractions of honeycomb structures to an aircraft designer is that there is no distortion or buckling under load until shortly before the ultimate strength of the panel is attained. In this they differ markedly from the conventional skin and stringer structures where the skin, as is so often the case even in high-speed aircraft, has to be thin. Till now the aircraft designer has had to accept the fact that much of his skin covering, particularly in shear, will show considerable buckling even at quite low loads. Inset 14 shows a well-respected bomber

on the ground, and under this gentle loading condition there is considerable diagonal wrinkling in the sides of the fuselage. This is not a sign of weakness, however; long ago H. Wagner showed that such a thin skin, properly designed, must wrinkle at a fraction of its ultimate strength. Nevertheless, in these days of high speeds and of laminar flow wings, such wrinkling cannot be tolerated, and to use a honeycomb structure is one possible solution. We may expect to see much more of it in future.

FURTHER READING

On fundamentals of adhesion:

Tabor, D.: 'Basic Principles of Adhesion', *Report on the Progress of Applied Chemistry*, 1951, **36**, 621.

de Bruyne, N. A.: 'Fundamentals of Adhesion', *Research*, 1953, **6**, 362.

On applications to aircraft:

de Bruyne, N. A.: 'Structural Adhesives for Metal Aircraft', *Proceedings of the Fourth Anglo-American Aeronautical Conference* (Royal Aeronautical Society, London, 1954).

The above papers give full references to the very large literature on the subject of metal adhesives.

APPLIED BIOLOGY AND ECONOMICS

S. A. BARNETT

GOVERNMENTS of all complexions and in all countries are increasingly committed to planning. Despite the controversies which the idea of planning has aroused, many of the plans are themselves acceptable to everyone, except in detail. Nearly every country has a public health service, and modern industrial communities cannot function without a highly organized system of preventive medicine. In two ways this example is typical of contemporary trends. First, the problem arose as a result of the application of science: physics and chemistry were a necessary basis for the industrial revolution which produced the malnourished, disease-ridden people of the big cities. Second, the solutions to the problem also came from science: in this instance, especially from bacteriology and biochemistry. Of a very different kind, but equally examples of successful planning on a vast scale, are the schemes of conservation and development such as the Tennessee Valley Authority or the Volga River Plan.

As increasingly large numbers of men and women come to be employed in such planned activities, a new problem arises. Very generally, the question is: what is the optimum effort to be put into any given activity? The object of this article is to give examples which illustrate the importance of asking questions of this sort, and to show how neglecting the scientific approach to planning and government policy can lead to unnecessary inefficiency and waste.

PEST CONTROL

There is urgent need for quantitative assessment in economic terms wherever attempts are made to control losses of food

due to pests. This is a suitable field from which to draw examples, since it is one in which scientific and administrative problems are obviously interlocked. G. Ordish, an agricultural economist working for a large commercial undertaking, has published an economic study of pests and diseases of crops which at least exposes the deficiencies of 'estimates' of losses, and of savings through control measures; he politely calls most of the published figures 'intelligent guesses' (1). No comparable study has however been undertaken by the large body of disinterested government biologists.

Economic data are needed for each individual pest or group of closely related pests. To illustrate the nature of the problem, it is convenient to take at some length an example from a single species. The common brown rat, *Rattus norvegicus* Berkenhout, is generally present, in temperate regions, on farms, in food stores, and in sewers, and at least in the port areas of the tropics. In all these places rats are regularly or sporadically killed by poison, traps, domestic predators, and other means, but, until the last two decades, virtually no scientific study had been made of any of these methods of extermination.

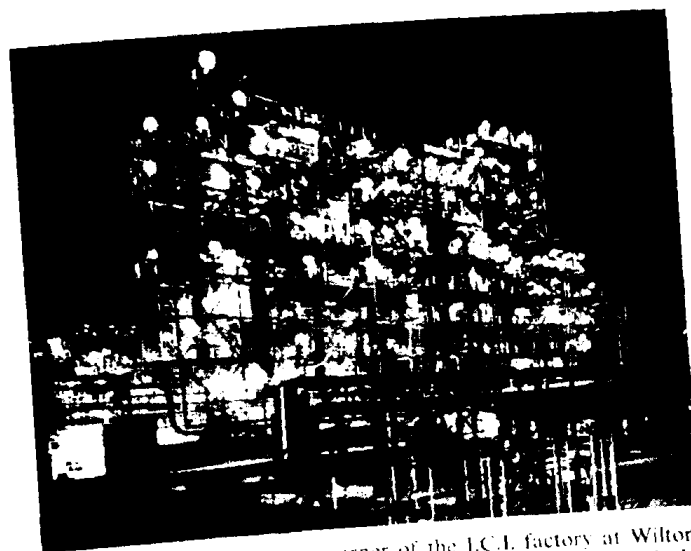
During the second world war the British Agricultural Research Council supported an extensive study of rats as pests (2). Most of the research was devoted to answering the question: given the presence of rats in a relatively small area, what method of killing them is most likely to give complete extermination? This question had to be answered within the framework of the available supplies of baits, poisons, and other equipment. One of the fruits of the research was a routine technique of control in which relatively unskilled men and women could be trained. The British government therefore employed numbers of biologists to give such training, and it set up a considerable organization throughout the United Kingdom to maintain a country-wide attack on rats. This was part of a wider group of schemes for protecting crops and preserving stored food.

Some organization of this sort was certainly necessary, especially since at that time large reserve stocks were stored for long periods in government depots. It is probable that there resulted

A CENTURY OF DEVELOPMENT



1. The birthplace of the synthetic dye industry: Perkin's Greenford Green Works in 1858. The plant used for producing the dye matched the simple exterior of the factory.



2. Chemical plant today: a corner of the I.C.I. factory at Wilton, the complexity of which depends largely on the extent to which the chemical industry has adopted automation.

GREYWACKÉ PROBLEM



3. Typical greywacké sequence near Aberystwyth in which the greywacké bands stand out as ribs. The major beds show convolutions faintly, while the base of the middle bed has *flute-casts*. (Photo: Prof. J. H. Taylor.)



4. Base of a greywacké bed showing strong *groove-casts*. The current flow was from right to left. The beds above and below show *flute-casts* with the same orientation. Silurian Grits, Aberystwyth. (Photo: Prof. J. H. Taylor.)



5. Base of a greywacké bed showing *flute-casts*. These were probably formed by the infilling of scour-marks made in the underlying mud by a swift current. Silurian Grits, Aberystwyth. (Photo: Prof. J. H. Taylor.)

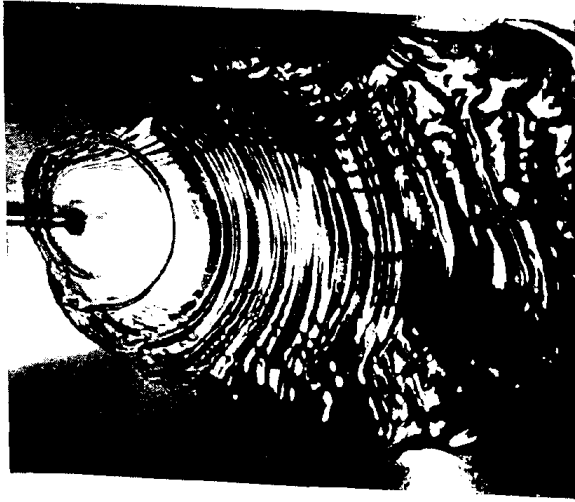


6. Greywacké bed showing internal convolutions (*convolute bed*). Tertiary Macigno, near Fiesole, Italy. (Photo: Prof. J. H. Taylor.)

METAL ADHESIVES



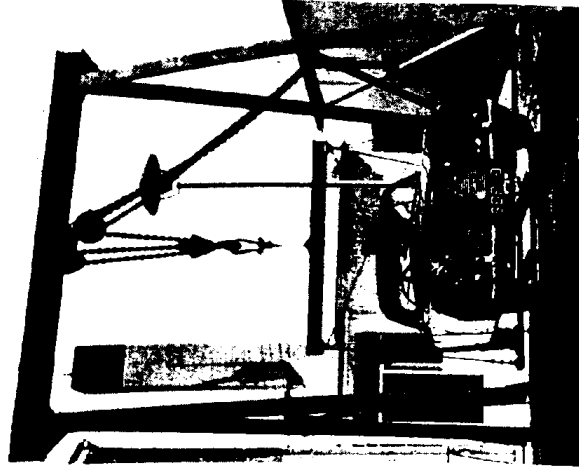
7. An electronic-flash photograph of a stream of water running down a polyethylene sheet. The water appears to be repelled by the polyethylene.



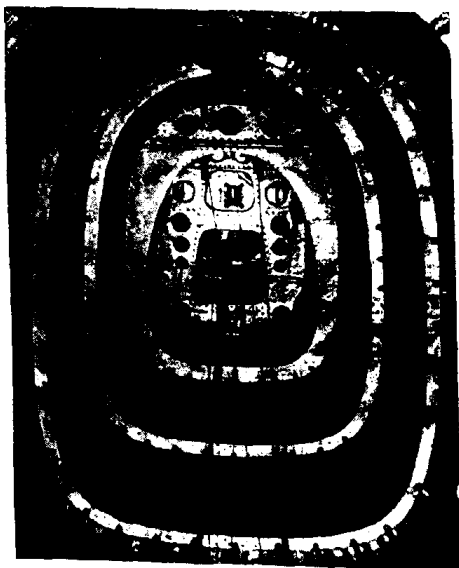
8. Here the polyethylene sheet has been 'flamed' with a bunsen burner. This makes the surface hydrophilic and so the water now spreads out.



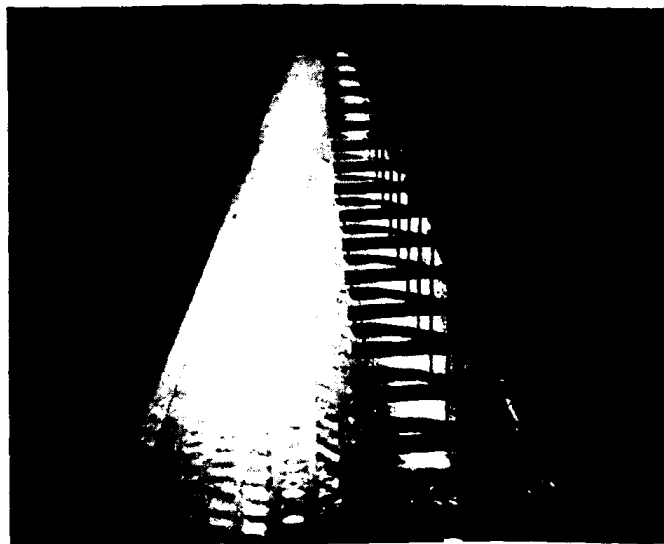
9. The Chance Vought 'Regulus' guided missile, the construction of which involves the use of a metal adhesive.



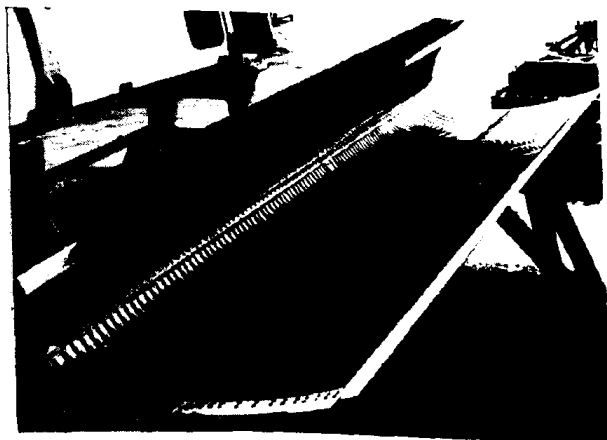
10. Car weighing 30 cwt. suspended on a 3.25 sq. in. adhesive bonded joint; the joint could carry three similar cars.



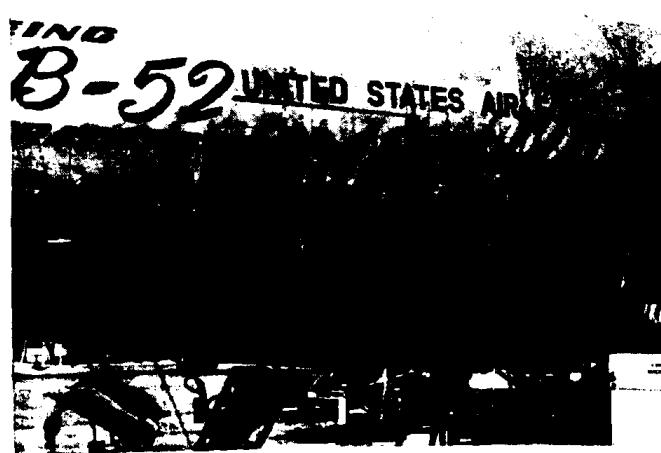
11. Fuselage of 'Dove' showing use of metal adhesives to attach stringers to panels.



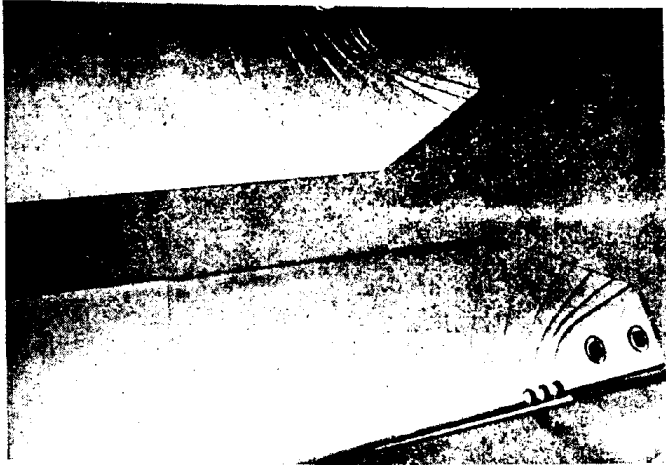
13. Wing of 'Dove' under test simulating air load. The wrinkles in the skin are suppressed where it is glued to the longitudinal stringers.



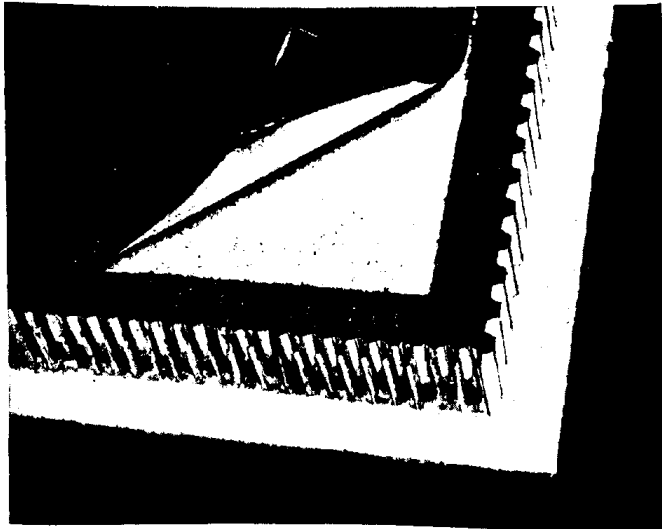
12. Section of Bristol 'Britannia' leading edge showing corrugated inner skin bonded with metal adhesive to the outer skin.



14. Wrinkling in the side of the fuselage of a bomber under the conditions of load while sitting on the ground.



15. Helicopter blade showing the use of adhesives to avoid the difficulties inherent in machining from the solid.



16. The principle of sandwich construction using aluminium foil honeycomb, to the open ends of which the panels are attached with adhesive.

a material reduction in rat and mouse damage in these depots. The question asked here is: what evidence is there that this effort was directed to the best economic advantage?

To answer this fully we need to know at least three things. First, it should be possible to assess the effect of routine control measures on rat populations. Second, an estimate of the losses caused by given numbers of rats is required. Third, for the area concerned, the approximate size of the rat population should be known.

The Effects of Control

Studies of the effects of control on rat populations are difficult to undertake, especially on a large scale, but some have been made. Working at Oxford, A. D. Middleton showed that the new methods permitted economic control on certain types of farms (3); but a later study, carried out by zoologists of the Ministry of Agriculture in two Devon villages in which residences and farm buildings were old, showed that in more difficult environments satisfactory control is, on any standard, less easy (4). Partial clearances of rat populations were followed within six months by a restoration of rat numbers to 'normal', that is, to the probable maximum for the area in the prevailing conditions; on the other hand, very thorough clearances, involving at least two successive poisonings, had a much more lasting effect – one which was still evident after a year. This had practical implications. In agricultural areas in England it was usual for rat treatments, by poisoning or by 'gassing' with cyanide, to be carried out at three-monthly intervals. A more economical procedure would probably have been a really thorough operation once a year.

Where rats have plenty of cover and food, as D. E. Davis, the American ecologist, has emphasized, it is difficult to reduce the population to near zero; and if rat numbers are only brought to, say, 30 to 50 per cent of the maximum, the survivors multiply at their highest rate, and rapidly restore their numbers (5). Davis and his colleagues, working in Baltimore, showed that both growth and fertility rates increase in rat populations which have

been decimated by trapping or other means: competition for food and space among the survivors is reduced, and conditions become more favourable for those that are left.

In some environments *Rattus norvegicus* is exceedingly inaccessible. This applies especially to sewers, of which old systems are commonly heavily infested and so constitute a regular source of infestation of buildings, via the drains or burrows in the surrounding earth. From 1943 onwards, therefore, a formidable effort has been devoted to killing sewer rats in all the main towns of England and Wales. It was supposed that initial clearances, by means of thorough poisoning campaigns, would so reduce sewer rat numbers that later they could be kept down with only a modest expenditure of labour and materials. This policy may have worked in some places; but a study made in 1947-50 in some London sewers by a Ministry of Agriculture research unit showed a very rapid restoration of the population after a probable reduction of about 97 per cent (6). The evidence was that this recovery was aided by reinvasion from the surface. A more recent study, also by Ministry zoologists, suggests that in some instances poisoning rats by baiting at the bottom of sewer manholes (the only practicable system) may sometimes fail to reach all the rats living in or visiting the sewers (7). Here then we have a case in which great effort, over a period of more than a decade, has been put into control, in advance of a satisfactory knowledge of even the population dynamics of the pest.

The obstacles in the way of complete extermination, and the expense and administrative difficulties of even attempting it, naturally suggest that environmental control, by the reduction of cover and accessible food, and by repair of drains and sewers, should be more profitable than direct destruction. Unfortunately, in many environments, this would involve large-scale replanning and rebuilding. At best, it can be only a very long-term aim.

A similar situation arises in regard to locusts – another group of food pests of world-wide distribution. There have been spectacular successes in locust control since 1940. These have been based on the discovery that locusts exist in two phases: in one,

they swarm in vast numbers; in the other, they exist as ordinary, large grasshoppers showing no gregarious tendency. Swarming depends on special environmental conditions, and these occur only in certain areas. For Africa these areas have now been mapped, with the result that advance warning of incipient swarms can be given, and the insects can be destroyed with poison before they become airborne. Despite the success of these measures, B. P. Uvarov, Head of the Anti-Locust Research Centre in London, has emphasized that in the long run the remedy must be prevention, by changing the environments in which the outbreaks start (8). In some areas this will involve an alteration in agricultural or stockbreeding practices.

Numbers and Damage

The examples of research on rat control described above are exceptional. They are based on a technique of census first described by D. H. Chitty at Oxford – one which, in skilled hands, can give reliable results. This depends on laying surpluses of a standard food such as wheat, acceptable to rats, at many points in the infested area, every night until the amount eaten levels off at a steady maximum. A control measure may then be applied, and the census repeated. The result of the second census gives an estimate of the reduction in rat numbers effected by the control operation. The data from ordinary poisoning campaigns provide no basis at all for estimates of 'success', and calculations of the rats killed, sometimes derived from such evidence, have no validity.

Estimates of total rat populations, for a country, a county, or other large area, are also usually worthless. If to make a census in a farm or a large warehouse is difficult, to do so for an administrative area requires far greater expenditure on field research than has hitherto been allowed. (Such expenditure would, of course, remain trifling compared with that on actual control.) However, C. S. Elton and E. M. O. Laurie at Oxford estimated the fluctuating numbers of rats in corn ricks in England – the most important habitat for rural rats – and showed that, over a period of five years during which rat control was

greatly expanded, little change took place in these populations (9).

Another example of a large-scale inquiry into rural rat populations is that of the two villages mentioned above. In them, minimum rat populations were estimated as 180 and 330 respectively; the corresponding human populations were 360 and 270. In both villages there was one cat or dog to every five persons. These figures of rat numbers, undoubtedly underestimates, cannot however be applied to other habitats; they merely indicate that inquiries of this sort are practicable.

As for damage, there is an even more notable dearth of quantitative data. The complexities may be illustrated from the one small group of experiments which has been done. Bagged wheat was exposed to attack by four small colonies of rats for periods of 12 to 28 weeks. The net cost of the rat infestations at the end was 18 per cent of the original value of the wheat plus the sacks. This included labour. More than half this loss was, however, due to damage to the sacks which were torn up by the rats for nesting (10). It is often said that rats cause more loss of food by fouling than by eating, but in this instance all the wheat fouled was, after cleaning, declared fit for human consumption. No doubt the picture would have been different had the rats been allowed to breed longer.

ECONOMICS AND HEALTH

The data above are all expressed in terms of rats as food pests. Where rats are to any important extent disease carriers (as they are in many countries) further difficulties arise. During a plague outbreak in Malta the government employed, on rat control alone, a labour force in the proportion of one operative to every 4,000 inhabitants; the Services employed many more (11). In the circumstances, this was worth while: it was followed, not only by the collapse of the plague epidemic, but also by a marked reduction in endemic typhus (also rat-borne) and by a general decline in the rat population. Afterwards it was possible to keep rat numbers low with a relatively small, permanent labour force. But there is no means of telling whether a similar effort would

have been economically justifiable had rats in Malta been food pests only.

In certain economic conditions it might be worth while to apply a large labour force, for a short period, to controlling rats or other pests, on the assumption that later, when a greatly reduced pest population had been established, a much smaller number of men could be employed on maintenance work. The initial effort would then correspond to a capital outlay which would not have to be repeated. The exact conditions in which such an outlay would be justifiable could, however, be established only on the basis of accurate quantitative data on the effects of the pests.

Until recently, rabbits in Britain represented just this sort of problem. Now, however, myxomatosis has made the first stage, of large-scale control, unnecessary: today the rabbit population is relatively small, and it can probably be kept small without uneconomic expenditure on control, provided that there is an adequate national plan and that the farming community co-operates.

A General Problem

The example of rats is a convenient one, since there are at least some facts which can be reported. But the problem is quite general. Locusts and rabbits have also been mentioned, and E. H. Graham, the distinguished American biologist, in an admirable book on land use, has assembled many examples of the need for quantitative studies (12). He cites an investigation of a campaign against 'vermin', in which many snakes were killed. About one-third were pilot blacksnakes, which eat small rodents. Careful and conservative estimates have suggested that the destruction of these snakes, in twenty-six United States counties, led in one pre-war year to a loss from rodent damage of crops worth \$132,000. Graham quotes another American authority, L. R. Dice:

When naturalists advocate that scientific studies be made before beginning a control campaign, they are told there is no time to make a scientific study while a farmer's crops are being eaten up or his

poultry devastated. This excuse would be more satisfying if it were not repeated year after year. . . . The ecologic and economic studies of wild life which should be made in every region before initiating a poison campaign are . . . not now being made, and with a few notable exceptions, never have been made anywhere by men competent to conduct such studies.

If facts of this kind have still to be discovered in most fields of applied biology – if, indeed, they are as yet not even being sought – we must be very far from answering the type of question put at the beginning of this article. For pests, the question in a simplified form might be this: if, in a given area, one hundred men are employed on pest destruction, will those men save more food than they would produce if they were farm workers? Or should there be fifty men, or two hundred?

A PROBLEM OF SOCIAL PSYCHOLOGY

Since a fully rational scheme of pest control is possible only if this sort of problem is solved, and since the same principle applies in far wider spheres of applied science, it is surprising that such questions for the most part remain unasked. The Report of the Working Party on the Nursing Services did raise the question of the optimum number of nurses in different types of area in England and Wales – in a minority report signed by only one member (13); but this is an isolated and rejected instance of resort to reason. What is the source of the resistance to this obvious line of inquiry? The answer is perhaps to be found in a counter-question, often made in reply to the argument given above: does this mean that the work in question is useless? Perhaps this starkly irrational response sometimes conceals an unacknowledged feeling of guilt that the work or the organization concerned is not objectively justifiable. It may stem from the fear that scientific scrutiny would justify a cutting down of establishments (although it might just as well have the opposite effect). In any case, inquiry is always likely to lead to a change of methods or routines, and to a demand for the application of an adaptable intelligence instead of a capacity to adhere unthinkingly to a set of regulations.

It is not yet understood that the whole practice of government and administration can be usefully made the subject of scientific inquiry. Scientists themselves are for the most part accustomed to thinking in this way. For some, the subject is too 'political'. It is indeed political (that is, pertaining to the state, its government and policy), but that is not a valid reason for regarding it as unfit for polite discussion. The aim must be, in the long run, for the whole of administration to be imbued with the objective, quantitative, and heuristic methods of science. But this will be possible only when we are freed from the belief, still held by influential people, that a scientist, being a manual worker, is inferior to persons who have made a special study of ancient literature and languages. There is still a notion that 'science' is some sort of machine or organization, into which certain sorts of problem can be fed, and which may then, if rightly treated, disgorge an answer. The fundamental error here is the belief that 'science' is a sort of thinking or type of method which applies only to a narrow range of problems coming under such familiar headings as physics, chemistry, and biology. In fact, scientific methods and thinking can and should pervade all human activities which are directed towards definable ends. This was seen clearly enough in the operational research of wartime, but the full lesson still remains to be learned. The learning will demand extensive re-education both of administrators and their scientific colleagues. One of the former once said during a discussion on organization: 'You scientists are never satisfied'. Unfortunately this is not always true. But it should be.

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THE ELECTRICAL CONSTANTS OF FREE SPACE

W. C. VAUGHAN

FROM the time of Newton's formulation of the laws of mechanics, almost every major advance in the field of physics has modified, to some extent, the contemporary attitude to what has come to be described as free space. Little short of a history of physical science during the past two centuries would suffice to describe this trend in ideas, which has culminated in the recognition of the free-space velocity of electromagnetic waves as the most fundamental of all physical constants. The main purpose of this article is to trace the consequences of this evolution in thought, and to show that implicit in the systems of units used by scientists and by engineers are two fundamental quantities that are termed the electrical constants of free space.

BASIC STANDARDS

Measurements in mechanics require the prescription of three basic standards; a unit of length, a unit of mass, and a unit of time. From earliest times it was realized that several important considerations governed the choice of these standards. It must be possible to define them unequivocally, they must be easy to copy, they must be invariable. Furthermore, methods must be available for subdividing and multiplying each standard. If such criteria can be met, the size of the unit may be arbitrarily selected. The essence of all measurements in physics is comparison with standards; the ultimate purpose in refining experimental techniques is to facilitate or to enhance accuracy in making these comparisons.

Length

The first reliable standards of length were measuring rods. When knowledge of astronomy had advanced sufficiently to enable the dimensions of the earth to be estimated, it was natural to relate the measuring rod to the circumference of the earth. This led to the proposal of a standard of length, the *metre*, which should be one ten-millionth part of the distance from equator to pole. Now it should be noted that to define a metre in this way is to make the terrestrial distance the primary standard; the measuring rod is then a secondary standard – obtained by subdivision. In terms of such a definition, measurement of the earth's quadrant is meaningless: observations purporting to do this, in fact, compare an arbitrary distance between two marks on a measuring rod with a much larger standard distance. The rod, not the earth, is measured. As precision in comparison improves, it becomes necessary to recalibrate all measuring rods if their inaccuracies are not to be transferred to other physical measurements for which they may be employed. Slight though these corrections might be, continual readjustment of the practical sub-standard would be intolerable. The terrestrial standard dimension is inconveniently large except for astronomical purposes; moreover, there is evidence that it is not quite constant. The international standard of length was therefore specified as the distance between two marks on a platinum-iridium bar, called the International Prototype Metre, deposited at the International Bureau of Metric Standards at Sèvres, near Paris. This standard, it should be emphasized, is an arbitrary distance. It is now known to be about 0.02 per cent less than a ten-millionth part of the earth's quadrant.

Elaborate means have been devised for reproducing copies of this standard, and in 1889 a number of these reproductions were distributed by lot to different countries. In 1894, Michelson and Benoit used an interferometer to compare the standard metre with the wavelengths of three lines in the spectrum of cadmium. This comparison has been repeated by other workers; recent results using the red component of the spectrum of this element

differ by less than one part in a million from that obtained over sixty years ago. The wavelength of the cadmium red line is inconveniently small for use as a standard of length. It does, however, furnish a satisfactory sub-standard against which the invariability of the standard metre and the accuracy of copies can be assessed.

Mass

In comparison with the metric standard of mass, the British standard, the *pound*, is of great antiquity. Originally it was specified as equal to the weight of 7,000 average grains taken from the middle of ripe ears of wheat. The present standard is a bar of platinum, called the Imperial Standard Pound, preserved at the Standards Office of the Board of Trade. The metric standard of mass, the *kilogram*, is a bar of platinum deposited at Sèvres. This unit was formerly defined as the mass of one litre of distilled water at the temperature of its maximum density. It may be desirable to link the standards of length and mass in this way, but this does not furnish a primary standard. Indeed, following the discovery of heavy hydrogen by Urey, Brickwedde, and Murphy, and the isolation of heavy water, in consequence of extremely refined experiments, an unexpected variability in the older specifications was revealed.

Time

The standard of time is the *second*. This is defined as the 86,400th part of a mean solar day. In this instance the standard is determined from astronomical observation of the period of the earth's rotation. This, however, is not quite constant, its irregularity being measurable by comparison with the period of vibration of a quartz crystal. Although a still more constant interval of time is provided by molecular vibrations, it would be inconvenient to use as a standard of time any interval not directly related to the mean period of the earth's rotation. Adoption of some new standard would, of course, be necessary if the variability of the present unit were sufficient to prejudice high accuracy. In the few instances where it might seem justified, the

The factor ϵ in this relation represents some property of the medium separating the bodies since this too was found to affect the force. The term ϵ is called the *permittivity*, or dielectric constant, of the medium. Coulomb's law applies even when the charged bodies are in a vacuum; indeed, the force is then slightly greater than under similar circumstances in air. Thus a permittivity ϵ_0 must be ascribed to free space. By means of Coulomb's law it is possible to define a unit of electric charge in terms of the C.G.S. units of force and distance and the permittivity of free space. If two bodies carry unit electric charge they will experience an electrostatic force of 1 dyne when separated by a distance of 1 centimetre in vacuum. This definition specifies an absolute unit termed the *C.G.S. electrostatic unit of electric charge*. This definition regards ϵ_0 as having unit value.

A rapid advance in the understanding of electromagnetism followed Ampère's quantitative formulation of the evidence from Oersted's discovery in 1820 that an electric current produced a magnetic effect. As a result, it became possible to compute the force between a pair of conductors due to the currents they carry. In particular, it was shown that if two long parallel wires separated by a distance r carry currents I_1 and I_2 , any small portion of conductor of length d experiences a force

$$F = \frac{2I_1 I_2 d}{r} \times \mu$$

due to the current in the other. It is necessary to introduce into this relation the factor μ , characteristic of the medium separating the wires, since this too affects the magnitude of the force. The factor μ is called the *permeability* of the medium. From this formula it is possible to define a unit of current. Suppose, for example, that the two wires form a long narrow loop so that they carry equal current in opposite directions. This current will have unit value if each centimetre of one conductor experiences a force of 2 dynes due to the current in the other when they are separated by 1 centimetre in a vacuum. Here μ_0 , the permeability of free space, has been given unit value, and, since C.G.S. units of force and distance have been employed, the absolute unit so

defined is called the *C.G.S. electromagnetic unit of current*.

Now an electric current is the consequence of the drift of electric charge along a conductor; if one unit of charge passes a point on a conductor in one second, there is unit current in the circuit. Thus a current of one electromagnetic unit is the passage of one electromagnetic unit of electric charge in each second. Implicit in the definition given in the previous paragraph we therefore have a definition of the *C.G.S. electromagnetic unit of charge*. An important question now presents itself; are the electrostatic and electromagnetic units identical?

COMPARISON OF ELECTROSTATIC AND ELECTROMAGNETIC UNITS OF CHARGE

In 1879, Ayrton and Perry carefully compared these two units by an indirect method which combined simplicity with a high order of accuracy. If a high-voltage battery is connected to a pair of well-insulated plates, the charge they acquire soon becomes steady, since none can leak away. In this steady state, the plates have an electrostatic charge that can be computed from a knowledge of the voltage, the area of overlap of the plates, the distance separating them, and the material between them. Now if the battery is disconnected and the plates joined by a wire, a current flows until the system is discharged. The number of electromagnetic units of charge carried by this current can be determined from the readings of an instrument known as a ballistic galvanometer, connected in the circuit. In this way Ayrton and Perry were able to show that the electromagnetic unit of charge was very nearly 3×10^{10} times the electrostatic unit.

In defining the electrostatic unit of charge, it was stated that a force of 1 dyne would be experienced by a body bearing one of these charges if a similarly charged body was situated in a vacuum 1 centimetre from it. If each of these charges were increased 3×10^{10} fold the force between them would be $(3 \times 10^{10}) \times (3 \times 10^{10})$ times greater. Thus, if each body bore 1 electromagnetic unit of charge, the force experienced would be 9×10^{20} dynes. The equation expressing Coulomb's law, which is true regardless of the choice of units, will only yield this result

if ϵ_0 is given the value $1/(9 \times 10^{20})$. This then must be the permittivity of free space in the C.G.S. electromagnetic system of units. From the relation for the force between two parallel conductors that carry currents, a precisely similar argument leads to the conclusion that in the C.G.S. electrostatic system of units, μ_0 , the permeability of free space, must be $1/(9 \times 10^{20})$.

It is evident that ϵ_0 and μ_0 must be electrical quantities of some sort. If this were not so, then the equations in which they appear would purport to relate electrical and mechanical quantities; they would, in fact, imply that electric charge could be described in terms of distance, mass, and time only. This would deny the existence of purely electrical phenomena. The mechanism of a force cannot be visualized; ϵ_0 and μ_0 are equally abstract concepts. Failure to appreciate this was responsible for the attempts made to identify an ether in which electromagnetic waves could be propagated. Maxwell's classical work had its origin in a realization that the mystery of ϵ_0 and μ_0 could be dispelled if they were considered together. As we shall see, suitable combinations of these two quantities evoke quite familiar concepts. To understand this, it must be appreciated that the two sides of any equation must balance not only arithmetically but also in respect of the types of quantities which it relates. Quite obviously, no equation can show a valid relation between, say, distance and weight. If distance appears on the left side, the quantities on the right must reduce to distance. By carefully examining the two equations that were given earlier, it is not difficult to show that these balance in terms of quantities only if,

$$\epsilon_0 \times \mu_0 = (\text{time})^2 / (\text{distance})^2$$

that is, if

$$1/\sqrt{\epsilon_0 \times \mu_0} = \text{distance}/\text{time}.$$

Now distance divided by time is, of course, velocity. If the quantities in the equations are expressed in C.G.S. units, then the velocity will be in centimetres per second. As we have seen, in the electrostatic system of units, ϵ_0 has unit value, and μ_0 is $1/9 \times 10^{20}$. Thus

$$1/\sqrt{\epsilon_0 \times \mu_0} = 3 \times 10^{10} \text{ centimetres per second.}$$

Exactly the same value is obtained if the electromagnetic system of units is employed. The velocity so calculated relates to free space: it is the velocity c of electromagnetic waves in free space. Thus,

$$1/\epsilon_0 \mu_0 = c^2.$$

This relation, which Maxwell concluded would be true in any consistent system of units, is one of the two most important equations known to physics. The other is Einstein's equation which relates mass and energy. It is significant that c^2 appears in both these fundamental relationships.

PRACTICAL UNITS

The choice of units in any applied science must, of course, take into account their suitability for practical purposes in technology. From the standpoint of the engineer, the system of units based on the centimetre, the gram, and the second, suffers from the drawback that it leads to a unit of work, the erg, which is inconveniently small. It therefore became necessary to devise a so-called practical system of units which are multiples of the absolute C.G.S. units. Instead of the erg, the engineer employs as a unit of work or energy the *joule*, which is equal to 10 million ergs. In this practical system, the unit of power, i.e., the rate at which work is done, is the *watt*. This represents the expenditure of 1 joule of work per second. The kilowatt is, of course, 1,000 watts, and this is equivalent to 1.34 horsepower; the horsepower is not a metric unit; it is derived from the foot, the pound, and the second, as fundamental units. If 1,000 joules of energy are expended in 1 second, the rate of working is 1 kilowatt, and if this is maintained for one hour, the energy expended is 1 kilowatt-hour. This is the quantity of energy colloquially referred to as a 'unit' when specifying the amount of electrical energy supplied to a consumer. Thus an electric fire that consumes energy at the rate of 1,000 watts will use one 'unit' per hour. Strictly speaking, the kilowatt-hour is not an electrical unit at all, but is a measure of energy. In the example quoted it refers to energy used for heating.

From the point of view of the electrical engineer, neither of

the absolute systems is well suited for practical measurement. Early experiments showed the electromagnetic unit of charge to be somewhat too large for convenience, and the electrostatic unit to be far too small. A practical unit, the *coulomb*, equal to one-tenth of an electromagnetic unit of charge, was therefore selected. The practical unit of current, the ampere, is then the passage of 1 coulomb per second. The work done in carrying unit electric charge from one point to another is termed the potential difference between the two points. Unit potential difference, called the *volt*, will therefore exist between two points if one practical unit of work, i.e., 1 joule, is expended in conveying 1 practical unit of charge, i.e., 1 coulomb, from one point to the other. The volt is of the same order as the potential difference existing between the terminals of a simple cell when disconnected. It is fairly simple to show from these definitions of the practical electrical units that when a current of 1 ampere is maintained between two points having a potential difference of 1 volt, 1 joule of work is expended in each second. The power is therefore 1 watt. The practical electrical units are thus conveniently and simply related to the practical mechanical units.

If in a conductor a potential difference of 1 volt produces a current of 1 ampere, its electrical resistance is said to be 1 *ohm*. The resistance of a conductor depends on its dimensions and on the material of which it is made, so that it is possible to specify a prototype standard ohm. Such a standard, called the International Ohm, consisting of a column of mercury of stated dimensions at a given temperature, was approved by the 1908 International Conference on Electrical Units. The same meeting also defined a secondary standard, the International Ampère, as that steady current which would deposit silver at a specified rate from a solution of silver nitrate. The prototype standards for a practical system of electrical units thus came into being.

GEORGI'S M.K.S. SYSTEM

In 1881, the First Electrical Congress in Paris had ratified as fundamental the C.G.S. electromagnetic system of units. Recog-

nizing the inconvenient size of some of the units in this system for engineering purposes, the meeting adopted at the same time five practical units, the ohm, the volt, the ampere, the coulomb, and a unit of capacitance, the *farad*. It seems inexplicable that for more than half a century following this decision, scientists and engineers should have tolerated three distinct systems of units, two absolute and one practical. Although the pitfalls of conversion from one system to the others bedevilled the work of students and advanced workers alike, no real progress towards ameliorating the complications of this situation was made until 1935. A highly satisfactory solution of the problem had however been proposed in a paper published by Professor Georgi in 1901. That this failed to capture the support it undoubtedly merited seems attributable, at least in part, to acceptance as immutable, of systems having the sanction of international agreement.

It is worth noting in passing that the C.G.S. units are not, as is often thought, based on the international prototype standards: the latter, it will be recalled, are the metre, the kilogram, and the second. Georgi's proposal was an absolute system of units based on these international standards, to be known as the M.K.S. system from their initial letters. The outstanding merit of such a system, he pointed out, was that it actually included the existing practical units. The thousandfold increase in the unit of mass, and the hundredfold increase in the unit of length, gave a unit of force a hundred thousand times larger than the dyne. David Rowland suggested in 1904 that this unit of force might appropriately be named the *newton*. The hundredfold increase in the unit of length, together with the hundred-thousandfold increase in the unit of force, lead to a unit of work equal to 10^7 ergs, namely, the joule. Because Georgi's system includes the joule, and retains the second as the unit of time, it must also include the watt as the unit of power. It follows that it will also include all the practical electrical units mentioned above. Here, then, we have an absolute system which also embraces the practical electrical units. The need for separate absolute C.G.S. systems disappears.

Despite the undoubted advantages of Georgi's suggestion, it did not receive general acceptance until the Scheveningen-Brussels meeting of the International Electrotechnical Commission in 1935. Even then, this body resolved that the new absolute system should supplement, but not replace, the existing systems. Support for the M.K.S. system was still restrained when, three years later, the commission discussed at its Torquay meeting the eventual replacement of the older systems. It was to take tremendous advances in the field of radio technology during the Second World War to convince large numbers of scientists and engineers that the tedious complications under which they had laboured for so many years need no longer be tolerated.

Impedance of Free Space

Workers in the field of radio communication are concerned with determining how energy in the form of electromagnetic waves may be most efficiently launched into free space. The transmitting aerial in these circumstances may be regarded as a source from which energy is supplied to a load, in this instance, free space. It is well known that the energy supplied to an electric fire in a given time depends on the electrical resistance of its elements; moreover, this is the only property of the load that affects the transfer of energy. More generally, we may regard the load resistance as that which determines the rate at which a load can absorb energy from a particular source. Accordingly, the radio engineer requires to know the value of the corresponding property to which he must match his aerial systems. This is termed the resistance or, to be more precise, the impedance of free space. Clearly this cannot be measured directly by experiment, but its value can be deduced from a knowledge of ϵ_0 , the permittivity of free space, and μ_0 the corresponding permeability, the two constants of free space that have been under discussion.

If the two equations given earlier are multiplied together and their terms rearranged, we arrive at the following interesting relation between the types of quantities involved,

The Electrical Constants of Free Space

$$\frac{\mu_0}{\epsilon_0} = \frac{(\text{force} \times \text{distance})^2}{(\text{charge})^2} \times \frac{1}{(\text{current})^2}$$

or

$$\sqrt{\frac{\mu_0}{\epsilon_0}} = \frac{\text{work}}{\text{charge}} \times \frac{1}{\text{current}}$$

Work divided by charge is, from the definition given in a previous paragraph, potential difference. Furthermore, potential difference divided by current is resistance. Thus $\sqrt{\mu_0/\epsilon_0}$ represents a resistance, which, because μ_0 and ϵ_0 are free-space constants, must therefore represent some property of free space.

We have seen that in electromagnetic units μ_0 is unity and ϵ_0 is $1/9 \times 10^{-20}$, so that $\sqrt{\mu_0/\epsilon_0}$ is 3×10^{10} C.G.S. electromagnetic units of resistance. By applying the principles of conversion already outlined it can be shown that the practical unit of resistance, i.e., the ohm, is equivalent to 10^9 electromagnetic units of resistance. This being so, then $\sqrt{\mu_0/\epsilon_0}$ is 30 ohms. The theory of wave propagation indicates that the value of impedance required by the radio engineer as a basis for his aerial calculations is 4π times this result.* The impedance of free space is therefore 377 ohms.

For convenience, the data pertaining to the electrical constants of free space are summarized in Table I.

The Meaning of ϵ_0 and μ_0

In the present state of knowledge, there seems no possibility of being able to assign any precise meaning to the constants ϵ_0 and μ_0 that will give any physical picture of the mechanism of propagation in free space. These are concepts which, in common with the notion we classify as force, emphasize our complete ignorance of the fundamental mechanisms of nature. Neverthe-

*The multiplier 4π comes in this instance from the fact that the surface area of a sphere of unit radius is 4π . For reasons beyond the scope of this article, account is sometimes taken of this multiplier by writing ϵ_0 as $1/4\pi \times 9 \times 10^9$, and μ_0 as $4\pi/10^7$. These are said to be respectively the rationalized M.K.S. values of the permittivity and permeability of free space.

CONSTANT	SYSTEM OF UNITS		
	C.G.S. Electrostatic units	C.G.S. Electromagnetic units	M.K.S. units
Permittivity of free space ϵ_0	1	$1/(9 \times 10^{20})$	$1/(9 \times 10^9)$
Permeability of free space μ_0	$1/(9 \times 10^{20})$	1	$1/10^7$
Velocity of electromagnetic waves in free space $c = 1/\sqrt{\epsilon_0\mu_0}$	3×10^{10} cm./sec.	3×10^{10} cm./sec.	3×10^8 m./sec.
Impedance of free space $Z = 4\pi\sqrt{\mu_0/\epsilon_0}$	$4\pi/(3 \times 10^{10})$	$1.2\pi \times 10^{11}$	377 ohms

less, as we have seen, they are in no sense the consequences of abstruse speculations about the unknown. Indeed, it is symptomatic of the spirit of modern physics that the seemingly insuperable barriers which they mark neither limit the expansion of knowledge, nor does lack of knowledge of fundamental processes rob technological advancement of its vigour.

THE PARASITE'S POINT OF VIEW

GEOFFREY LAPAGE

THE WORD parasite, which is derived from the Greek words *para*, beside, and *sitos*, corn or food, means, to the average healthy human being, a sponger, a hanger-on, a person who does not earn his keep; and this meaning makes us dislike the human parasite, or we regard him with feelings stronger than that. We like to believe we are independent, self-supporting individuals, who rightly despise those who are not; and, when we hear biologists say that some animals, or that some plants, are parasites, we transfer the meaning of the word just described to these creatures and recoil from them. We think of parasitic animals or plants as creatures that are unpleasant, ugly, and undesirable; and, as we learn more about them, we find considerable justification for this very natural attitude.

For parasites undoubtedly do human beings and human society a great deal of harm; they cause illness, suffering, and death. They also do other animals and plants a great deal of harm. Many crops and many domesticated animals are severely harmed by various parasitic animals. The harm that these animals do, in fact, compels man to defend himself continually against their activities, and a large company of biologists, medical men, veterinarians, and agriculturists are all the time trying, all over the world, to minimize or abolish the harm done by parasitic animals. The job of these men is not, however, to pass moral or ethical judgements on the parasitic way of life. Their job is to study parasites objectively, by scientific method, and to put themselves, so to speak, in the shoes of the parasite; for only by this method can the parasite be properly understood. If it should happen – and it often does happen – that biologists lose their natural dislike of the animals they study, or even learn to see in them that beauty of structure and that more difficult

and more abstract beauty of adaptation shown by all living creatures, that is an outcome with which this article is not concerned. The aim here is to show how the world looks from the point of view of a parasite. Especially this article tries to present the point of view of animals that are parasitic; for parasites may be bacteria, which are plants; or viruses, which are neither animals nor plants; or animals, such as tapeworms, flukes, roundworms, mosquitoes, horse flies, fleas, lice, and other parasitic insects which, with the ticks and mites, are more or less familiar to us all. We need not be ashamed if we have experience of some of them, for no animal on the earth is free from parasites, and man has been plagued by them since the earliest days of his history.

Approaching our subject in this way, we may first ask what we mean by the term parasitic? What, that is to say, is the scientific meaning of the two words parasitic animal? Basically we can say that parasitism is simply a method of getting food. Some animals, the typical carnivores like the lion and the wolf, get their food by killing other animals; they feed on flesh. Other animals, such as the ox or horse, are herbivorous; they get their food by killing and eating plants. But parasitic animals also feed on animals or plants, so it is not the kind of food that distinguishes the parasitic animal, but rather its method of getting its food. Unlike the carnivores or herbivores which consume animals or plants, the parasites learn to live either inside, or on the surface of, the bodies of the other organisms from which they get their food. They form an *association* with these other organisms; the animals or plants with which they associate are called their *hosts*.

Parasites do not necessarily kill their hosts. Unlike man, who cultivates animals and plants for the purpose of killing and eating them, the parasitic animals – the successful ones, at any rate – preserve, so to speak, the goose that lays the golden eggs. They always, however, inflict some kind of injury on their hosts. They must do this, for they feed on the tissues and tissue-fluids of their hosts and, in doing this, they inflict other kinds of harm.

They may, for instance, (a) nibble off portions of the host's

body; human hookworms, for instance, suck in, by means of powerful pharyngeal pumps, plugs of the lining of the small intestine and nibble off portions of these plugs of living tissue with the teeth and cutting plates inside their bell-shaped mouths; they also suck blood in prodigious quantities; (b) inflict in various different ways small injuries on the tissues of the host; this causes irritation and inflammation with subsequent permanent changes in the anatomical make-up of the tissues affected, e.g., formation of scar-tissue, or even tumours of various kinds; (c) block up the host's vital channels such as blood vessels or the ducts (bile ducts) that bring bile from the liver to the intestine; (d) exert, as they grow, mechanical pressure on the tissues of the host, with the result that these tissues are destroyed or vital channels in them are occluded; (e) remove from the host, not only blood, but other essential elements of the host's food, such as the sugars and vitamins; (f) introduce into the host, bacteria, viruses, or other organisms; (g) produce substances that poison the host; and finally (h) parasites may lower resistance (immunity) to diseases caused by other organisms.

These are some of the ways in which parasitic animals injure their hosts and they serve to show that parasites cannot be welcome to the host. The host suffers inevitably; and the host, of course, reacts against the parasitic animal. The inflammations caused by parasitic animals are but one form of the host's reactions; they result in changes in the tissues of the host, in the formation of scar-tissue, or of fibrous tissue that walls the parasitic animal off or otherwise limits its activities. The immunity that hosts develop is another form of reaction against parasitic animals. This is, for instance, a very important means by which man defends himself against malarial parasites. There are also other forms of reaction, all of which constitute what we call the signs and symptoms of the disease caused by the parasite.

The parasitic animal, which thus provokes the host to react against it, does not itself get off scot-free. It suffers from the reactions of the host: and we find, when we trace its history, that its way of life, the parasitic way of life, produces, in all kinds of parasitic animal, changes of structure and physiology that can

be grouped together as changes due to parasitism. In general the structure of the parasitic animal is simplified. The structure of some parasitic animals may, indeed, be so profoundly altered that they no longer look like their relatives. Few people, for instance, would believe, unless they were told that it is so, that the small, reddish, wormlike or almost shapeless creatures we sometimes see in our fish-shops attached to the gills of plaice, sole, and other fish, are relatives of shrimps and crabs. It is only by studying them carefully, and especially by studying their development, that we realize what their relationships are. It is then that we find that there appears, in the course of the development of these creatures, a young stage, which appears only in the life histories of Crustacea. This is proof that these remarkable parasites are also Crustacea. They are, of course, far gone in parasitism, so far gone that they must live attached to their hosts.

Among human parasites tapeworms and flukes must also attach themselves to their hosts. We find therefore that most of these sedentary species of parasites have suckers, or hooks, or both, by means of which they hold on to their hosts.

The simplification of structure mentioned above may be only a simplification of certain organs, or it may go further and lead to the loss of organs that are no use to the parasite. Some parasitic insects, for instance, especially those which, like the lice, live all their lives on the surface of a host, have lost the wings of their ancestors, as also have fleas and bedbugs. Another parasitic insect that has got rid of the wings is the sheepked that lives all its life in the wool of sheep. Some of the relatives of the sheepked show us how this has come about; for some of them, such as the New Forest fly found on horses in the New Forest, keep their wings although they live their adult lives on the horse's skin, to which they hold on tenaciously with their claws. Related to these flies are the deer-lice, the females of which begin life with wings, but use them only for making contact with the host and, once contact is made, throw them off. Another organ that is absent from some parasitic animals is the food canal. Tapeworms and thorny-headed worms, for instance, have

no food canal: they feed by absorbing food through the soft and permeable skin.

The loss of certain organs is, on the other hand, counter-balanced by the modification of existing organs to serve new purposes, or to perform their original functions in a more favourable manner. Among the most striking instances of this are the modifications of the jaws (mouthparts) of blood-sucking insects to enable them to pierce the skin of the host and to suck its blood and tissue juices. The jaws of mosquitoes, tsetse flies, and horse flies, for instance, have become elongated stylets; and associated with this modification of the jaws is a specialization of the pharynx to form an efficient muscular pump which sucks in blood much as the pharyngeal pump of the hookworms mentioned above also does. Ticks and mites, which also suck blood and tissue juices through the skin, have gone a step further. They have also developed a projection from the head (called the hypostome) which is thrust into the host's skin. This is an organ for holding on to the host while its owner feeds. On its surface it has teeth that project backwards and prevent its withdrawal from the skin.

These instances of modifications caused by the adoption of parasitic life are a few only of the many remarkable and beautiful structural adaptations that parasitic animals show to their particular mode of life: their physiological adaptations are equally remarkable and beautiful. Even more remarkable, and more important to man, are the answers that parasitic animals find to those other basic problems that they have to meet, the problems of reproduction and the maintenance of the species in the struggle to survive.

The first of these problems, reproduction of the species, is met by parasitic animals by methods that all kinds of animals use. Thus most kinds of parasitic animals, like their non-parasitic relatives, perform, at some time in their life history, an act of sexual reproduction which involves the fusion of a male spermatozoon (male gamete) with a female ovum (female gamete) to form a fertilized egg (zygote), from which an individual of the succeeding generation develops.

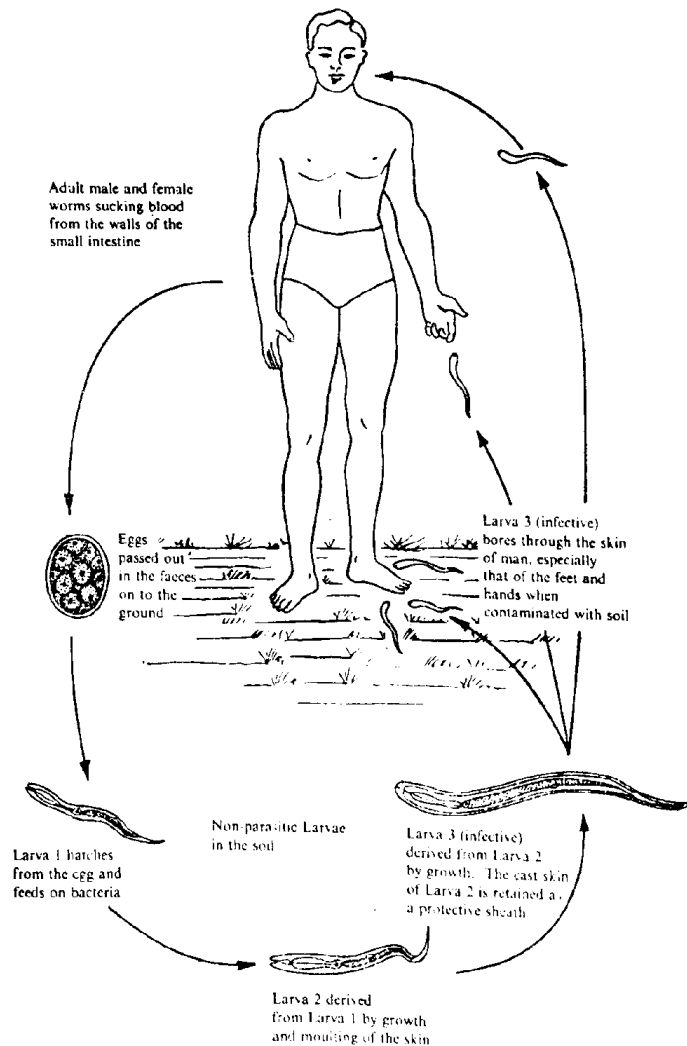


Fig. 1. Life History of Human Hookworms.

Most parasitic animals, at some time during the life history of the individuals, reproduce sexually like this. The sexes may be in separate individuals, as they are in insects, ticks, and mites; or they may be in a single hermaphrodite individual, as they are among the tapeworms and flukes. But, whatever the distribution of sexes among the individuals, sexual reproduction always effects an interchange of genes between male and female to give a zygote, or fertilized egg. It is when we consider the descendants of the zygote that we see how different kinds of parasitic animals increase their chances of survival and of establishing themselves in a host.

DIRECT LIFE HISTORIES

Human Hookworm

Consider, in the first place, the life history of a human hookworm shown in Figure 1. The adult male and female, which are about 0.3 to 0.5 inches long, live in the small intestine of man, nibbling off portions of its lining and sucking prodigious quantities of blood from small arteries that they ferret out. They produce fertilized eggs, which pass out in the faeces on to the ground. From each fertilized egg a single young worm (larva 1) hatches out, feeds on bacteria in the soil, grows, and eventually casts its skin to become a second larval stage (larva 2), which, in its turn, feeds and grows till it becomes the third and last larval stage (larva 3). This third larva cannot feed. It is enclosed in the cast skin of the second larva and must live on reserves of food in its body until it makes contact with the skin of a human being, or is carried by the hands or in some other way to the mouth, or gets into food or drink and is swallowed. It then infects man. This, as biologists say, is the infective larval stage. Its job is to make contact with a host and to establish itself inside. It is the only one of the three larval stages that can do this.

In this life history the infective larva can infect man either through his mouth or by penetrating his skin. Usually hookworms enter man through the skin, especially when people work with bare feet and hands in warm, moist soils where the infective

larvae have developed from eggs in human faeces deposited on these soils. These conditions prevail, for instance, in paddy-fields or tea-plantations in the East or in mines where the infective larvae are sheltered beneath the surface of the earth.

Looking at this life history we see that it is what is called a *direct* life history. The parasitic animal can pass directly from one host to another through the medium of its infective larval stage. It leaves its host in the form of the fertilized egg, goes through a period of development in the world outside, and then passes into a new host. It must therefore live in two worlds. One is the world outside inhabited by larval forms which live a non-parasitic life and are exposed to the risks and dangers common to all non-parasitic animals; the other is the world inside the host, which the older larvae and adults inhabit. This, too, is a hostile world, for the host will always try to get rid of the parasite, whose task is therefore formidable. It has to become adapted to both these worlds and also to quick changes from one to the other. The greatest danger, no doubt, is to the non-parasitic younger phases that live outside and encounter frost, drying, sunlight, and changes of temperature, all of which kill large numbers of them.

How does the hookworm meet these risks? It must overcome them or fail to make contact with a host and so complete its life history. Even if it does successfully enter a host, it still must ensure that both males and females do so; for unless they do, and unless sufficient numbers attain maturity, succeeding generations will not be provided and the species will not survive. Its principal handicap is that only a single larva is derived from each fertilized egg, and from each larva only a single male or female adult worm. Numerous larvae are therefore required, for many fail to find a host and many succumb to the risks of the outside world.

Because one larva only comes from each fertilized egg, eggs must be numerous; and this, in fact, is exactly what happens. Each female hookworm produces, when her egg-production is in full spate, some 30,000 eggs a day. A hookworm can live in the human intestine for 5 years or so, and the hookworm called

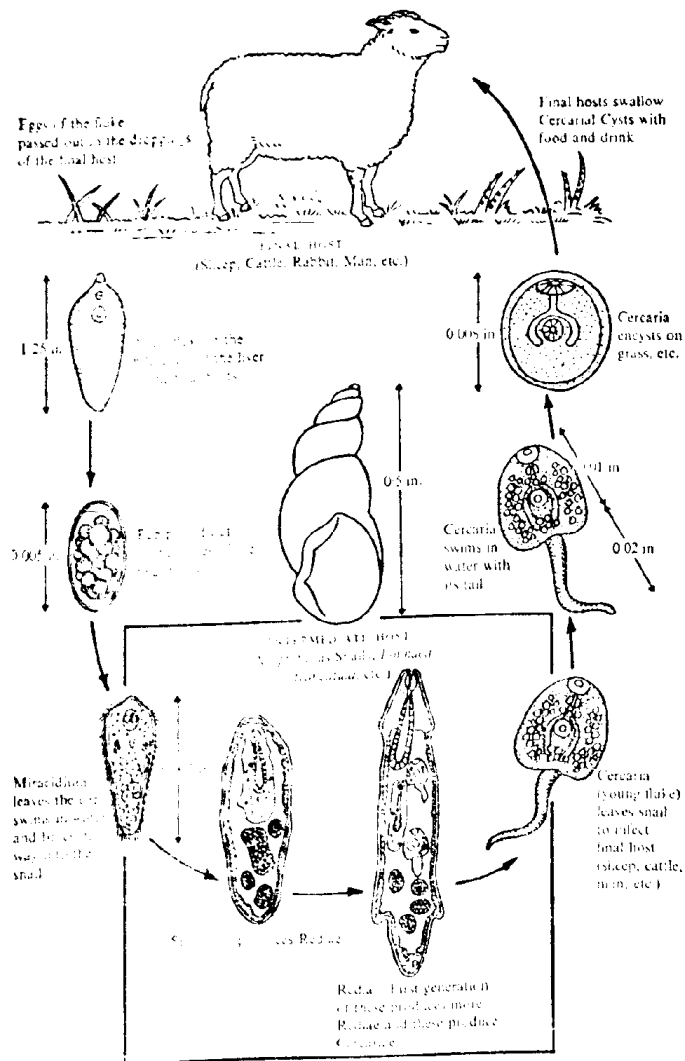


Fig. 2. Life History of the Liver Fluke of Sheep, Cattle, etc.

the American murderer can live for 15 years. While this rate of egg-production is not kept up all this time, clearly the number of fertilized eggs produced is prodigious.

This, then, is one of the ways in which parasites meet the risk of failure to become established in a host and the added risks of destruction in the outside world. What other answers do they find? One of them is not so much the production of large numbers of fertilized eggs as multiplication of the number of infective phases that are derived from each fertilized egg. This device multiplies the chances of infecting a host. The life history of the common liver fluke of cattle and sheep, shown in Figure 2, shows how it works. This diagram also illustrates certain other important features of parasitic life.

INDIRECT LIFE HISTORIES

Liver Fluke

An important feature of the liver fluke is the fact that it is hermaphrodite. Each individual fluke contains both male and female sexual organs. Cross-fertilization between different individuals nevertheless occurs and is probably necessary, at any rate at times, so hermaphroditism itself confers no special advantages. An adaptation shown by one group of flukes is, however, an advantage in the sense that it helps fertilization. These flukes, called *schistosomes*, live in the blood vessels of man and other animals and the different sexes are in different individuals. Fertilization of the eggs of these unisexual flukes is assisted by more or less permanent attachment of the male to the female, the male schistosome holding the female in a groove formed by the folding over of the edges of its body.

What other principles of parasitism does the life history of the liver fluke illustrate? The adult worms live in the bile ducts of the livers of sheep, cattle, rabbits, and many other vertebrate hosts, including man, and there they produce fertilized eggs, which, like the eggs of the hookworms, pass out in the faeces of the host. From each egg a single larva, a *miracidium*, hatches out. It is covered with short protoplasmic hairs (*cilia*), by means of which it swims in moisture on the pastures on which

hosts live and feed. The miracidium cannot, however, directly infect the vertebrate host again. It must itself first become parasitic inside a different kind of host. In this particular instance it must bore its way into and become parasitic in an aquatic or an amphibious snail. Inside the body of the snail it starts on a process of multiplication. The miracidium becomes a kind of sac, the *sporocyst*, on the walls of which develops a third larval stage, the *redia*. The rediae may then produce a second generation of rediae and from these the fourth and last larval stage, the *cercaria*, develops. The cercaria is the infective larval stage. It alone can infect new vertebrate hosts. It leaves the snail, swimming with its tail, but soon casts off its tail and settles down on aquatic plants or on grass blades near the edges of pools and streams and there it makes for itself a protective envelope or cyst-wall. Inside this cyst it waits until it is eaten by a sheep or cow or other host as this host crops the pasture. Man may become infected by eating watercress and similar uncooked salad plants on which the cercariae have encysted. Once it is in the mouth, the cercaria, which is, in fact, already a young fluke, makes its way to the liver and grows there into the adult hermaphrodite parasite.

Comparing this life history with that of the hookworm, we see that the liver fluke has multiplied the number of its infective larval phases, i.e. the number of infective cercariae, each of which is a potential adult fluke. During the life histories of some species of flukes multiplication in this way may increase the number of infective phases derived from each fertilized egg to a remarkable degree. For example, it is estimated that a single snail discharging the cercariae of one of the three species of flukes that can live in the blood vessels of man (*Schistosoma mansoni*) may go on liberating about 3,500 cercariae a day for a considerable time and that the total number set free by a single snail may be 100,000 to 250,000. It is clear that a species that does this has enormously increased its chances of survival. Possibly this relatively enormous increase of the number of potential adults derived from a single fertilized egg has been provoked by the restriction of this particular fluke virtually to

one final host, namely, man, with the consequent reduction of living room, so to speak, for its adult phases. Some tapeworms show a similar multiplication of their larval phases. For instance, the larval phase of the small tapeworm of the dog (*Echinococcus granulosus*), which takes the form of a cyst called a hydatid cyst, may contain thousands of tapeworm heads, each of which may become an adult tapeworm should the cyst be eaten by a dog.

Pork Tapeworm of Man

The life history of the common liver fluke of sheep and cattle reveals that a species may increase its chances of survival in another way. Its vulnerable larval phases are all, excepting the miracidium, protected either inside the body of the snail in which the earlier larval phases develop, or inside the cyst-wall that encloses the infective cercaria. Other species of parasitic animals which are intermediate hosts also protect these larval phases in these ways. There are some that go even further. They develop inside intermediate hosts that are eaten by the final hosts, so that the larval phases of the parasitic animal never enter the outside world at all. The pork tapeworm of man (Figure 3) passes out eggs that are eaten by the pig and develop in the muscles of the pig into a larval stage called a bladderworm (*cysticercus*) in which a single tapeworm head develops. If man eats pork that has not been cooked sufficiently to kill the bladderworms, the tapeworm head in the bladderworm develops into the adult worm. The beef tapeworm of man has a similar life history, except that its larval stage occurs in the ox and man infects himself by eating beef containing these larval stages.

Malarial Parasites

Human malarial parasites (Figure 4) never enter the world outside the host at all. The female anopheline mosquito sucks them up from human blood and they pass, after development in the mosquito, back into the blood of man when the mosquito later on takes another meal of blood. This elimination of the need to enter the world outside the host has certain disadvan-

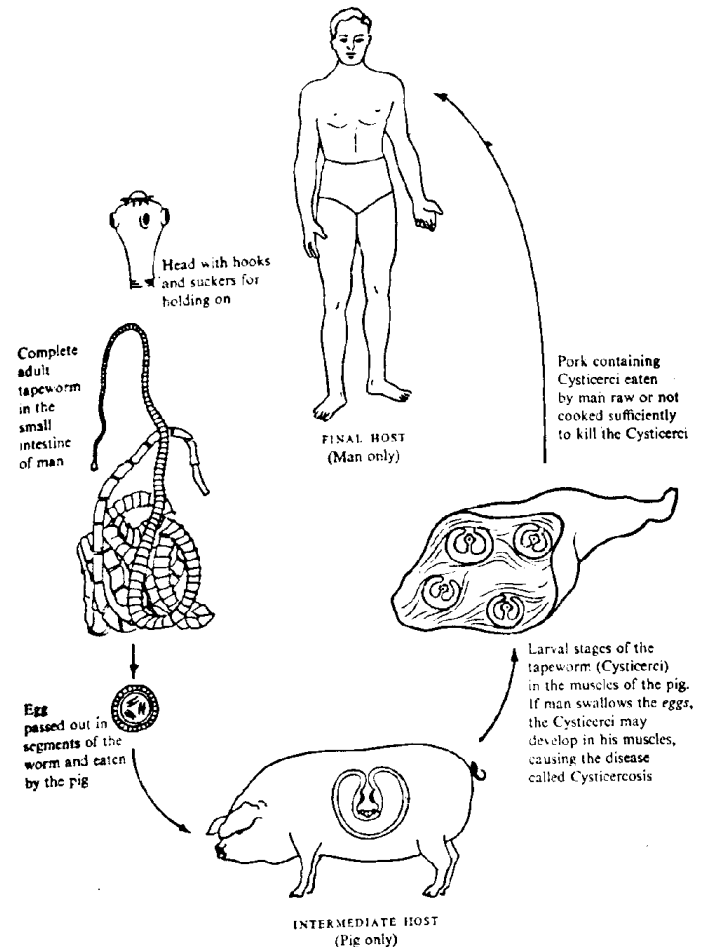


Fig. 3. Life History of the Human Pork Tapeworm (*Taenia Solium*).

tages for the parasite, especially when it is narrowly restricted, as human malarial parasites are, to one kind of intermediate host (man), and to the females only of one kind of final host (anopheline mosquito), but it does remove at least one of the major risks of parasitic life.

The use of an intermediate host, whose body protects the vulnerable larval phases of the parasite, is certainly an advantage, but against it must be set the fact that the life history then becomes what is called an *indirect* life history. The parasitic animal must become parasitic twice, or when more than one intermediate host is used, more than twice, in the course of one life history. The liver fluke cannot pass directly from one sheep or cow to another; it must first become parasitic in a different animal, in this instance an aquatic or amphibious snail. The snail intervenes between one generation of adult flukes and the next. It is therefore called the *intermediate host*. In it the larval development of the parasite takes place. In the other host, which need not be a vertebrate animal, the other larval phases and the adults of the parasite live and reproduce their kind. This host carries the final stages of the life history and it is called the *final host*, or sometimes, though less usefully, the *definitive host*.

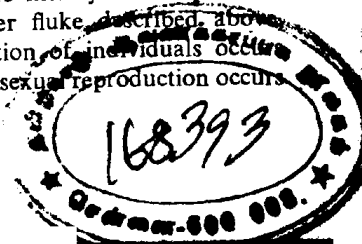
We have noted already that parasitic animals with indirect life histories must become parasitic at least twice during each life history. They therefore become dependent on at least two hosts. This may seem, at first sight, to be a disadvantage, but it is, in fact, much less disadvantageous than it seems. For the two hosts, the intermediate one, in which the larval phases develop, and the final one, in which the adults live and reproduce, usually live in situations which enable the eggs that leave the final host, or the first larvae that hatch of them, to enter the intermediate hosts. Thus snails live on pastures which sheep and cattle normally graze, or in pools and slow-running streams on the pastures; and the habits of both the snails and the sheep and cattle favour the transference of the larval phases of the parasite from one host to the other.

The fact that the habits of the intermediate and final hosts

bring them into close association has no doubt led naturally to the development of indirect life histories. The anopheline mosquitoes, which are the final hosts of the human malarial parasites, habitually visit man to suck his blood and, as they suck, they transmit the malarial parasites to man. The same thing happens during the life histories of other parasites. Tsetse flies suck human blood and transmit to man the trypanosomes that cause African trypanosomiasis. Blood-sucking leeches transmit trypanosomes to fish, and mosquitoes carry filarial worms to man. Remarkable, too, is the habit of the South American human warble fly, which glues its eggs to the abdomen of mosquitoes and other blood sucking species and, when these species suck human blood, the larvae of this warble fly hatch out and establish themselves in the skin of the person bitten by the mosquito, developing there in painful abscesses similar to those caused on the backs of cattle by the ox warble flies. There are thus parasites which use other animals as means of transport, these other animals being called *transport hosts*.

The method just described of multiplying the numbers of the infective phases derived from each fertilized egg is remarkable enough, but it is excelled by the method of doing this used by some species of parasitic single-celled Protozoa. The Protozoa multiply their numbers either (a) by division of each individual into two descendants, a process called *binary fission*, which in a favourable environment can quickly produce a large number of individuals; or (b) by a process of multiple division (called *schizogony*) of an individual into several descendants produced simultaneously, which can, if repeated rapidly, produce an even greater number of individuals. Both methods may be reinforced, at intervals, by sexual reproduction, which effects the interchange of genes. This occasional interchange of genes seems to be necessary for the survival of most parasitic Protozoa, but there are some, such as the trypanosomes, that are able to do without it altogether. When the life history of the parasitic protozoan is, like that of the liver fluke described above, indirect, the non-sexual multiplication of individuals occurs inside the intermediate host, and the sexual reproduction occurs

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inside the final host. This is shown by the life history of a human malarial parasite illustrated in Figure 4.

In this instance the final host, in which the sexual reproduction occurs, is an anopheline mosquito. This host sucks up human blood in which the parasite has formed the mother cells (gametocytes) from which its male and female sex cells are derived. The male and female sex cells are formed in the food canal of the mosquito and there the male fertilizes the female cell. A zygote is thus produced, which is exactly comparable to a fertilized egg. From it, by a series of divisions, thousands of minute individuals (sporozoites) are formed. There is thus an immediate enormous multiplication of the number of individuals derived from the zygote (=fertilized egg). These individuals (sporozoites) congregate in the mosquito's salivary glands, and when it sucks human blood, the sporozoites are injected into man. They pass to the cells of the human liver and there they undergo multiple division which still further increases the number of individuals derived from the product of the single sexual union. The individuals thus formed in the human liver pass into the blood, enter the red blood cells and, growing there, destroy these cells. When growth has been completed, each individual undergoes further multiple division and liberates a number of descendants into the blood, which then attack other red blood cells. Multiple divisions of this kind may be repeated many times, so that enormous numbers of individuals may be produced. Eventually, however, multiple division ceases and the individuals grow up, not into individuals which divide, but into mother cells of the male and female sex cells. It is these that are sucked up by the mosquito when it takes its meal of blood and the life history returns to the point at which this description of it began.

This process of non-sexual multiplication may produce astonishing numbers of the parasites. It has been estimated, for instance, that the protozoan parasite *Eimeria tenella*, which causes coccidiosis, can produce about 1,800,000 individuals in 4 or 5 days, and that the human malarial parasite that causes malignant tertian malaria could, if unchecked, produce enough

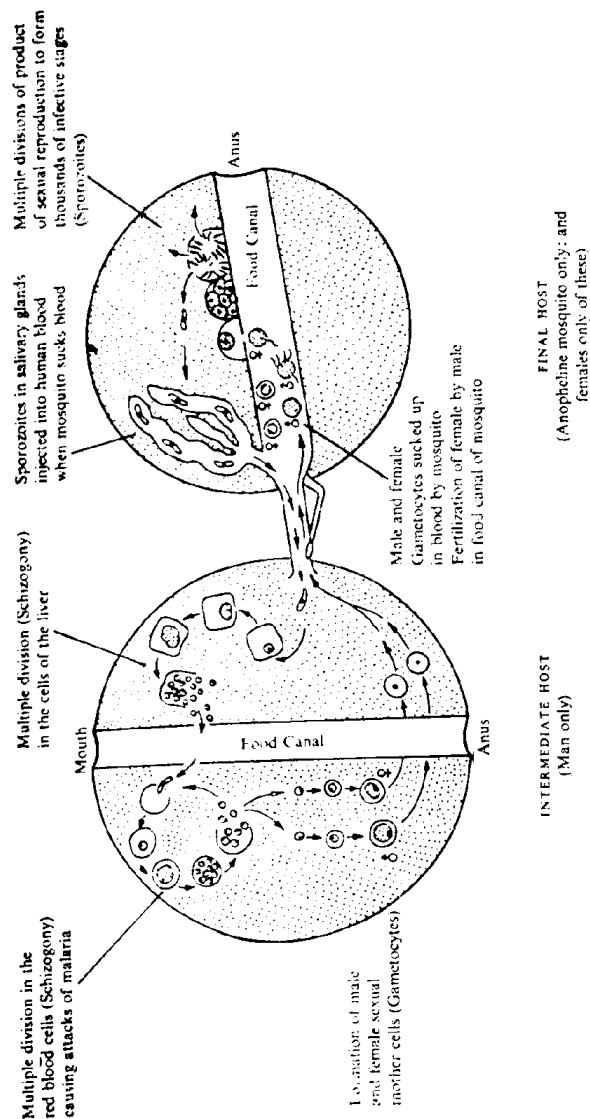


Fig. 4. Life History of the Human Malaria Parasite (*Plasmodium Vivax*).

individuals to infect and destroy some 10 to 20 per cent of the red cells of the blood, that is to say between three and six million parasites.

These two examples of ability to multiply are, it is true, exceptional, but they show that Protozoa resemble bacteria and viruses in this respect. The ability to multiply no doubt increases the power of the parasite to establish itself in the host and to maintain itself there, but, if it is excessive, it is a disadvantage. It enables the parasite to deliver a mass attack on the host, but the attack may kill, and the death of the host means death to the parasites in it. In any event the host fights back. It may, for instance, develop immunity. Human beings, for instance, develop an immunity to their malarial parasites, and this curbs the power of the malarial parasites to multiply, so that people repeatedly exposed to infection suffer relatively little, whereas immigrants into malarious areas are quickly overcome by the mass attack and may be killed.

PROTECTION OF THE YOUNG

What other methods do parasitic animals use to facilitate infection of the host and survival of their species? Lack of space will not permit us to mention them all, but methods by which the young of the parasitic animal may be protected and given a better chance of infecting the host may be briefly described.

One of the advantages of having an intermediate host, namely, the protection afforded by its body to immature larvae, has already been mentioned. But the egg itself, upon which everything depends, may also be very effectively protected inside a thick and resistant shell. The eggs of the large roundworm of the pig and man can, for instance, survive outside the host for as long as five years. The first larvae that come from the eggs are usually very vulnerable and may be destroyed before they meet with a suitable host. The intermediate host may itself be the victim of accident and the larvae in it may be destroyed at the same time. But some species of parasitic animals avoid these risks by relying on the fact that the intermediate host is normally eaten by the final host. The larval phases of the beef tapeworm

of man develop in the muscles of the ox, and unless the beef containing them is eaten by man, either raw or not treated in such a manner that the larvae are killed, this tapeworm cannot reach man.

Another method used by some parasites to protect their young is to develop the young inside the body of the parent female that produces it. The sheep ked, for instance, lives its whole life in the wool of sheep, and the female lays, not eggs, but living larvae ready to turn into the chrysalis stage, so that the risk of the young of this species becoming detached from the host on whose surface it must live is greatly reduced. Tsetse flies, which transmit to man the trypanosomes that cause African trypanosomiasis, also lay larvae ready to turn into the chrysalis stage, and they lay these in sheltered positions, such as in warm, moist soil or under fallen trees, where conditions for their further development are good.

This practice of placing the young where the chances of their survival and infection of the host are favourable is well shown by some insects whose larvae are parasitic on eggs or larvae of other insects. With their ovipositors the adult females of these insects actually pierce the eggs or the bodies of the insects on which their young will develop and place their eggs, or, if they lay larvae and not eggs, their larvae, inside the bodies of the animals that are to be the hosts of the parasitic phases of the life history. Some insects are even able to detect whether a prospective host for their larvae is already occupied by the eggs or larvae of another insect. Incidentally these insects are, like the warble flies and bot flies of horses, examples of animals whose young phases only are parasitic, the older phases and adults being non-parasitic animals.

Mention of the warble flies and bot flies reminds us that attachment of the eggs to the hairs or feathers of a host is another method by which some insects secure for their larvae good chances to survive. The lice of man and other mammals and birds do this, their eggs being called nits. The warble flies of cattle glue their eggs to the hairs of their hosts, and they can do this almost instantaneously, while they are on the wing, an

act that is one of the marvels of animal skill. The eggs are glued to the bases of the hairs in a position in which the hatching of the eggs is favoured by the heat of the body of the host and in a position from which the larvae can readily penetrate the host's skin. On the other hand, the larvae that come from the eggs of the bot flies of horses enter their host through its mouth and their hatching is favoured if the horse licks the eggs; and these eggs are attached, it is interesting to note, not to the bases of the hairs but nearer to their tips, where licking can affect them.

PEACEFUL COEXISTENCE

The instances given above of the adaptations used by parasites to establish themselves in association with their hosts and to maintain themselves in these associations, so that their species may survive, are only some of many that could be described. But the facts given may be enough to show that parasitic animals, seen as living beings battling in the natural world, are by no means the lazy, unpleasant creatures that the word 'parasitic', as used of the human hanger-on or sycophant, suggests. On the contrary, theirs is a difficult and risky way of life, not in any way less exacting than that of animals that get their food in other ways.

For the parasitic way of life is, in essence, just a particular method of getting food. If parasitism involves, as it certainly does, dependence on other animals or plants for food, this does not distinguish the parasite from its fellows in the world of life. If, indeed, dependence on other living creatures were the only criterion of the parasite, man himself would have to consider whether he is not the greatest, the most destructive, and the most cunning parasite in the world. For he breeds animals and cultivates edible plants, only to kill and eat them; and everything that does him harm he seeks to exterminate.

Destruction of other living things, either because they are needed as food, or because they are enemies, is, of course, no more than an expression of the instinctive urge that man shares with the parasite to survive in a difficult world; and for this reason man will go on trying to exterminate parasites. For man

is menaced, not only by parasitic animals in, or on, his body, but also by the other species parasitic on domesticated animals and crops. The damage done by these latter species is prodigious. In 1942, for instance, American experts calculated that, in the United States alone, parasites on domesticated stock in that country were costing some 400 to 1,000 million dollars a year, and this estimate takes no account of the incalculable damage done to agricultural and horticultural crops.

So far as parasites of man himself are concerned, there are some that do immense harm. Malaria, for instance, was formerly our Public Enemy No 1. Its history consists largely of repeated massacres of human populations. In 1938, to take a typical instance of its power, in two months it killed 20,000 people in Brazil; in 1916 it stopped the fighting in Macedonia; during the Second World War in the Far East it forced the Army Commanders to conquer mosquitoes before they could tackle the Japanese, and even then it put out of action some 5 to 30 times as many men as bullets or other military weapons did. Nowadays, of course, malaria is rapidly coming under control. Large areas of the world that were formerly uninhabitable are now prosperous and well populated. But malaria, according to the World Health Organization, still kills two and a half million people every year, and some 250 million have clinical attacks. If we add to this the estimate, made by a distinguished American parasitologist in 1947, that more than two thousand million people in the world are infected with parasitic worms, we see that the parasitic animal certainly makes a success of its difficult way of life.

Thus man has plenty of reasons for battling with the parasitic animals that do him so much harm. His victories, most of them achieved in the last eighty years, have been remarkable. But the war goes on; it is not by any means won. It is wiser, indeed, to assume that it never will be won. For the urge to survive that drives the parasite as it drives all other living things, including man, is a force that the human brain, with all its ingenuity, can never hope to suppress. We can, no doubt, at the cost of great effort, bend this force to the human will; but it has a way of

hitting back, of getting round our defences, of infiltrating through them and taking a fierce revenge. Indeed, it is worth considering whether peaceful coexistence, or as biology puts it, the tolerance of one species by another, their mutual adaptation to one another's needs, will not in the long run prove to be the only method of dealing with the parasitic animal.

RESEARCH REPORT

A. W. HASLETT

HIGH-ENERGY PHYSICS

PLANS and ideas for the acceleration of nuclear particles to high energies were discussed at a conference held lately in Geneva by the European Organization for Nuclear Research (C.E.R.N.). The object of the conference was one that came naturally to C.E.R.N. The reason for its existence as an organization is that the biggest machines needed in nuclear research are now so expensive that only the United States and the U.S.S.R. can afford, as individual countries, to build them; and C.E.R.N., formed by twelve countries, is engaged on a machine budgeted, in round figures, at £7,000,000. The object of the conference was to find ways of building such machines which shall not become too astronomically expensive as the energies reached are increased. And the upshot was to bring from Professor V. I. Veksler, of the U.S.S.R., a suggestion for a wholly new mechanism of particle acceleration; from speakers in general an enlargement of ideas already talked about between individuals, and to some extent published; and from Dr J. W. Blamey, of the Australian National University, Canberra, a progress report on the construction of what may fairly be called a 'poor man's' proton synchrotron.

From this multiplicity of material it may be useful to go back to the beginning and consider what is the object of these machines, and what are the main types which already exist. Both questions have been discussed in earlier numbers of *Science News*.*

*For example, in the articles by P. E. Hodgson in *SN31*, by R. M. Tennent in *SN35* (correction in *SN36*, p. 122), and by G. Feldman in *SN35*; on types of accelerators, the key article was by L. L. Green in *SN22*.

The object, in the most general terms, is to enable observations of kinds, which hitherto have been limited to the comparatively small number of particles provided naturally by cosmic radiation, to be made in the laboratory, with larger numbers of particles available, and with the energies of the particles known. For comparison, the highest useful energy of cosmic radiation is of the order of 10^{15} electron volts; and the highest energy planned to be reached by a machine is 5×10^{10} electron volts (50,000 MeV). In terms of energy, the advantage of cosmic radiation is of the order of 10,000 to 1. But the frequency with which primary particles of cosmic radiation of all energies enter the atmosphere is only about one per square centimetre per second; the energy of each particle detected and used must be individually deduced; and occasions when particles of the highest energies engage in collisions with nuclear particles under conditions which can be usefully studied are of extreme rarity. On the other hand, even those machines which produce particles of the highest energies produce them at the rate of 10 or 12 pulses a minute, and in each pulse tens of thousands of millions of particles are accelerated. There is thus a continuing pressure irresistible on every ground but cost – for the transfer of new areas of research from cosmic radiation to laboratory-accelerated particles.

Machines for the acceleration of charged nuclear particles to these very high energies have three requirements in common. There must, first, be a source of the particles (usually protons) and, in the case of the bigger machines, means for their preliminary acceleration up to an energy such that the final machine can use them. Secondly, conditions of high vacuum must be provided, in order that the particles accelerated should be scattered as little as possible by collisions with gas molecules. Thirdly, there must be means for keeping the particles together, or at least enough of them to provide a useful final output.* This means that there must both be a focusing effect – whether in the main design or added to it – and also stability in point of time;

*Possibly only 1 per cent of the particles injected, in the case of the bigger machines.

the particles, in other words, must neither stray (too many of them) from the course, nor spread out too much along it. The extent to which these two requirements will be met in practice cannot easily be computed; and, until any new type of machine has been made to work, there remains always an element of uncertainty.

All machines of the kind, existing or planned, work on the same general principle. There is in all of them a series of step-wise accelerations, brought about by an electric field which it is arranged shall be in the required direction whenever the particles pass from one section of the machine to the next. And, in general, there is also a magnetic field, the function of which is to constrain the particles, while being accelerated, to follow the path provided for them.

The successive sections may be disposed in a straight line, and are then traversed only once by each particle. This is the linear accelerator. It is used commonly to provide the preliminary acceleration already mentioned; it has yet to be used in its own right to yield particles in the highest range of energies. Or the sections may be coiled, in effect, so that each is a half-turn of a spiral. Partitions between neighbouring sections being unnecessary, there remains a circular vacuum chamber, and within it two hollow electrodes – half-circles in plan view – between which the particles pass repeatedly as they spiral outwards from the centre, being accelerated twice in each circuit. To constrain them within the required limits of path, there is a magnetic field across the whole area of the vacuum chamber. This leads to a magnet with large circular pole-pieces, one above the chamber and the other below it, both of them vacuum-sealed to the chamber. It is here that machines of this type become expensive. With conventional, iron-cored electromagnets, the strength of the magnetic field attainable is limited by the saturation of the iron of the pole-pieces; and this, in turn, limits the curvature of the particle tracks at maximum energy, and increases the size and cost of the magnet. These facts have determined the main sequence of development.

In the synchrocyclotron – the circular type of machine which

gives the highest energies – the magnetic field remains constant, but the electric field is varied to take account of the increase in mass of the particles during acceleration, as the speed of light is approached. This modification – the beginning of pulse operation – was suggested independently by Professor Veksler, already mentioned, and by Professor E. McMillan, of the University of California, in 1945. It enables the particles to reach the limit of energy set by the magnet.

We arrive now at the proton synchrotron, the most advanced type of machine already working. From this point onwards the aim is to reduce the size, weight, and cost of the magnet needed for particles of a given energy. In the proton synchrotron, the magnetic field, as well as the electric field, is varied. As a result, the particles can be made to follow roughly the same orbit at all stages of acceleration. There is thus a transition from the circular shape to ring-shaped or annular, and a reduction in the size of magnet needed. But the focusing of the particles is weak, and the paths which they follow are not, therefore, closely limited. In the University of California 'bevatron', the largest of these machines yet working, the width of the vacuum chamber is about 1.2 metres – small compared with the orbit radius of 15.2 metres, but leaving room still for reduction – and the width of the pole tips is 1.68 metres. The weight of iron in the magnet is about 10,000 tons, and the protons reach an energy of 6,200 MeV. In a Russian machine, now approaching completion, the weight of iron in the magnet is 36,000 tons, and the energy reached will be about 10,000 MeV.

For a more economical approach to higher energies, there are two main alternatives, each at the stage of prototype construction – and the new *ideas* discussed at the conference. The first alternative is to use a stronger, more precise, system of focusing. The vacuum chamber can then be of smaller cross-section, and a further saving on the magnet can be effected. With this approach, there can be no reduction in overall size; so long as iron-cored magnets are used, the curvature of the particle tracks is still limited, and the circumference of the machine increases remorselessly as the final energy of the particles is increased.

The second alternative – which is the one being followed in Australia – is to tackle the trouble at its source: to forsake the iron-core of the conventional magnet, and to obtain a stronger magnetic field by using bigger currents and an air core.

The method of stronger focusing was independently proposed by workers at the Brookhaven National Laboratory in the United States, and by Christophilis in Greece. Machines using it are being built by C.E.R.N. at its site at Meyrin near Geneva, and at the Brookhaven Laboratory. These two machines are designed to accelerate protons to energies of 25,000 MeV and 30,000 MeV respectively. Work on the C.E.R.N. machine was begun first, and has made the most progress. The Russians, with a variant of their own, plan to reach energies of the order of 50,000 to 60,000 MeV. Theirs is, so far, the biggest machine planned.

The basis of a stronger-focusing system follows more or less directly from a difficulty encountered in all machines from the cyclotron onwards. With a straightforward magnet, although the pole-pieces may be made larger than the vacuum chamber, there is still a falling off in magnetic field towards the outer part of the chamber. This causes vertical focusing. But the effect produced is limited; and it turns out that strong vertical focusing can be obtained only at the cost of radial instability. The conclusion that the functions of vertical and horizontal focusing should be separated was one of those simple ideas which look self-evident in retrospect. The trick is to divide the magnet into sections, so designed that, while the effect of one section is to focus in the horizontal plane and defocus vertically, that of the following section is to reverse these effects. In that way focusing in both planes can be strengthened, although at no time is there an alternation of magnet sections, such that, in one, the field strength increases from the inside outwards, and in the next the other way about. The arrangement is known for this reason as the alternating-gradient proton synchrotron.

The gain from this method can be shown simply in figures. Because of the high final energy of the particles, the diameter

of the C.E.R.N. machine is increased to 200 metres, so that a cricket ground, as it has been said, could be placed in the middle. But by strong focusing, the vacuum chamber is reduced to an elliptical section no more than 15 centimetres wide by 8 centimetres deep; and, although the energy reached will be four times as great as in the 'bevatron', less than a third as much iron will be used in the magnets. The precision of control which is being demanded implies precision also in construction. This applies both to the material of the magnets and to the accuracy with which they must be positioned. The uniformity of magnetic properties which is demanded is without precedent, and the 100 sections of the magnet have to be positioned with a mean error of not more than 0.6 millimetres radially and 0.3 millimetres vertically. After a survey of local ground movements, it was decided to support the magnet units on pillars resting on bed-rock. What is to be seen at the present stage of construction is a concrete-built tunnel such as might house a double-track railway. Yet all of it, supporting pillars and magnets, will be in aid of that small vacuum chamber, less than a hand's span across.

The Australian solution leads to a great reduction in size for particles of a given energy. Compared with the Russian proton synchrotron, designed for nearly the same energy (10,000 MeV, Russian; 10,600 MeV, Australian), there is a reduction in orbit radius in the proportion of about six to one, and there is no use of iron in the main magnet. On the other hand, the frequency of pulses is reduced from five a minute to one every ten minutes, and there is a host of new problems. To obtain the advantage of a high peak magnetic field (80 kilogauss) from an air-cored magnet, extremely large currents must be used. They are got by short-circuiting an alternating current generator – a similar approach to that developed in the 1920s by the Russian physicist Kapitza. In the Australian plan, four discs of mild steel, each of 19 tons weight, are to be spun at 900 revolutions per minute between the poles of a magnet 12 feet in diameter; and peak currents of up to 1,600,000 amperes taken from the discs through jets of molten sodium or sodium-potassium alloy. Under this treatment, the rotors are expected to 'brake from 900 revolu-

tions per minute to zero in 0.8 second (and then accelerate in the opposite direction)'. The design of the more intricate parts of this generator, Dr Blamey told the conference, had already been several times revised. But whatever the difficulties, the saving in size and cost is potentially so great that this machine may well, as he suggested, 'point the way to future development'.

Among new ideas expressed at the conference, the greater part consisted of elaborations on one or other of two themes: the use of steeper magnetic gradients in iron-cored magnets, and that of discontinuities introduced by physical ridges or otherwise. All that can be said usefully is that the amount of ingenuity shown on paper was such as to make short summary impossible. A more general point, which has been in mind for some time, is that with larger beam currents it should be possible ultimately to make use, in research, of collisions between opposing beams of accelerated particles. The advantage of so doing arises from a relativity effect which becomes increasingly important as the energies reached are increased. Its origin is a difference in viewpoint between the designer and that of two nuclear particles about to collide. For the designer, the velocity of an accelerated particle is that relative to the machine; and, as the speed of light is approached, more and more of the energy which he supplies goes to increasing the mass of the particle. From the point of view of the particles (one 'moving', the other in a 'stationary target') what matters is the velocity of each relative to their common centre of mass. In this new frame of reference much of the energy imparted (from the designer's point of view) to the 'moving' particle does not exist. Hence, collisions between two opposing beams of particles would offer better value – if there were enough of them to be useful – than would collisions made with a fixed target by particles with twice as much energy.

The suggestion of a wholly new mechanism of acceleration came, as stated earlier, from Professor Veksler, and aroused the greatest interest of the conference. The idea, in principle, is that, just as a particle moving with a velocity close to that of light loses energy by emission of radiation in the direction of motion (Čerenkov radiation), so it should be possible, in reverse, for

energy to be imparted to a particle by a medium moving at high velocity past it. The 'medium' might, for this purpose, be another group of charges, a highly ionized gas (plasma), or electromagnetic radiation. And for a useful effect, the particles accelerated (e.g., protons) must consist of a geometrically small group, when the extent of acceleration produced should be proportional to the number of particles present. For this reason, Veksler proposed the name 'coherent' for this general mechanism of acceleration. Theoretical investigations by half a dozen or more workers, he said, made it clear that between the statement of the principle and its realization there were 'a good many complicated problems'. In a following contribution, Professor Ya. Feinberg referred to possible experiments on the use of high-speed oscillations in an ionized gas as a source of acceleration, and stated in discussion that by the next such meeting they should have the answer. In Professor Veksler's view, this approach was suitable for the acceleration of nuclear particles to 'not too great energies'; for acceleration to very high energies, he was more hopeful of electromagnetic radiation as the medium of acceleration, notwithstanding that very great powers would be required.

The C.E.R.N. meeting on high-energy accelerators was, in its way, a counterpart to the conference on atomic energy, held a year earlier, also in Geneva. It was the first at which contributors from all the principal countries concerned have met in extended discussion, and the opportunity was quite obviously appreciated. It was followed by further sessions on the detection and counting of nuclear particles, and on research in high-energy physics. Included in the latter was a review by Professor E. Segrè, of the University of California, of work on the antiproton, or negative proton, the discovery of which was recorded in *Science News* 39.

The proceedings of the conference, which included other aspects of high-energy physics, are to be published in full by the European Organization for Nuclear Research (C.E.R.N.)

HAZARDS OF NUCLEAR RADIATION

The outburst of public concern which in March of last year led to the appointment of the Medical Research Council's committee on the hazards to man of nuclear and allied radiations arose primarily from a report by the United States Atomic Energy Commission on the effects of high-yield nuclear explosions. The emphasis at that time was on the possibility of long-term genetic effects, operating through the whole population, and on the extent to which the total exposure to penetrating radiation had been increased by test explosions up to date. Now the committee has reported, and there has been a shift in emphasis as a result.

The most important danger to be expected from an increased rate of thermonuclear explosions is shown to be an effect on the individual - that which would result in a proportion of people from the accumulation of strontium-90 in bone, as is already taking place. Hence, if this figure is watched, the question of genetic effects can be forgotten, so far as thermonuclear explosions are concerned. The reason for this is the great height in the atmosphere (possibly up to 100,000 feet) to which the fine dust from such explosions penetrates, and the relatively slow rate (from 10 to 20 per cent a year) at which it comes down again to ground level. The main mass of relatively short-lived fission products is thus of only small importance; world distribution is comparatively uniform; and interest is in the longer-lived products, of which strontium-90 is the most important. Because of the ease with which strontium-90 can take the place of calcium in bone, the internal effects of this one isotope are potentially more significant than the so far very small addition to total irradiation made by fission products as a whole. On assumptions based on British conditions of living (but probably over-optimistic for tropical peoples), this increase is estimated at not more than 0.04 per cent of the natural dose rate, allowing for delayed fall-out from thermonuclear explosions already made at the time of writing of the report. This conclusion postpones for the present the need to arrive at standards of the total extra dosage taken to be acceptable from the point of view of

genetic effects. Standards of the latter kind will be needed eventually, none the less, for other purposes, including the peaceful development of atomic energy. There are thus two main – and quite distinct – interests in the report: the immediate need for a watch on strontium-90, and the scientific problems presented by the long-term requirement of arriving at standards of total permissible irradiation.

The position about strontium-90 can be summarized in figures from the report. The maximum level accepted by the International Commission on Radiological Protection for adult occupational workers corresponds with 1,000 micro-microcuries of strontium-90 per gram of calcium in bone. For a general population, including young children, a limit of 100 micro-microcuries is suggested. The greatest strontium-90 activity which has so far been found (in the skeletons of one-year-old children) is 1.2 micro-microcuries per gram of calcium. But the effects of delayed fall-out must be allowed for; and if the concentration 'showed signs of rising greatly' beyond 10 micro-microcuries, there would be cause for 'immediate consideration'. In sum, therefore, there is no immediate cause for anxiety, but neither is the margin in hand large.

With the long-term development of atomic energy, it may be expected that fission products will be produced in power stations to the extent of 1,000 tons or more annually. But strontium-90 is unlikely in this case to be a limiting factor. Partly for use, and partly as a help in disposal, it is planned to separate both this isotope and also caesium-137 from the mixed fission products produced. With most of the strontium-90 removed, the addition to total radiation will be a relatively more important consequence of the large-scale operation of nuclear power stations than it is of thermonuclear explosions. Also, although any standard within reason could be worked to, it will be necessary, if only for economy, to arrive at more rationally based figures than seem at present to be possible. Finally, for the purpose of working to these figures, it will be necessary to take account of all sources of extra radiation, medical and industrial. Of these the use of X-rays in diagnosis makes the biggest contribution to

gonad dosage. The dosage contributed by this source in Britain is estimated at 22 per cent of the natural dose rate, and it may well be bigger in the United States.

The analysis of genetic issues made by the committee is of special value as calling attention to the many weak links in what is thought to be the most valid chain of argument. The fundamental, and most difficult, problem is to determine the relation in man between a given extra exposure to radiation and the increased rate of mutation to which it leads. This would be no problem if it could be assumed that all mutations were caused by radiation, that the natural mutation rate was the same in all species, and that all genes were equally sensitive to radiation. But not one of these generalizations can be made. In *Drosophila*, for which there is most information, only one mutation in every 10,000 is attributed to natural radiation. But the effects of radiation are cumulative within the range of dosage for which evidence exists; and the span from conception to breeding is longer in man by a factor of about 1,000. Up to this point, therefore, one in every 10 mutations might be attributed to natural radiation. But the question of the mutation rate then arises. If this is higher in man than in *Drosophila*, the effect of extra mutations would be less in proportion. The mutation rate in man can be estimated approximately from the incidence of lethal conditions, of which the genetics is known. It is thought to be higher by a factor of 5. So the proportion of mutations caused by radiation is now reduced again, from one in 10 mutations to one in 50. The last question is the sensitivity of human genes to radiation. The answer is taken from the mouse, not from man, and is unsatisfactory at that. Mainly on account of a high sensitivity to radiation shown by one mouse gene – out of seven tested – human genes are taken provisionally to be 10 times as sensitive as those of *Drosophila*. And the proportion of mutations in man taken to be caused by natural radiation now goes up again to one in five. Various other arguments are introduced. But the final conclusion is that there is an uncertainty of 50-fold in the dosage of extra radiation needed to double the mutation rate. It will be the duty of the committee to make recommendations

for research. The practicability of an experiment designed to determine directly the difference in mutation rates between two human populations exposed to markedly different dosages of natural radiation has been under discussion since the Geneva conference on the peaceful uses of atomic energy. Suitable populations with a ratio of ten to one in natural dosage are said to exist in India, and there are also other possibilities. In most countries, and certainly in India, there would be need for a major effort in medical organization to secure the required notifications on which estimates of mutation rates could be based. There are clearly many different experiments which could be done and would improve the type of argument already quoted. But the case for a human experiment would remain; and the strongest case is for one done under international auspices on the most favourable pair of populations that can be found.

The Hazards to Man of Nuclear and Allied Radiations. London, H.M.S.O., 1956.

ROYAL SOCIETY CONVERSAZIONE

Among many interesting exhibits shown at a conversazione held lately by the Royal Society in London was one from the Post Office Research Station which might be described as an artificial voice based on applied physiology. The idea behind the apparatus is that the characteristics of individual speech can be most economically analysed in terms of the movements made by the talker's vocal organs; and that, this done, an acceptable reproduction could be synthesized electronically. The signals needed to convey information from analyser to synthesizer would then take up only a small fraction of the line space occupied by normal telephony – perhaps as little as a hundredth. The analysis, though in fact acoustic, is thus unrelated to the conventional study of the wave forms produced in speech. A first distinction is made between sounds of a humming character like the vowels, and those of a hissing character like S, SH, and F. The analyser notes the loudness of these two types, and also the pitch of the

hum. Further characteristics are supplied by the resonances which take place in the throat, mouth, and nose, and modify the timbre of the sounds emitted. These resonances, or 'formants', move continually up and down the frequency scale as different sounds are articulated, and their positions are measured in the analyser. The same characteristics are reproduced by the synthesizer from information transmitted to it. In the present stage of development, the synthetic voice is recognizably that of the speaker, but further improvements are considered to be necessary before it could be accepted as 'natural'.

Crystal Defects

Electron micrographs believed to give the first direct observations of crystal lattices were shown by Dr J. W. Menter, of Tube Investments Research Laboratories, Cambridge. The lattices shown were those in crystals of copper phthalocyanine and platinum phthalocyanine. The molecules of these compounds have the form of flat, square plates, with the metal atoms in the middle. The lattice planes are known by X-ray methods to be about 10^{-7} centimetre apart in the copper compound, and 1.2×10^{-7} apart in the platinum compound. Lines with the same spacings are seen, clearly resolved, in the electron micrographs. In some micrographs all the lines are regular and parallel. In others there is a direct view of a dislocation in the lattice, as first postulated by Sir Geoffrey Taylor to explain the weakness of real crystals. One line (plane of molecules) is seen to terminate in the crystal, and the neighbouring lattice structure is disturbed. Although the types of crystal which can be studied by this direct method will necessarily be limited, the claim seems justified that entirely new vistas are opened up for the study of solids.

Ice-age Preservation

The discovery of organic remains of water and water-side plants, and of more than a hundred species of beetles, as well as other small animals, especially insects, all dating from a period tentatively estimated at 25,000 years ago, was illustrated in an exhibit shown by Mr J. Balfour-Browne of the British

Museum (Natural History), and Mr G. R. Coope, Professor F. W. Shotton, and Dr I. Strachan of the Geology Department, the University of Birmingham. These remains have been preserved, many in a surprising state of perfection, in a series of black bands in the lowest 10 feet of a gravel pit at Upton Warren, midway between Bromsgrove and Droitwich. The gravels, which are up to 29 feet thick, were laid down by the River Salwarpe at the time of the Irish Sea Glaciation. At this time, the ice front was some 20 miles to the north, and shallow pools on the flood plain became colonized by plants and animals. It is these pools which are now represented by the black bands in the gravel, needing only to be washed to reveal this fantastic richness of organic material.

Duration of Insect Flight

An apparatus for the study, in free flight, of insects which, like aphids, fly upwards towards the open sky and are then transported by the wind, was shown by Mr C. O. Booth and Dr J. S. Kennedy, of the Agricultural Research Council's Unit of Insect Physiology at Cambridge. The apparatus is, in effect, an air treadmill in which flight is maintained by balancing the insect's attraction to light against an air jet, the strength of which is recorded. The interest in the case of the aphid (which was seen in flight) is that it will settle down to feed and multiply on a new host-plant only after a certain amount of flying time has been put in. The use of the apparatus is to enable the flight response to be studied.

HONEYBEES AND PRAWNS

In the paragraph published under the above heading in *Science News* 40, it should have been made clear that the account of sex reversal quoted from Dr Carlisle referred to the Mediterranean prawn, *Lysemata seticaudata*. There are only two other species of decapod crustacean which certainly reverse sex - *Pandalus borealis* (in which the phenomenon was discovered earlier than in *Lysemata* and *Calocaris macandreae*). I am indebted to Dr Carlisle for this information.

SOME BOOKS RECEIVED

ROBERT HOOKE by Margaret 'Espinasse (London: William Heinemann, 1956), pp. 192, 21s.

To be neglected for two centuries seems a high price to have paid for having incurred the enmity of one of the great men of science, but that is the contention of Mrs 'Espinasse in her biography of Robert Hooke to explain why this interesting post-Restoration character is practically only known today by 'Hooke's Law of Spring'.

But by his contemporaries he was considered one of the greatest of English scientists: indeed he was of the vintage that included Boyle, Pepys, Wren, Flamsteed, and Grew. In 1662, at the age of 27, Hooke was appointed Curator of Experiments to the recently founded Royal Society of London, and there he remained for forty years, at the very hub of English intellectual life. Hooke died early in 1703 and in the autumn of that year Newton accepted the presidency of the Royal Society, personal and professional animus having kept him away while Hooke yet lived.

While those who knew Hooke were still alive his reputation remained high, but, with the passing of the years, the eye of history became more and more focused on Newton, to the almost complete neglect of Hooke. Mrs. 'Espinasse has done well to redress the neglect of Hooke. Her text is entirely readable, and it is decorated with contemporary illustrations of Hooke's activities in the fields of microscopy, meteorology, horology, mechanics, and architecture. A useful list of relevant books, excellent notes, and an adequate index are included.

SCIENCE UNFOLDS THE FUTURE by J. G. Crowther (London: Frederick Muller, 1955), pp. 254, 18s.

Scientists are not prophets, but in this age few are in a better position to make extrapolations into the future than they. Even in science, fashions change, and preoccupation with technological matters during the long war years left little leisure for speculation. Once again it has become possible: Sir Charles Darwin and Sir George Thompson, two distinguished physicists, have had a go, and now Mr J. G. Crowther, the science-writer, is having his turn. But despite his forward-looking he keeps his feet firmly on the ground all the time.

His queries, to which the future will be the answer, do not call for idle speculation. Successive chapters deal with radio-astronomy and radio-spectroscopy; the future of farming and of industry; man's efforts to surpass the physical achievements of his predecessors; a review of the organization of living matter, and the prospects that man in the future will be able to imitate what nature achieved in the past.

AUTOMATION, FRIEND OR FOE? by R. H. Macmillan (Cambridge: at the University Press, 1956), pp. 100, 8s 6d.

The social implications and repercussions of automation have become headline news sooner than many technologists had expected, particularly as they see automation, not as something explosively new, but as the continuation of a process, albeit accelerating, that has been going on for the best part of two centuries.

This is the background against which Mr Macmillan has brought together this valuable little book. It started as a number of talks in the BBC Third Programme, developed into a series of lectures given at the Royal Institution, and now appears in expanded form. The author has considerable gifts of clear exposition, and, at the present vital cross-roads in technological history, his book deserves to be widely read. Anyone who takes the trouble to read its hundred-odd pages will have a far better picture of automation and its implications than can be derived from scare headlines in the press. Those who wish to follow up the subject will find a valuable guide to further reading and a useful index.

THE MICROBE'S CONTRIBUTION TO BIOLOGY by A. J. Kluyver and C. B. van Niel (Harvard: University Press; London: Cumberlege, 1956), pp. 182, 32s.

The guinea-pig has long held pride of place as the biologist's living experimental tool, but to think that only 'macro-biology' contributes to our understanding of living processes is to get a distorted picture of the whole field of biology. To correct this misconception is the function of this book, which is based on the 'John M. Prather' lectures given at Harvard in 1954 by A. J. Kluyver, the distinguished Dutch micro-biologist and professor at Delft, and his American associate C. B. van Niel, who also started his micro-biological career at Delft. Their book is directed particularly to general biologists and

students of the natural sciences, because it is the authors' contention that workers in such fields are hardly even aware of the great contribution that has been made by the study of micro-organisms to the development of broader concepts covering the whole of the life sciences. There are six lectures dealing with microbial metabolism, phototrophic bacteria, microbial adaptation and mutation, and evolution as seen by the micro-biologist, in the course of which the authors do much to establish the notion of the essential unity in the mode of operation of all living creatures.

THE WEATHER AND THE LAND: Bulletin No. 165 of the Ministry of Agriculture, Fisheries, and Food (London: H.M.S.O., 1955), pp. 35, 3s.

If Government publications are not available on station book-stalls at all times, they certainly ought to be, because *The Weather and the Land* is an ideal three shilling's worth for a journey. In an hour it will dispel a dozen misconceptions about the climate of different parts of the British Isles: Torbay wetter than the Firth of Forth; the mean January temperature of the extreme north of Scotland higher than that of East Anglia, and so on: perhaps most surprising, the records for a remarkable frost hollow which lies in the valley bottom among the foothills of the Chilterns between Rickmansworth and Chorley Wood in Hertfordshire. Although within twenty miles of the centre of London, this district enjoys, if we do not misconstrue the meaning of the word, ground frost on an average on 20 per cent of the nights in June, 11 per cent in July, and 13 per cent in August. But the reader must not imagine that the whole publication is made up of a collection of *recherche* statistics; it contains much of value to gardeners, farmers, and above all, that connoisseur of the weather, the average Englishman.

THE CHEMICALS OF LIFE by Isaac Asimov (London: G. Bell and Sons, 1956), pp. 159, 12s 6d.

Isaac Asimov is assistant professor of biochemistry in the Boston University Medical School. When not engaged in research on nucleic acids he has found time to write many successful books of science fiction for adults and a couple for teenagers. *The Chemicals of Life* is not fiction, but it has all the fascination of high scientific adventure. The level at which the author has aimed is that suitable for boys

and girls towards the end of their school curriculum, but there are many older students and adults who will find Professor Asimov's book difficult to put down once they have opened it. And those who aspire to write about science, or even more to write science, might well take it as a model of lucid exposition. Would that more professors could come off their perches and tell us in the same simple way what they are doing. There might then be less of a gap between those who are in the forefront of scientific advance and the many who wish to understand them but are repelled by the style of official scientific pronouncements.

Professor Asimov sees the cells of the body as chemical factories in which thousands of different chemical processes are taking place, the chemical processes that are life itself. These processes are under the control of other chemicals called enzymes, whose ways of working are discussed in detail – how they work in harmony, how vitamins and hormones assist them, how their failure spells death, how a drug can spike the guns of a disease germ by putting one of its enzymes out of action, and how it is that such a minute quantity of cyanide can kill a man in an instant. In a nutshell he gives scientific embodiment to the scriptural phrase: 'we are fearfully and wonderfully made'.

ABOUT OUR CONTRIBUTORS

S. A. BARNETT is an Oxford zoologist who from 1946 to 1950 was head of a Government pest-control research unit in which his own work was mainly on rat behaviour and populations. He has also had experience in the sub-tropics on rat control during outbreaks of plague. He now teaches Zoology in the University of Glasgow, and carries out research on social behaviour in wild rats and on the effects of low temperatures on mice. Author of *The Human Species*.

N. A. DEBRUYNE graduated at Cambridge in 1927 and researched in the Cavendish Laboratory for a number of years. In 1934 he founded Aero Research Ltd and has been managing director since. Awarded Simms Gold Medal by the Royal Aeronautical Society in 1937 for a lecture on 'Plastic Materials for Aircraft Construction'. Invented and developed the 'Redux' process of metal-to-metal bonding used in the Dove, Comet, Britannia, and Service aircraft. In 1940 published with Gough and Tapper the first analysis on sandwich structures.

G. LAPAGE was born in Nantwich and studied medicine at the University of Manchester, but changed to zoology and graduated in 1911. A graduate scholarship enabled him to work at the Lister Institute on protozoology, and he saw war service in Iraq as Special Pathologist to the 32nd British General Hospital. Taught zoology in the University of Manchester from 1919-28 when he went to Exeter to organize the new Department of Zoology there. From 1930-54 held various posts in Cambridge ending as lecturer in Animal Pathology in the School of Veterinary Medicine. His publications range from contributions to scientific journals and scientific books, to volumes of verse, and a boys' story. Although he retired in 1954 he is still writing and has at least two books on the stocks. Has broadcast in *The Naturalist* and in other programmes.

J. E. PRENTICE was educated at Spalding Grammar School, Lincolnshire, and at University College, Nottingham. After a few years as Geologist with H.M. Geological Survey he became an assistant lecturer at Manchester University, and since 1948 has been lecturer in Geology at King's College, London. While officially a palaeontologist, his researches in North Staffordshire and Devonshire have led him into the fields of structural geology and the study of sedimentation.

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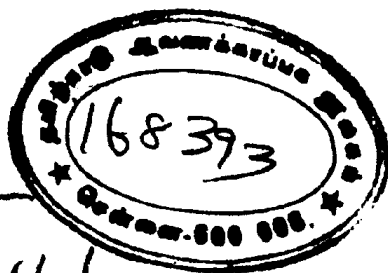
P. SYKES was born in 1923 and graduated in chemistry at the University of Manchester in 1944, subsequently obtaining an M.Sc. degree. Moving to Cambridge he received a Ph.D. in 1947 for work on the chemistry of the Penicillins. Is now a University Lecturer in Organic Chemistry at Cambridge, and has worked for a number of years on the chemistry of vitamin B₁₂; main interests are in the organic chemistry of sulphur, and in the history of science. Has taken part in adult education work in East Anglia for the past ten years, and has given many broadcasts on scientific topics.

W. C. VAUGHAN, M.B.E., is a Wing Commander in the Royal Air Force, stationed at present in Wiltshire. He was awarded the degree of Ph.D. for experimental work in radio physics in the University of London. He is the author of a number of scientific papers and has previously written in *Science News* on the velocity of electromagnetic waves.

D. H. M. WOOLLAM received his medical education at Peterhouse, Cambridge, and St George's Hospital, London, qualifying in 1948. He became a member of the Royal College of Physicians of London in 1949 and took the M.D. in 1953. Has been a lecturer in Anatomy at Cambridge since 1953.

J. W. MILLEN received his medical education at the Queen's University of Belfast, graduating in 1937. He took M.D. with gold medal in 1943 and D.Sc. in 1955. He has been a lecturer in Anatomy at Cambridge since 1950.

Drs Woolam and Millen have collaborated closely in the study of the circulation of the cerebro-spinal fluid and the vascular supply of the central nervous system. Grants from the Nuffield Foundation have enabled them to study the relationship between vitamin A deficiency and hydrocephalus.



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