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THE GEORGE BIDDER LECTURES

The Society for Experimental Biology, with the generous support of the Company of Biologists Ltd., have instituted a series of formal public lectures to be given by distinguished members of the Society, and subsequently to be published in the *Journal of Experimental Biology*. The series is named after Dr George Bidder, who played an important role in the founding of both the Company and the Society.

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The first George Bidder lecture, given at the Imperial College of Science and Technology, 5 January 1971:

EXPERIMENTAL BIOLOGY, PURE AND APPLIED

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There are those who really believe that the purpose of science is to increase human welfare. That was the vision which inspired Francis Bacon, writing of the 'Novum Organum' at a time when modern science scarcely existed, and advocating a scientific procedure which, by and large, has proved unproductive. It was the vision, also, which inspired Joseph Priestley, writing 150 years later when experimental science was really getting under way. Priestley predicted the profound effects that the new knowledge was going to have on human affairs.

That has duly come to pass; and the process is still going forward at an ever-increasing pace. But it is my object in this lecture to assert that that is not the *purpose* of science. The purpose of science is to increase knowledge. Science is the formulation of our knowledge about natural phenomena in a co-ordinated fashion by the establishment of principles and theories which epitomize that knowledge and thus provide enduring tools for thought. Scientific knowledge so formulated becomes common property and can be drawn upon for the solution of practical problems of every kind.

Sometimes, in effect, it is the scientific investigator who himself turns to apply new knowledge to practical ends; so that the boundary between these totally different kinds of activity becomes blurred. Moreover, as everyone knows, scientific research depends on asking the right questions; and some of the most pregnant questions arise from the field of practice. For centuries the problems for the physiologist sprang from the experiences of clinicians. It seems a pity that today academic physiologists tend to cut themselves off from this source.

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I do not myself find the distinction between 'pure research' and 'applied research a good one. The important distinction is between 'useful research' and 'futile research'. Useful research adds effectually to knowledge; research may be futile because the wrong questions are being asked, because it has gone on too long on set lines in one direction, and for many other reasons. But it is not my intention in this lecture to regale you with profound generalizations of this kind. I shall offer you only a personal saga; and first I must explain how it is that I have any claims to speak about applied biology.

TRAINING IN APPLIED BIOLOGY

After a brief experience, of a couple of years, in academic research in biochemistry under Gowland Hopkins, I was trained in medicine, an art based largely upon applied science; and then for twenty years I was occupied in teaching medical entomology. I travelled extensively, and in some of the less healthy places of the world: in the rat-infested shanties that made up much of Lagos during the plague outbreak of 1928; and the areas of Northern Nigeria where epidemics of sleeping sickness were rife; in some of the most malarious areas of India, such as the tea gardens of the northern foothills of Bengal and Assam and in the so-called 'Valley of Death' in the Anamallai Hills of South India. I visited many of the less salubrious locations in Malaya, Burma and Java; and was present in Ceylon during the great malaria epidemic of 1934 in which some 100000 persons died.

Then, in the early nineteen-forties I switched from medicine to agriculture and entered the employ of the Agricultural Research Council. I travelled throughout the United Kingdom to visit all the main centres where research in agricultural and veterinary entomology is done; and I followed this up with an intensive tour in which I visited some sixty of the corresponding centres in all four corners of the United States and Canada. More recently I have been able to travel in agricultural and in medical entomology in Egypt, in East Africa (where one could witness the transformation in outlook since the pre-DDT days and the advent of modern antimalarial drugs) and in Japan; and, only last year, throughout the Commonwealth of Australia.

I can therefore claim to have covered a varied practical course in applied entomology - including also forest entomology, stored-product entomology and veterinary entomology. I am not, of course, an applied entomologist; it would be most unwise for any of you to commission me to handle an actual problem in either the medical or agricultural field. But I know the people who do this work, I understand their language and their way of thinking, and have the greatest respect for their achievements.

PURE AND APPLIED SCIENCE IN THE UNITED STATES

Now as you must all be aware, there is alarm and despondency among scientists in the United States because Congress has issued a fiat demanding concentration upon practical problems; and the grant-giving bodies are all being pressed to favour and support only projects that are likely to lead to practical results. There is widespread fear for the ruin of American science and the downgrading of all the outstanding fundamental research that is being carried out.

But let us look a little more closely at this matter. Widespread interest in basic research in the United States is something new. There was, of course, a long tradition of good academic research in the American universities. But, by and large, the United States looked to Europe for the fundamental discoveries of science. What caused the change in outlook? The answer is: the needs of applied science. If you look up the *Atlantic Monthly* for the summer of 1945 you will find an article by Dr Vannevar Bush, then President of the Carnegie Institute in Washington, who held the position of Director of the Office of Scientific Research and Development from 1941 to 1947 and was one of the chief scientific advisors to President Roosevelt during the war years. It was Vannevar Bush and J. B. Conant who advised Roosevelt to proceed with the project of the atomic bomb. The thesis developed in the article to which I refer was that the war had revealed the deficiency of the United States in basic science. The extent to which physicists had necessarily been recruited from Europe for the development of the atomic bomb was stressed, and the need to make good this deficiency was emphasized.

These thoughts bore fruit. The National Institutes of Health were established in the early post-war years; the Atomic Energy Commission was set up; in 1950 the National Science Foundation was formed; in the same year, with the election of D. W. Bronk as President of the National Academy of Science, that august body entered vigorously into the political arena of science; and as part of the general enthusiasm for basic research the armed services in the United States distributed largesse in the way of research grants for almost any scientific topic – not only within America but overseas as well. Support from these sources expanded for nearly twenty years; but now a reaction has set in. Support for foreign research began seriously to be cut in 1964. Now retrenchment is hitting the home market; and pessimists in the United States feel that they are witnessing the beginning of the end of the 'U.S. age of science'. What will the future be? I shall return to that question a little later.

DDT AS AN ILLUSTRATIVE EXAMPLE

It happens that in the same volume of the *Atlantic Monthly*, in the December number (1945), there appeared another article which is relevant to my argument. At that time I had recently returned from the United States, where I had been humbly sitting at the feet of the American agricultural entomologists, trying to learn the elements of their trade, and was taking part in an autumn meeting in Cumberland to discuss problems of sheep dipping, when I was called to the 'phone at our inn in Eskdale. It was a call from the Central Office of Information who had received a request from the United States that I be invited to contribute an article on DDT to the *Atlantic Monthly*. Such indeed was the dependence of the United States on European science! The article was entitled 'DDT and the Balance of Nature'. It appeared under the editorial caption: 'A scientist looks at tomorrow' – but I am afraid that my prophetic perspicacity was not of a very profound order.

'DDT', I wrote, 'is a valuable supplement to hygiene and cleanliness. It will not take their place...When strong solutions, such as are used for spraying forests from the air, fall on water, not only are all the acquatic insects...killed, but...fish are destroyed and the streams rendered practically devoid of animal life...Only careful experiments can prove whether birds will suffer or not...It is obvious enough that DDT is a two-edged sword. We can see how seriously it may upset the balance locally between insect enemies and friends...It can bring about within a single year disturbance that it would take other chemicals a good many years to produce.'

The manner in which insects develop 'resistant races' was described – with the implication that this would surely happen with DDT; and a plea was made for increased study of insect ecology and the search for insecticides of a more selective type. All this has a terribly familiar ring today.

At that time there seemed to be an immense amount of work to be done in the study of DDT and its use. But it was all accomplished within a year or two years at the most. That is my point. 'Applied science' consists mainly in doing useful jobs with the help of scientific knowledge. Nearly always some local adaptations are necessary, sometimes quite difficult ones, so that highly intelligent investigation is required. Indeed the formidable difficulties of applied science are commonly greatly underestimated by the academic scientist. But in a broad sense it is true that the amount of thoroughgoing research is relatively limited. When new ideas or new methods emerge there will be a burst of activity as they are tried out under all varied conditions – and then the cry is for more knowledge. The knowledge that is used for some practical purpose lies at the apex of a pyramid that represents the corpus of Science. The deeper strata of this pyramid represent the accumulated knowledge of the basic sciences.

THE NATURE OF THE CONTRIBUTION OF PURE SCIENCE

My own real interests lie some way up this pyramid, but not at the apex. How did it come about that I should get caught up in the applied sciences – first in medical and then in agricultural entomology? It was the demand from the applied people for more knowledge. In 1926 when Patrick Buxton was appointed head of the Department of Entomology at the London School of Hygiene and Tropical Medicine he wrote a letter to *Nature* in which he pointed out that medical entomology was being held up by lack of knowledge of the physiology of insects. He sold this idea to Morley Fletcher, then Secretary of the Medical Research Council and an influential member of the Board of Management of the School, who believed ardently in 'watering the roots' of science. After a memorable interview with Fletcher, and backed by his friend and former collaborator Gowland Hopkins, I was recruited to enter this field; and so started on some 45 happy years of 'experimental biology' – 'pure', and on the insect.

During the war years, in the time off from crash courses for service medical officers and War Office committees, this work still continued. I became involved in an inquiry, initiated by W. W. C. Topley, then Secretary of the Agricultural Research Council, into insecticides and what could be done to improve them. Much evidence was taken and the outcome was that more *knowledge* was needed – particularly about the physiology of insects. In that way the A.R.C. Unit of Insect Physiology came into being.

That, in principle, is what will happen in the present crisis of science in the United States. Cut off the continuing supply of new basic scientific knowledge and the applied sciences quickly run out of steam. They set up such a call for help that the whole vast machine of fundamental research has to be set going again.

At the outbreak of war in 1939 everyone felt that they ought to do some science that would help the war effort. Even the Council of this Society set going a search for seaweeds to yield agar, and for brambles or briars that would furnish an improved source for gunpowder. And at the London School of Tropical Medicine we all became more self-consciously 'applied' in our outlook. But by the end of the war it was realized that the main shortage was of *knowledge*. War Office committees were funding all kinds of basic pieces of research; and in 1945 when I visited the United States I found that precisely the same thing was happening there. Insect physiology was a word to conjure with.

At a luncheon in Winnepeg during my tour I was invited by B. N. Smallman to speak (off the cuff) on 'The contribution of insect physiology to medical entomology'. To the alarm of my hosts I started by saying that it made 'no contribution' – that is, no *direct* contribution. As I had written earlier (April 1944) in *Discovery:* 'Lip service is often paid to the importance of pure science as an aid to practice. But even the loudest advocates sometimes fail to make out a convincing case. That is because it is rare for the results of research in pure science to have an immediate practical application.* It is only when the intervening links are interposed that the connexion becomes apparent. It is then seen that the practical measures directed against an insect, for example, depend first upon an accurate recognition of that insect species; then upon a thorough knowledge of its habits. As soon as its habits are closely studied, problems in its physiology arise for solution. These wait upon a knowledge of the physiology of insects in general; and so in turn on general physiology, chemistry and physics.' I propose now to illustrate the point by reference to the physiology of the insect cuticle.

FORTY YEARS RESEARCH ON THE INSECT CUTICLE

I first became interested in the insect cuticle in the early 1930s. During the previous decade two important points had come to be realized. Firstly, that the hard and horny component of the cuticle was something quite different from the chitin of Odier (as, in fact, Odier himself in 1823 had clearly recognized), and secondly, that the cuticle was not to be regarded solely as an external skeleton, but that its waterproof properties were of equal importance in the life of the insect.

Cuticle hardening

The hardening or 'sclerotization' of the cuticle was attributed to impregnating substances or 'Inkrusten' considered by the German authors to be probably carbohydrate in nature. Working on the cuticle of the blood-sucking bug *Rhodnius*, I suggested that the sclerotizing material was a mixture of lipid and protein that I called 'cuticulin'. This mixture by itself was believed to form the 'epicuticle'; and in the deeper horny layer (the 'exocuticle') it was believed to impregnate the chitinous framework. Cuticulin was supposed to be hardened by lipid polymerization – due perhaps to an oxidative condensation of unsaturated chains, as in the formation of a varnish. Physically the substance resembled shellac in hardness; and shellac is now known to be a lipid polyester (Cockeram & Levine, 1961).

The deposition of this lipid-containing material ran parallel with the secretory activity in the oenocytes which were at their maximum size when the deposition of

* DDT was synthesized by O. Zeidler in 1874; it was nearly 80 years before it found a use as an insecticide.

new cuticle was about to begin; they were completely exhausted at the time of ecdysis when the exocuticle was complete. The bulk of the cuticle (the unimpregnated endocuticle) is laid down after moulting when the oenocytes are inactive. Moreover the oenocytes are very rich in bound lipid. These cells, whose function is usually regarded as enigmatic, are to be thought of, I believe, as ectodermal cells (they commonly continue to arise from the epidermis throughout post-embryonic development) which have become specialized for this one function among many that reside in the epidermis: the secretion and storage of structural lipids or lipoprotein (Wigglesworth, 1933).

Then in 1940 Mark Pryor put forward his illuminating theory that the horny component of the cuticle, which he named 'sclerotin', is just protein that is tanned by quinones produced from the oxidation of diphenols secreted into the cuticle at the time of moulting. In my enthusiasm for this new interpretation I unwisely abandoned my belief that lipids were involved – though Dennell & Malek (1955) firmly maintained that there was a large element of truth in the cuticulin theory.

There is now a very extensive literature on the nature of the tanning process in the cuticle. Notably the work by Karlson and Sekeris and others (Karlson & Sekeris, 1962) in Germany, by Brunet (1967) in this country and by Hackman (1964) in Australia. The enzyme chemistry of the process, notably in the öotheca of the cockroach and in the puparium of blowflies, has been extensively studied. It appears that the proteins are linked directly to the benzene ring of the quinone and are irreversibly bound by what must be a somewhat violent reaction. But very recently a much more gentle form of phenolic polymerization has been described by S. O. Andersen (1970) in which acetyl dopamine seems again to be the precursor; but the proteins are linked to the β-carbon atom of the side-chain and the two phenolic groups on the benzene ring survive intact.

Structural lipids

But this is not the whole story. Quinone-tanned protein is not the same thing as sclerotin. Moreover there is refractile semi-hardened cuticle which shows no evidence of the presence of phenolic substances and is not regarded as being tanned – such as the 'mesocuticle' which lies below the tanned exocuticle in the cockroach, or the 'taenidia' which form the stiffening threads of the tracheae, or the walls of the wing scales of Lepidoptera. Reinvestigation has shown that all these structures are in fact heavily impregnated with lipid. That has been shown histochemically by Sudan-black staining after the oxidative fission of the protein in the cuticle with dilute hypochlorite (Wigglesworth, 1970).

These observations are in agreement with the chemical analyses of the cuticle of various insects that have been carried out in recent years. Far more lipid can be extracted by prolonged treatment with hot chloroform and methanol than is likely to exist in the invisible layer of free wax on the surface. The following are a few of the results reported for total extractable lipids on a dry-weight basis: mealworm, *Tenebrio molitor*, cast larval skins, 5% (Bursell & Clements, 1967); Mormon cricket, *Anabrus simplex*, whole abdominal cuticle, 4·3% (Baker *et al.* 1960); blowfly, *Lucilia cuprina*, empty puparia, 2·6%; the same, cast pupal skins, 31·4% (Gilby & McKellar, 1970); and the following are some preliminary results obtained recently by Dr J. T. Martin (personal communication): *Dermestes maculatus*, cast larval skins, 9%; *Oncopeltus fasciatus*, cast larval skins, 15%.

There is no doubt that phenolic or quinone tanning is of prime importance in the sclerotization of the hardest parts of the cuticle, but quite firm cuticle can be produced in the absence of tanning or before tanning takes place. The nature of this process is not known. I suggested in a recent paper (Wigglesworth, 1970) that the lipid might be a polyester comparable with the plant cuticle or with shellac; but hydroxy fatty acids are not common among the lipids that can be extracted from the cuticle. Perhaps the change is merely a physical one: a denaturation of protein by interaction with lipid and the consequent exclusion of water.

Waterproofing properties of the cuticle

The importance of the waterproofing properties of the cuticle in the life of insects was appreciated much later than its skeletal function. This appreciation goes back I think only to the theory put forward in 1927 by Hazelhoff that the function of the spiracular valves on the tracheal system of insects is to prevent the loss of water by evaporation. This theory carried with it the assumption that the cuticle itself is highly waterproof. In 1935 I extended Hazelhoff's observations to the control of respiration in the flea and Mellanby (1934) confirmed that if the flea is obliged to keep its spiracles open (by exposure to carbon dioxide) it rapidly loses moisture. It had been pointed out by Kühnelt (1928) that soft-skinned insects, such as larvae of the clothes moth *Tineola*, are just as successful in retaining water as are sclerotized insects, such as larvae of the mealworm *Tenebrio*. Clearly the waterproof layer must be at the surface of the cuticle.

The first indication of the nature of the waterproofing system was obtained by Ramsay (1935), who observed that minute droplets of water sprayed on the surface of the cuticle of the cockroach *Periplaneta*, instead of evaporating in a few moments, remained unchanged for hours. They had been covered by a waterproofing lipid film which had spread over them from the cuticle. When the temperature was raised above about 35 °C there appeared to be a phase change in the lipid coating and the droplets evaporated immediately. Likewise when the whole insect was exposed to a temperature above 35 °C there was a more or less abrupt increase in the rate of transpiration. Thus a thin layer of lipid, perhaps a mono-molecular layer in the case of the water droplets, was highly effective in preventing transpiration.

Abrasive and absorptive dusts

It had long been known that fine inert dusts were lethal to insects. Indeed the protection of stored grain against insect attack by the addition of fine road dust had been practiced in North Africa since Roman times. In the early 1940s it was found that certain refined dusts, notably of silica and of crystalline alumina (synthetic sapphire powder) were exceedingly effective. It was generally agreed that the insects died from desiccation, but, as was noted by Alexander, Kitchener & Briscoe (1944), in many species the dust was active only when applied to the living insect. The explanation of this curious observation proved quite simple. Experiments on *Rhodnius* (Wigglesworth, 1945) showed that in many parts of the body the waterproofing layer is quite superficial, but it is not broken down by simple contact with the fine dust – that is, by adsorption; it can be interrupted only by superficial abrasion. When the insect is alive and moving the dust gets into the joints and elsewhere and rubs away a part of the waterproof covering (Wigglesworth, 1945, 1947*b*).

In the recently engorged larva of *Rhodnius* the distended abdomen is drawn along the surface as it runs. If it is moving on filter paper lightly dusted with alumina, the surface of the cuticle is abraded at the point of contact and within 24 h in a dry atmosphere the larva is completely dried up and dead. The abraded areas are readily detected by immersing the insect in ammoniacal silver hydroxide; the exposed diphenols in the epicuticle produce deep brown areas of silver reduction. But if, under these same conditions, the abdomen is held away from the surface with a little knob of paraffin wax, the larva survives with very little loss of moisture (Wigglesworth, 1945). In certain other insects, such as the cockroach and some termites, the waterproofing material is quite mobile and is readily removed by adsorption in the dead and motionless insect (Wigglesworth, 1945; Ebeling, 1961; Collins & Richards, 1966).

Waterproofing waxes

These superficial waterproofing waxes vary in character from a soft mobile grease as in the cockroach, through soft waxes as in caterpillars and sawfly larvae, to waxes of increasing hardness in the mealworm, in *Rhodnius*, in the honey bee, and finally in the pupae of Lepidoptera (*Pieris*) which must withstand exposure for many months. All these insects show the same pheomenon as the cockroach: there is a more or less abrupt increase in the rate of transpiration when the temperature is raised – but the transition temperature at which the break occurs rises from about 33 °C to about 58 °C as the waxes increase in hardness (Wigglesworth, 1945). And Beament (1945, 1961) using the wax extracted from the cast skins of these same insects, applied to artificial membranes, got comparable results.

Even when the waterproofing wax is a solid crystalline material on the surface of the cuticle it is a very fragile barrier against the drying power of the environment; it is indeed invisibly thin. It turned out that in most insects, just at the time of moulting, a further protective layer, the so-called 'cement layer', is poured out by numerous dermal glands and spreads evenly over the entire surface of the waterproofing wax (Wigglesworth, 1947*a*, 1948). In the cockroach the 'cement layer' seems to be of a sponge-like nature and to be permeated by the waterproofing grease (Kramer & Wigglesworth, 1950).

The cuticular grease of the cockroach is readily obtained by dripping chloroform over the surface of the living insect. I found that when it was stored in contact with the air for some months this grease changed into a hard wax. With my prejudice in favour of the polymerization of unsaturated lipids in the cuticle I was inclined to regard this as the result of autoxidation. At my suggestion the nature of the change was looked into by Beament and he obtained some evidence that it resulted from the evaporation of volatile solvents (he suggested a mixture of short-chain paraffins and alcohols) (Beament, 1955). Gilby & Cox (1963), however, using gas chromatography were unable to confirm the presence of such solvents. The major component proved to be the unsaturated hydrocarbon *cis-cis*-6,9-heptacosadiene (Beatty & Gilby, 1969). Atkinson

& Gilby (1970) have recently shown that when the grease is isolated and exposed to the air this unsaturated hydrocarbon undergoes autoxidation, with the formation of the waxy solids stearal and stearic acid. Polymers formed by free radicals may also contribute to the hardening. In the living insect the free protocatechuic acid, which is believed to be the primary source of the *o*-quinone involved in tanning (Brunet, 1967), has the additional function of serving as an antioxidant which prevents the oxidative degradation and polymerization of the cuticle lipid (Atkinson & Gilby, 1970).

Of course the 'cement layer' is not proof against gross abrasion. Insects in the soil (wireworms, chafer beetle larvae, etc.) become so scratched by abrasive particles that if they are exposed in a dry atmosphere they lose water rapidly. But if a larva of the wireworm *Agriotes*, for example, is taken from the soil and kept in a moist atmosphere, and allowed to moult under conditions where it does not come into contact with abrasive particles, it lays down a good waterproof cuticle which has a sharp 'critical temperature' and it does not suffer rapid desiccation under dry conditions (Wigglesworth, 1945).

Wax secretion

Where does the wax in the cuticle come from? Until very shortly before the old skin is shed the new cuticle is not waterproof. Indeed the digested product of the inner layers of the old cuticle are being absorbed through it. Only in the last hour or so does the surface of the new cuticle become dry and hydrophobe and waterproof. The wax is exuded through the substance of the new cuticle, which has no visible ducts. It was observed in the 1830s that the cuticle is traversed by fine canals, named by Leydig in 1855 the 'pore canals', which extend outwards from the epidermal cells. But the pore canals, which are only a fraction of a micron in diameter, end blindly below the epicuticle, which is usually rather less than a micron in thickness.

In 1942 I noted that if any small insect is immersed in a drop of oil, such as medicinal paraffin, covered with a coverslip and observed under the microscope, minute droplets of water soon begin to exude from the cuticle into the oil. This happens both over areas covered by soft cuticle, such as the intersegmental membranes, and, more slowly, over areas with horny cuticle (Wigglesworth, 1942). This was a highly suggestive observation because it implied that there must be a connexion between the pore canals and the surface.

Further evidence of this was obtained by exposing the surface of the new cuticle to ammoniacal silver hydroxide at different stages during the time when the wax layer is being formed. The medium which carries the wax or its precursors forms a precipitate with the silver solution. This blackened precipitate spreads radially from points overlying the pore canals. And it is often possible to see that the precipitate is penetrating the substance of the epicuticle and connecting up with a pore canal (Wigglesworth, 1947*a*, 1948).

The explanation was ultimately found by Michael Locke (1961) in an electron-microscope study of the cuticle. Locke showed that beyond the distal endings of the pore canals, and connected with the tips of these canals, there are excessively fine tracks, no more than 100–130 Å in diameter in *Tenebrio*, which spread out fan-wise to penetrate the epicuticle and lead to its free surface. These tracts doubtless provide the looked-for outlets from the epidermal cells. In the wax-secreting epithelium of the honey-bee there is the same arrangement in more exaggerated form. The cytoplasm of the epidermal cells contains whorls of filaments which become bundled together and form a sort of rope in the pore canal and then continue into the individual tracts to the surface. Locke calls them 'wax canal filaments'.

At the light-microscope level one cannot see these structures. But with nitric acid and potassium chlorate it is possible to dissolve away the rest of the newly formed cuticle to liberate the contents of the pore canals as fine strands which are rich in lipids. These lipids are set free and become stainable with Sudan black on oxidation with dilute sodium hypochlorite (Wigglesworth, 1970).

Locke (1961) also showed that the pore canals contain an esterase. This could well be a protease (for most proteases, such as trypsin and many peptidases, have esterase activity) and may perhaps be concerned with liberation of the fluid medium that spreads over the surface of the cuticle and from which the waterproofing wax crystallizes out. It seems likely that this is a continuing process in the life of the insect, and that the pore canals provide a constant reservoir of waterproofing wax. In *Rhodnius*, if the surface of the cuticle is lightly abraded with alumina dust and the powder is then washed off and the insect kept in a humid atmosphere to avoid desiccation, new wax is secreted and forms a white bloom over the scratched area, and the impermeability of the cuticle to water loss is restored (Wigglesworth, 1945).

Many other interesting things have been discovered about the insect cuticle in recent years: on the interrelations of protein and chitin by Hackman (1964) and by Rudall (1963), on the rubber-like protein 'resilin', which occurs in all those regions where a high degree of elasticity is required, by Andersen & Weis-Fogh (1964); on the reversible plasticity of the soft cuticle, by Bennet-Clark (1962); on the nature and variety of lamination in the chitin-protein micelles of the cuticle by Neville (1965, 1967); and much more besides. I have confined my remarks to those aspects of the subject in which I happen to have been involved.

Conclusions

No one can be concerned in thinking deeply about contact insecticides or about the ecology of insects in adverse climates without constantly reflecting on the properties of the cuticle. In that sense what we have learned in the past forty years is a great contribution to applied entomology: it has provided essential tools for thought. But one would find it difficult to point to a *single* discovery, taken by itself in this field, and claim that *this* has been of practical value.

Besides joining in these investigations of the cuticle, I have been engaged in studying insect digestion, respiration, excretion, and water conservation, ionic and osmo-regulation, the nervous system, sense organs and behaviour, the control of growth and form and various other matters. As with the insect cuticle, the general body of knowledge that has been built up about all these topics by a small army of insect physiologists now forms part of the intellectual armoury of the applied entomologist.

Perhaps the last item on my list, the control of growth and form, is the most academic of the lot, with the least bearing upon applied science. And yet, curiously enough, this is the only topic that has hit the headlines in respect to insect control. When the chemical nature of the juvenile hormone was finally established by Röller and his colleagues (1968) it turned out to be a terpenoid. And many other terpenoids, more or less related, had already been found to have similar effects on growth and reproduction; or abnormal effects, causing malformation or sterility. As a result a new potential field for the synthesis of new kinds of insecticides is being opened up with tremendous energy at the present time. And yet, when I described the hormonal control of moulting and metamorphosis in 1934, and demonstrated the existence of the hormone which we later called the juvenile hormone, I was unable to persuade Patrick Buxton to include a reference to these discoveries in the annual report on the work of the Department of Entomology at the London School.

Man is an arrogant animal. In the euphoric state engendered by her Centenary in 1969, even *Nature* was betrayed into claiming that 'the directions of scientific advance are no longer left to chance but, rather, are charted almost deliberately in advance'. In his famous address to the combined Darwin Centenary and International Congress of Zoology in the Albert Hall in 1958, Julian Huxley assured us that man was no longer subject to natural selection. As one who does not believe any of these things I hold that there are still unexpected discoveries to be made, and that there is still room for the enquiring mind and the untrammelled researches of the experimental biologist.

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