fall into two sharp groups; in the archæogastropods they are predominantly acid-soluble, pyrrolic substances, whereas in all pulmonates and most higher prosobranchs they are non-extractable protein-bound materials. Uroporphyrin occurs in large amounts in archæogastropod shells, and also in a few other groups (tectibranch opisthobranchs, certain Cypraeidae, etc.). In others (*Turbo*, *Haliotis*), it is apparently replaced by linear tetrapyrroles often of an unusual kind and in mixtures which paper chromatography has shown to be highly complex. *iso*-Uroporphyrin also occurs in some Trochidae. Coproporphyrin has not been found.

The source and function of these substances are not known, but are possibly dietary, the shell providing a means of disposing of porphyrins or their degradation products. The colour of pulmonates (*Cepaea*) has, however, been shown experimentally to influence selection by predators, and the complexity of shell pigmentation in other forms makes it difficult to believe that it has no similar adaptive function.

Dr. D. R. Crofts (Queen Elizabeth College, London) dealt with the subject of "Muscles and Torsion in Gastropods". Garstang, in 1929, made the suggestion that torsion might have originated ancestrally during pelagic larval development in response to larval needs, bringing the mantle cavity with its contents into a dorsal position behind the head and so allowing for the withdrawal of the head and foot within the shell for protection. This position of the mantle cavity was by no means an advantage to the adult, allowing no free elimination of the waste products of respiration and excretion. Garstang emphasized that further changes, therefore, became necessary in the creeping adult because of torsion. Garstang's hypothesis was that a genetic mutation, having its phenotypic expression effective in the veliger stage, could have involved a pair of asymmetrical larval retractor muscles, namely, a right-hand head retractor with a posterior shell attachment and a left-side foot retractor with a more forward shell attachment, working more or less at right angles to one another. Ancestrally these two muscles might have brought about the whole 180°-torsion which Boutan (1898) thought took place in a few minutes.

From recent work on muscle development in primitive gastropods it is obvious that only one of the two muscles postulated by Garstang exists at the time larval torsion begins. This is the asymmetrical retractor developed from the mesoderm band of the pretorsional right side, having a posterior shell attachment on that side: the anterior attachments on the right retract the mantle and head, while those on the left curve dorsally over the gut and retract the left side of the head and foot. The retraction of this single asymmetrical muscle is responsible for the first part of the rotation and thus this muscle appears to be the primary ontogenetic cause of torsion. It might be the right member of an ancestral pair of muscles; the other member might be the post-torsional muscle of the right side (the adult columellar muscle), which is delayed in development until the second phase of torsion, during which the shell fixation of the original larval retractor migrates towards the final left side. At the completion of torsion the two muscles are equal in size. Their further modification does not occur until post-larval development. The two laterally placed equal muscles closely correspond with those of the adult *Scissurella* and might represent the two symmetrical retractor muscles of ancestral gastropods, the scars of which were discovered in the Palæozoic bellerophonts by Knight (1947). Contrary to general supposition, the early larval retractor does not become the columellar muscle. Lemche's study, at the Copenhagen Museum, of the organization of the muscle cells in the living monoplacophoran, which has not undergone torsion, is awaited with great interest.

In the ensuing discussion, to which a number of those present contributed, Dr. John Morton remarked that the long adapical canal of *Rimella* corresponds exactly in position to what would be needed for an efferent canal were the mollusc to burrow, as appears likely, like *Aporrhais* and *Struthiolaria*. In general, the expanded outer lip in the Strombacea could be an adaptation, perhaps as a canopy against the fall of sediment; a small sinus low on the lip is to let out the right eye stalk, the left one coming out from the anterior canal. Dr. Comfort's picture of the distribution of porphyrin pigments in shells, chiefly in archæogastropods, primitive tectibranchs and primitive mesogastropods, previously difficult to explain, makes very good sense if fitted in with a postulated radial derivation of pulmonates, opisthobranchs, and higher mesogastropods from archæogastropods.

L. R. Cox

# AEROBIOLOGY

AEROBIOLOGY may be defined as the study of the aerial transport of plants and animals or viable parts thereof, including flying animals (such as insects) in so far as passive movement is a major factor in their dispersal. A three-hour symposium on the subject was held by the Linnean Society of London on February 21, the president, Dr. H. Hamshaw Thomas, being in the chair.

The first speaker, Dr. J. M. Hirst (Rothamsted Experimental Station, Harpenden), said that, although spore dispersal is essential for the fertilization of many plants and for the wide distribution of saprophytic moulds, these aspects had received less attention than had the harmful effects of spores to man: direct effects in the form of allergic reactions or indirect in the form of plant diseases. For the study of both these kinds of effects it is necessary to catch spores. Critical examination by Prof. P. H. Gregory of the various kinds of spore trap in use up to 1950 showed that freely exposed traps could never provide unbiased estimates of all constituents of the air spora at the frequent intervals necessary to show that their numbers were affected by changing weather. A new trap based on May's cascade impactor was therefore devised. This, the automatic volumetric spore trap, catches plant spores of all sizes with a high efficiency, and in particular it is much more efficient as a collector of small spores than is a freely exposed horizontal surface; though *per contra* the agar-coated Petri plate allows identification of colonies of fungi, the spores of which cannot be recognized microscopically. The daily trace obtained by the automatic volumetric spore trap is often clearly banded, and counts made of the

spores on traverses across the slide give estimates of spore concentration at intervals throughout the day. Almost every group of spores investigated has been found to show a typical diurnal periodicity if examined over a sufficiently long period. Thus the sporangia of potato blight (*Phytophthora infestans*) are most abundant in the air at 11 a.m.: their release seems to be influenced by radiation acting either directly or indirectly by local change in relative humidity. The new spore trap has also been used for finding when the two kinds of spore of the apple scab fungus (*Venturia inaequalis*) are dispersed and so to improve the timing of fungicidal sprays.

Mr. H. A. Hyde (National Museum of Wales and Asthma Research Unit, Cardiff) described the results of a 15-year census of pollen grains and mould spores made in the interests of the study of allergic disease. The horizontal ('gravity') slide had been used continuously at Cardiff from 1942 and at fourteen other centres for periods of a year or more; the Petri plate at Cardiff from 1948 and also at seven other centres in 1952; and the Hirst trap from 1954 at Cardiff only. Empirical comparison between simultaneous counts made by gravity slide and Hirst trap showed that gravity slides reflect the general trend of atmospheric incidence so that conclusions drawn from observations made by this method are still valid. Such counts made over many years indicated that the average incidence of the principal kinds of tree pollen might oscillate in successive years up to 400 per cent or down to 4 per cent (or less) of the 15-year average. This variability probably hinders the development of allergic sensitivity and, together with variable phenology, certainly complicates diagnosis. Grass pollen makes up nearly one-half the total trapped in the course of the year. Hourly counts of grass pollen caught by the Hirst trap have confirmed conclusions on time of flowering of grasses and its relation to external factors and to atmospheric pollen incidence. There is a close relationship in time between atmospheric grass-pollen concentration and the severity of allergic symptoms.

Grass-pollen concentrations are highest in the lowlands and lowest in mountain areas, but probably at no point on the mainland of England and Wales or within thirty miles of the coast do they remain during the season (June–July) below the level of tolerance. The mould *Cladosporium*, which had been shown by the Petri plate census to be by far the most abundant culturable mould in the air and which Hirst had stated was numerically the most abundant of all fungus spores caught in his traps during the period covered by his observations at Harpenden in 1952, has been shown to be, among culturable moulds, the most frequent cause of allergic symptoms. Both diagnosis and treatment of inhalant allergy demand a comprehensive pollen and spore census.

Mr. L. R. Taylor described work done at Rothamsted Experimental Station under the leadership of Dr. C. G. Johnson on the origin of fluctuations in aerial aphid density and their significance in dispersal. Insect densities were measured hourly at five heights up to 1,000 ft. Spatial and temporal fluctuations in these densities depend upon the available upward transport acting upon the flight rhythm of the insect at ground level. The profile of insect density plotted against height as it changes from hour to hour is in effect an expression of these two major elements in dispersal, which have been related respectively to known meteorological and biological factors.

The flight curve of *Aphis fabae*, for example, at crop-level is commonly bimodal: its amplitude depends on the rate of hatching out of winged adults and its timing on the length of their teneral (drying out) period. Rate of upward transport depends in part on atmospheric circulation and in part on the aerodynamic characteristics of the insects. Preliminary analyses suggest that the rate of exchange of aphids is fairly high; that is to say, they may rise to thousands of feet in the air and return to ground level again within the hour. This suggests that alighting behaviour must play an important part in determining the horizontal distances travelled. Consideration of density/height and density/time profiles for other insects leads to the conclusion that many insects other than aphids are dispersed to heights similar to those reached by aphids and hence they must be dispersed laterally in a similar way. A segregation into 'active flight' of insects at low levels and 'passive drift' at high levels is probably highly artificial and misleading.

Dr. R. C. Rainey, of the Desert-Locust Survey, Nairobi, considered the effects of air movements upon adult locusts on two different scales. He first described how atmospheric turbulence affects the height of flight, density and detailed structure of flying swarms. Thermal upcurrents can rise only to a 'ceiling' height which varies from time to time, and is determined by the corresponding vertical distribution of air temperature. Large high-flying swarms have been observed to extend up to this ceiling height, at 3,000–6,000 ft. On the other hand, swarms have been observed flying below 30 ft. under conditions of isothermal temperature gradient, when turbulence could be expected to be at a minimum. Direct evidence on strength and distribution of turbulent air movements—the gusts recorded by aircraft—has also been obtained during a flight within and around the upper part of a swarm.

The density and distribution of flying locusts *in the vertical* are thus profoundly affected by turbulent air movements such as are utilized by soaring birds. There is, on the other hand, good evidence that the behaviour of locust swarms is strikingly opposed to *lateral* turbulent dispersal, that is, to spreading out in plan like a cloud of inert airborne material; the apparently purposive orientation of locusts is not in general related to the movement of the swarm as a whole, which movement in fact is often (and probably usually) directly downwind and therefore in general into zones of convergence and potentially of rain.

Locusts, under the influence of mutual stimulation, are perhaps among the most regularly airborne of insects. Once they are in the air, their subsequent distribution and movement are profoundly influenced by the atmospheric processes of turbulence, operating over distances of hundreds or thousands of feet, and of divergence and convergence, operating over hundreds or thousands of miles; and the part played by convergent wind flow in the production of rain would appear to confer a substantial survival value on the flight in arid regions.

Certain aerobiological problems which had not been dealt with by the four principal speakers were referred to by others. Mr. L. Ogilvie (Ministry of Agriculture, Bristol) referred to observations which he and his staff had been making for many years on epiphytotics of black rust of wheat in south-west England. Their conclusion that these may be initiated by airborne inocula from southern Europe

or north Africa had been supported in 1955 by Mr. Hyde, who had registered uredospores in the air around Britain at the relevant times.

Mr. P. K. C. Austwick (Veterinary Laboratory, Weybridge) directed attention to an aspect of intramural biology, namely, the indoor conveyance of airborne fungi pathogenic to man and animals. The inhalation of airborne spores is now accepted as the major epidemiological feature of coccidioidomycosis and histoplasmosis, and although these diseases are fortunately rare in Britain there are others, such as aspergillosis, which are not uncommon. One form of aspergillosis in animals appears to be bovine mycotic abortion, in which infection is thought to be primarily respiratory, spreading to the placenta from the lungs. Spore sampling by means of the Hirst automatic volumetric spore trap has been carried out in an ordinary cowshed at the Ministry of Agriculture, Veterinary Laboratory, Weybridge, by Prof. H. K. Baruah, University of Gauhati, Assam, with the kind co-operation of Prof. P. H. Gregory, who also lent the equipment. The number of spores encountered have been extremely high, varying from 300,000 to 1,300,000 per cubic metre, and it has been found that the majority of these are of *Aspergillus* or mucoraceous species. These are the fungi which are predominant in cases of mycotic abortion and they also occur in quantity in hay and straw. The aerospora of farm buildings therefore seems to be very different from that of the outside air both in quantity and quality, and its investigation should lead to a better understanding of both respiratory mycoses and the allergic diseases of the 'farmer's lung' complex.

All aerobiological investigations so far made seem to have arisen out of diverse practical needs, but as the symposium showed, studies which began with quite different approaches have led to entirely compatible conclusions: all, at least so far as they are concerned with the outdoor air, lay emphasis on the conditioning of spore and insect release by meteorological factors and on the reliance both of spores and (with modifications) of insects on the dynamics of the atmosphere. The study of particulate dispersal in general falls within the scope of meteorology, and meteorologists are exploring this field experimentally[1], but the need for planned observational work on the airborne biota still remains and is not likely to be satisfied for a long time to come. H. A. Hyde

[1] Pasquill, F., *Nature*, **177**, 1148 (1956).

# SYNTHESIS OF PENICILLIN V

THE accomplishment of a total synthesis of penicillin V (phenoxymethylpenicillin) at the Massachusetts Institute of Technology by Dr. J. C. Sheehan and Dr. R. K. Henery-Logan[1] brings to an end the long search for the first rational synthesis of one of the biosynthetic penicillins.

Dr. Sheehan, while a member of the Merck laboratories research team, took part in the combined attempt by thirty-nine American and British laboratories during the Second World War to synthesize benzylpenicillin. The stage reached when this collaboration came to an end in 1945 was the synthesis of benzylpenicillin in minute yield by groups of workers at Oxford and in the United States[2]. This synthesis gave no information about the structure of penicillin, and in spite of much effort could not be improved to give a better yield of the antibiotic. Sheehan was one of the few people who continued to entertain the hope that a satisfactory synthesis of the unstable penicillin molecule could be achieved. In 1948, two years after he joined the faculty of the Massachusetts Institute, he began the series of carefully planned researches which systematically led him to his latest achievement.

One of Sheehan's earlier successful ideas was the use of penicilloates that could not give azlactones by rearrangement. This idea led to the synthesis of the methyl ester of phthalimidopenicillin[3], which is biologically inactive, and then to a synthesis of the methyl ester of benzylpenicillin sulphone. The infrared spectrum of the latter was identical with that of the same derivative prepared from natural benzylpenicillin, thus providing the first direct chemical proof of the fused β-lactam thiazolidine structure of the penicillins. Further exploitation of the same idea, combined with a new method for synthesizing penicilloic acids that have the configuration corresponding to the natural penicillins, led to the synthesis of a penicillin analogue having a benzylsulphonamido group in the side chain[4] in place of the phenylacetamido group of benzylpenicillin. This substance was the first biologically active synthetic 'penicillin' to be made. It has not so far been obtained by fermentation.

Two further factors arising out of unrelated researches have a bearing on Sheehan's latest achievement. The first was the discovery, independently by Sheehan and Hess[5] and by Khorana[6], that aliphatic carbodiimides can be used as condensing agents for the formation of peptide bonds in the presence of water. The second was the observation by Brandl and Margreiter[7] that phenoxymethylpenicillin is stable in acid solution. Sheehan and Henery-Logan used N,N′-dicyclohexylcarbodiimide to bring about the cyclization of a β-lactam ring in the penicilloic acid of penicillin V. This reaction, which is the key step in the synthesis, is carried out in aqueous dioxan solution at room temperature and yields about 12 per cent of penicillin V.

The new methods of synthesis may not, at present, compete economically with the established fermentation processes. However, the production of new synthetic penicillins, of which some ten have already been made at the research laboratories of Merck, Sharp and Dohme[8], opens up exciting possibilities of improving the already established position of the penicillins in medicine. For example, penicillins effective against a wider range of pathogenic bacteria, including organisms producing penicillinase, may now be within reach. The key to a penicillin structure resistant to penicillinase may emerge from the completion of the structural studies[9] on the antibiotic cephalosporin C, which resembles the classical penicillins in many of its chemical properties. However, it is resistant to the action of penicillinase, and is