These life cycles are tied in with metabolic changes, muscle autolysis, and so forth. R. Wootton (University of Exeter) dealt with the fossil record and insect flight. No insect fossils exist from the Devonian when winged insects are believed to have appeared, but from consideration of the earliest fossil forms he supported a monophyletic origin of insect flight by way of a gliding phase in Devonian insects with thoracic paranotal lobes. V. B. Wigglesworth (University of Cambridge), after reviewing theories of the origin of wings, supported the gill theory and suggested that wings evolved from the styli of the thoracic coxae in a secondarily aquatic apterygote, perhaps of thysanuran type; and he restated his 'dispersal theory' of the origin of flight on this basis.

LEPROSY

New Treatment?

from a Correspondent

ONE of the many enigmas of leprosy concerns the particular predilection of the causative bacillus for human nerve tissue, a site which no other infective bacilli are found to occupy. The disease has received little attention from research workers, so that the nature of the causative organism remains unknown.

Since 1967 Prabhakaran's group have been concerned with the presence and implications of an unusual tyrosinase in *Mycobacterium leprae*, and in the current *Leprosy Review* (**44**, 112 ; 1973) Prabhakaran reports their latest findings in a comprehensive review of the activity and function of this enzyme. This work may point the way to a chemotherapeutic agent for treating leprosy.

Tyrosinase is utilised in the oxidation of DOPA (dihydroxyphenylalanine) in the formation of pigment. The enzyme is present in animal and plant cells, and exhibits in *M. leprae* (as in other cells of low phylogeny) a wide substrate specificity. Manometric, spectrophotometric and more recently radio-isotope tracer techniques have demonstrated the rapid oxidation of DOPA in viable organisms isolated from humans and armadillos (the nine-banded armadillo has recently been found to be susceptible to *M. leprae* infections). Certain properties of the bacillary enzyme which distinguish it from the plant and mammalian enzymes have also been intimated.

In contrast to tyrosine of mammalian and plant origin, no substrate inhibition of the bacillary enzyme has been demonstrated and neither is the enzyme inhibited by penicillamine or mimosine. The intermediary quinone produced in the conversion of DOPA to melanin in mammalian and plant cells is dopachrome ; in *M. leprae* it is indole-5-6-quinone. In plants and mammals reducing agents regulate the activity of tyrosine by inhibiting the production of quinone from DOPA, whereas in *M. leprae* the enzyme is not affected (although the further oxidation and polymerization of quinone to melanin is prevented). In plants tyrosine is a soluble enzyme; in mammalian cells the enzyme is particulate and can be released by deoxycholate. In *M. leprae* the enzyme is also particulate and can be released by the anionic detergent sodium dodecyl sulphate but not by deoxycholate. The existence of differences between the mammalian and bacillary enzyme indicates that *M. leprae* enzyme may be a suitable site for the action of chemotherapeutic agents, particularly because it seems to have a key metabolic role in the growth of the bacillus.

Prabhakaran points out that the sites invaded by *M. leprae* in man are all sites where free DOPA is present—skin and peripheral nerves, the eye (ciliary body ,and iris), testis, adrenal medulla and Schwann cells of dorsal root ganglia of spinal nerves. All these tissues including the melanocytes inhabited by the bacilli in skin and mucous membranes are derived from neural crest cells of the embryo. *In vitro* the production of melanin by melanocytes is suppressed in the presence of viable *M. leprae* organisms, indicating utilization of the DOPA by the bacilli.

A requirement for DOPA would therefore explain why the leprosy bacillus occupies such a unique environment in the human host. The most important implications of these findings, however, are concerned with chemotherapy. Knowledge of biochemical differences between host and causative organism induces a rational approach to the design of chemotherapeutic agents. In the case of leprosy, where an alarming degree of resistance to the sulphone drugs is becoming evident, new chemotherapeutic agents are urgently required. In this respect inhibitors of *M. leprae* tyrosinase activity may prove to be of great value.

Diethyldithiocarbamate (DDC) was found to be the most potent inhibitor of *M. leprae* tyrosinase both *in vitro* and *in vivo* where it suppresses multiplication of the bacillus in mouse footpads and results in a loss of viability. DDC probably inhibits the tyrosinase by binding with the copper moiety of the enzyme. Acting in this way, any mutation in the amino acid sequence of the enzyme, which is the cause of drug resistance in some instances (for example, in some bacteria resistance is induced in this way to rifampicin, a drug which has recently proved to be of value in the treatment of leprosy), would not result in decreased activity of the drug. The structure of DDC is such that the compound can pass easily through lipid predominant pores of the membrane, so that resistance due to a permeability barrier (as occurs in many instances of bacterial resistance) is unlikely to occur.

DDC and other compounds designed to inhibit the utilization of the apparently essential DOPA may therefore prove valuable in the treatment of leprosy.

NAVIGATION

Homing by Pigeons

from our Animal Behaviour Correspondent

IT is one thing for an animal to be able to take up a consistent orientation and find its way home using a simple compass (Sun, star and magnetic compasses are found throughout the animal kingdom). It is, however, a feat of a quite different order for the animal to be able to home consistently from wherever it is released, that is to say to take up a different compass direction depending on where it is in relation to home. Pigeons are able to do this over long distances

Terminator Anticodons in 18S rRNA

IN *Nature New Biology* next Wednesday (October 31) Dalgarno and Shine report that they have sequenced the eight nucleotides at the 3′ end of 18S RNA from yeast and *Drosophila* by stepwise degradation, followed by condensation with labelled isonicotinic acid hydrazide, and compared them with the same sequence in rabbit reticulocyte 18S RNA. The sequence, $GAUCAUUA_{OH}$, was the same for all three eukaryotes. Sequences at the 3′ end of RNA isolated from the large ribosomal subunits show no similar homology.

Dalgarno and Shine suggest that conservation of this fragment in such distantly related species implies a particular role in some cellular processes, and advise inspection of the antiparallel RNA complement of the sequence for an indication as to what this role might be. The complement (UAAUGAUC) contains two sequences, UAA and UGA, which are terminator codons in messenger RNA and one other, UAG, if "wobble" occurs. Since it is known that transfer RNA is not involved in recognising terminator codons, it seems likely that the octanucleotide sequence at the 3′ end of 18S DNA molecules has this function.

The authors tentatively propose that the conserved sequence "scans" the mRNA during translation until the 3′ oligonucleotide forms base pairs with the terminator codons in the mRNA, at which a factor is activated, so that the ribosome can be released.