Crenidens crenidens.

easily on account of this relative poverty of the native fauna, there being more unfilled ecological niches than there would be in the western basin. Their spread within the present century has, however, been rapid and at least sixteen species must now be regarded as common, some even as far afield as the coasts of Cyprus and Anatolia.

Very little seems to be known about the effects of this influx of Red Sea forms on the native fish fauna. As Ben-Tuvia observes, these fish, and especially the common ones, must be important in food chains and the general biological balance in the area. It may be significant that better than average catches of the immigrant lizard-fish, *Saurida undosquamis*, coincide with years when the native Atlanto-Mediterranean hake, *Merluccius merluccius*, is scarcer than usual. The connexion may not be direct, for *Saurida* and the Red Sea red mullet, *Upeneus moluccensis*, are noticeably more abundant in years of above average temperatures than in cool years in Israeli waters.

It is clear, however, that although this form of biological pollution of the eastern Mediterranean has reached considerable proportions, it is still continuing. With the drastic control exerted by the Aswan dam on the freshwater inflow of the Nile to the Mediterranean further changes in the marine fauna of this area could well take place.

TOXINS

The Perfect Poison

from our Molecular Biology Correspondent

VENOMS, it seems, are frequently more effective than their separated toxins. The ingenious rattlesnake for example, as Hendon and Fraenkel-Conrat (*Proc. US Nat. Acad. Sci.*, **68**, 1560; 1971) now show, secretes a pair of proteins, which act concertedly, one evidently softening up the victim for the other. Crotoxin, as isolated, behaves as a single component in the usual fractionation systems. When, however, amino-groups are chemically modified, an insoluble fraction appears, which is a basic protein, separated from its acidic partner. In ion-exchange chromatography crotoxin separates into two peaks, which, however, seem functionally identical. A tryptic digest of the material from these peaks shows only small differences, sug-

gesting that at least one of the two proteins is heterogeneous, but the acidic and basic components have not separated. In 6 M urea, however, the results are very different, two protein peaks appear of very different amino-acid compositions—one acidic and one basic—eluting at widely different positions. The molecular weights, by detergent gel electrophoresis, are about 8,400 and 13,000.

The acidic protein is not neurotoxic, and does not cause haemolysis, though it is able to cleave lecithin. The basic protein, on the other hand, carries all the haemolytic activity of the venom. Between them the two proteins manifest ferocious neurotoxicity. As Hendon and Fraenkel-Conrat note, enzyme systems that function only when two components are both present are by no means unknown, one subunit species in an oligomer directing the specificity of the other. Alternatively it might be conjectured that lysis of a membrane is necessary before the neurotoxin can go to work.

A rather similar situation has been uncovered by Lowy, Sarmiento and Mitchell (*Arch. Biochem.*, **145**, 338; 1971) in a study of bee venom. This

contains a variety of proteinaceous materials, including a hyaluronidase, a phospholipase, and several physiologically active peptides. This package turns out to be lethal to larvae. Lowy *et al.* have purified two peptides—melittin, which is well characterized and has been sequenced, and is the principal component of the venom and one other—and have examined their effects on *Drosophila* larvae. The new peptide is called minimine, for its physiological effect is nothing less than to minimize the insect. Its molecular weight is some 6,000 and it contains cysteine, or cystine. In appropriate doses it does not kill the larvae, but induces a condition of lethargy, in which the effort of feeding seems to be beyond the creature's will-power.

In a second article, Mitchell *et al.* (*ibid.*, 344) report the effects of melittin, which is an oligopeptide of twenty-six residues (molecular weight, 2,800). It is known to possess haemolytic activity, and it now seems that it is also a neurotoxin for the larvae. It is a non-competitive inhibitor of acetylcholinesterase, antagonized by cations—the first case, apparently, of such an effect by a polypeptide.

Cooperation Between Hapten and Carrier *in vitro*

IN recent months, cellular immunologists have been turning their attention to the hapten-carrier. Some of the questions being asked are do B (bone marrow derived) cells and T (thymus derived) cells respond to hapten and carrier respectively, are they specific in their responses, and what are the receptors on the responding cell populations?

An ingenious combination of techniques using *in vivo* and *in vitro* systems has been adopted by Christina Cheers and her colleagues to investigate these problems and they report their results in next Wednesday's *Nature New Biology*. 3,5-Dinitro, 4-hydroxyphenylacetic acid (NNP) was coupled to fowl gammaglobulins (or ovalbumin as a carrier specificity control), and the hapten protein conjugate thus formed was injected into mice, of which the spleens were later harvested. Primed spleen cells in culture in the presence of antigen were shown to be antibody producing by a plaque assay technique using sheep erythrocytes coupled to NNP as target cells for lytic antibody.

In the initial experiments the carrier used for priming *in vivo* and recall *in vitro* was varied, and it was shown that homologous carrier was required to obtain a satisfactory recall response. On the other hand, if cells primed to heterologous carrier were added to cultures in which recall was being attempted by the use of a heterologous

carrier-hapten antigen, significant enhancement of the anti-hapten antibody was observed. If either the carrier primed cells or the hapten primed cells were incubated with an anti-immunoglobulin serum there was a marked inhibition of the immune response. The inference here is that both the carrier and hapten primed cells have immunoglobulin-like receptors for the antigens to which they are primed. When combinations of parental and F_1 cells were used in conjunction with specific anti-allosera it was possible to show that the antibody was derived chiefly from the hapten primed cells.

In a further series of experiments Cheers *et al.* injected thymocytes and antigen into irradiated mice. The primed thymocytes were harvested from these animals and were shown effectively to substitute for carrier primed whole spleen cells in enhancing the anti-hapten response of cells primed to a heterologous NNP-protein conjugate.

This whole series of experiments tends to confirm and extend the results of, among others, Raff (*Nature* **226**, 1257; 1970) and his colleagues. There is little doubt that in the fullness of time studies *in vitro* of immune responses in association with the use of cell populations of defined anatomic origins will greatly assist understanding of the nature of immunological responsiveness.