clonal nature of these diseases. Dr Allison felt that understanding of internal regulatory mechanisms which are likely to affect the growth of some tumours in their early stages is inadequate, but suggested that the immune response is likely to be the most accessible to study.

REPRODUCTION

Monogamous Mosquito

from our Insect Physiology Correspondent

THE female of the yellow fever mosquito (*Aedes aegypti*) has often been described as mating repeatedly from very soon after emergence throughout a life which may last several months. Some forty matings before the first blood meal, fifty successful copulations with eleven different males during one hour, are typical records. But during the past few years a very different picture has emerged. In 1967, Craig (*Science*, **156**, 1499) found that a substance from the male accessory glands, received during mating, rendered the female permanently refractory to further insemination. This substance turned out to be a peptide to which the name "matrone" has been given. The effect can be produced in the absence of copulation by implanting the male glands into the abdomen of the female mosquito.

The nature of the refractory state has been studied in detail by Gwadz *et al.* (*Biol. Bull.*, **140**, 201; 1971, and *J. Insect Physiol.*, **18**, 152; 1972). It had been suggested that the female ejected the sperm received at all subsequent matings after the first; but it now seems that no sperm is received. The positioning of the vaginal orifice guarded by the cerci is such that the male cannot copulate successfully with the refractory female; the apparent repeated copulations of females are merely mechanical "couplings", of the same duration as copulation (about 12 seconds) but no sperm transfer takes place.

The female mosquito is indeed monogamous. On emergence from the pupa she is refractory to copulation; she becomes receptive within about 40 hours. This change results from the action of the juvenile hormone and can be speeded up to occur within 8 or 12 hours by treating the pupae or the freshly emerged adult females with a synthetic analogue of the juvenile hormone. Conversely, as was shown by Lea (*J. Insect Physiol.*, **14**, 305; 1968), the onset of receptivity can be prevented by removing the corpora allata from the newly emerged female and can be restored by re-implanting the glands. The peptide pheromone "matrone" from the male accessory glands exerts its action on the terminal

ganglion of the abdomen, which has long been known to control the mating behaviour of insects. It acts by the nervous route; and if the terminal ganglion is excised from a refractory female she will engage in repeated copulations so that the bursa copulatrix becomes distended with sperm received from several males. A similar cycle of controlled insemination was described in the housefly *Musca domestica* by Adams and Hintz (*J. Insect Physiol.*, **15**, 201; 1969).

It is remarkable that the refractory female continues to attract males which attempt copulation, whereas in other insects the refractory female is usually unattractive. Perhaps the reason is that in many insects mating is induced by male and female sexual scents, or pheromones, which are not secreted during the refractory state, whereas in mosquitoes the male is attracted by the flight tone of the female and this remains unchanged. It has long been known that male mosquitoes will endeavour to copulate with a tuning fork emitting the appropriate note.

ANIMAL LEARNING

Learning Laws Repealed

from our Experimental Psychology Correspondent

THE past two or three years have for many psychologists seen the abandon-

ment of some of the previous goals of learning theory. Partly, at least, animal learning had been studied in order to derive general laws of learning, applicable in all situations. Recent work by P. Rozin and J. Kalat of the University of Pennsylvania (*Psychol. Rev.*, **78**, 459; 1971), however, squarely rejects this approach. These authors point out that though sharing some common principles, learning mechanisms and their characteristics are for the most part various. Having been subject to selective pressures of widely different environments, these mechanisms, rather than exhibiting general laws of some slightly mysterious process called learning, represent specific adaptations of different animals to particular ecological problems.

Rozin and Kalat deal principally with how animals learn to avoid poisons and the related issue (and area of their experiments) of how they learn to select diets which relieve vitamin deficiencies. In this kind of learning some alimentary or other internal sensation such as a feeling of illness becomes associated with the taste or smell of a substance or substances most recently eaten. What is striking about the phenomenon is not just the efficiency with which it taxes the ingenuity of pest exterminators, but that the learning requires as little as one trial, spans delays of many hours between the occurrence of the taste and the onset of illness, and appropriately associates the internal sensation with

Putrescine, a Cell Growth Factor

MOST cells when placed in tissue culture require serum for their survival and proliferation and over the past several years numerous attempts, meeting with varied success, have been made to identify and to isolate those molecules or macromolecules which keep cells alive in culture and trigger cell division. Serum is, however, not only a complex but also a variable mixture of molecules and in order to identify cell growth factors cell biologists have turned their attention to so-called conditioned medium—medium which has been in contact with living cells. As Pohjanpelto and Raina, for example, describe in next Wednesday's *Nature New Biology* (February 23) medium conditioned by adult human skin fibroblasts contains a factor, presumably made and secreted by the cells, which stimulates the proliferation of embryonic human fibroblasts.

The maximal yield of this factor is apparently obtained when medium is conditioned for 5–7 days. The growth factor passes through dialysis tubing, and its behaviour on 'Sephadex G-15' columns confirms that it has a low

molecular weight. Furthermore, the factor is not particularly heat labile, neither is it soluble in ether or phenol but it can be extracted with alkaline butanol.

This last mentioned finding, together with the fact that polyamines have been shown to prolong the multiplication of Chinese hamster kidney cells in culture, led Pohjanpelto and Raina to think that the growth factor in their conditioned medium might be a polyamine. Pursuing this possibility they compared the effect of growth factor with the effect of various polyamines and found not only that putrescine partially mimics growth factor but also that the conditioned medium contains amounts of putrescine significantly in excess of the amount in unconditioned medium. They suggest, therefore, that the growth factor released from adult human skin fibroblasts is probably putrescine. They further suggest that it might be advantageous to add this polyamine as a supplement to culture media because its availability may determine the extent to which at least some sorts of cells can proliferate *in vitro*.