insect extracts are several times as large as that of the control. Parallel tests carried out with extracts of grasshoppers, ants, dragonflies and a number of other non-poisonous insects did not show any greater spread than that shown by saline alone.

The invasion of the tissues by these insect poisons can not, however, be compared with the extraordinarily powerful spreading power of snake venom. Fresh or desiccated venom from rattlesnakes in high concentration gives areas of spread as much as 20 times the area of the control. Dilutions as high as 1/100,000 still give areas of spread larger than that from saline solution. Cobra venom has similar properties. As a control to these tests extracts from the supralabial glands of such harmless species as chicken snake and pine snake proved to be devoid of any diffusing factor. This spreading action of the poison is shared if at all only to a limited extent by the extracts of several organs studied, including testicle, both from poisonous and non-poisonous snakes.

Naturally, the striking invasive power of the snake venom, as shown by the intensity of the local and general effects following snake bite, has always been known. It has even been pointed out that some fraction in the toxic complex must favor the rapid passage of the active components into the tissues and the blood. It is obvious that such a tremendous local diffusion of the snake secretion is not indispensable for the toxin to exert its action on the nervous centers. For instance, we have studied the poison from six different species of toads and, despite the fact that some of them killed the rabbit after a few hours, the local symptoms were either negligible or simply non-existent.

The progress of the venom through the inoculated animal could perhaps be interpreted not as due to a selective permeation by a specific factor but to a sort of passive "flooding" of the highly damaged tissue by the venom components. In order to test this objection the rattlesnake venom has been treated by heat and hydrochloric acid, both of which treatments practically suppressed the local toxic power. Such detoxification left the spreading factor in the venom little impaired in activity. Moreover, the intradermal injection of unmodified venom into the dead rabbit or into the skin which has been nailed down on a board produces spreads which in their initial phases are identical with those taking place in the living animal. Of course, there is neither hemorrhage nor edema in the former case and a slight superficial necrosis around the needle puncture is noticed only with the venom at high concentration.

The simultaneous injection of venom together with vaccine virus or *Staphylococcus aureus* brings about a marked enhancement of the resultant lesions. The venom in these tests was used either heated and at high concentration or unheated and at high dilution. The heated venom also sharply and rapidly localizes the dyes injected into the blood stream, a phenomenon which has been noted with other materials having the spreading property.

From the experiments so far reported it would seem that the mechanism of invasion of the tissue by the venom of insects and *Ophidia* is essentially the same as the one already described by us for invasive bacteria.[1] In the case of staphylococcus a split of the necrotizing toxin from the spreading factor has been recently achieved in our laboratory. At present an attempt is being made to dissociate the spreading and toxic factors in snake venom.

Thus, a factor or a group of factors, the essential physiological property of which is to increase to a marked degree the permeability of mesodermic structures,[2] is found in such widely separated forms as poisonous insects, poisonous *Ophidia,* malignant mammalian tissues[3] and normal mammalian tissues, especially testicle.[4] It was the last-mentioned organ that was first found to possess a powerful enhancing action for infections.[5]

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SEXUAL PHASES IN THE QUOHOG*

THE question of change of sex in Pelecypod mollusks has received much attention during the past decade. Orton[1] has described the alternation of male and female phases in the European oyster (*Ostrea edulis*); Roughley[2] found that *O. cucullata* was likewise protandric and Amemiya[3] in his experimental work on *O. gigas* concluded that the sex of each oyster is determined during the winter, and that the preceding sexual phase has no influence upon the following ones. Coe[4]

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1 J. H. Orton, *Jour. Mar. Biol. Assoc.*, 14: 967–1045, 1926–27.

2 T. C. Roughley, *Nature*, 124: 793, 1929.

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4 W. R. Coe, *Bull. Scripps Inst. Oceanog.*, Tech. Ser. 3: 119–144, 1932.

found an alternating sequence of male and female sexual phases in *O. lurida* and later[5] showed the protandric nature of the primary gonad of *O. virginica;* Burkenroad[6] and Needler[7] have also presented conclusive evidence of a change of sex in the latter species. Similar sexual phases have been found in the Pelecypod Teredo,[8] nearly all females passing through a preliminary functional male phase before reaching the definite phase of sexuality.

In an investigation of the life cycle of *Venus mercenaria* the writer has found similar evidence of protandry. Young clams, when only 0.6–0.7 cm long, collected on the clam beds of Long Island Sound, near Milford, Conn., in October, were found to possess distinctly bisexual gonads with very strong male predominance. In the majority of cases fully ripe spermatozoa occupied the central part of the lumen, while small ovocytes and indifferent gonia constitute the inner walls of the follicles. Rapid spermatogenesis thus gives the primary gonad the appearance of a spermary. Apparently functional spermatozoa are found in the follicles of many young clams of this minute size throughout the winter.

The following spring the follicles are gradually extended dorsally and posteriorly until they occupy the spaces around the stomach and between the digestive gland and the muscular body wall. The character of gonads remains essentially similar to that described above. Unless carefully examined, many of the animals of this stage may be taken for true males, but the presence of young ovocytes, showing distinct mitochondrial bodies and yolk nuclei, indicates the bisexual character of the gonads. It is interesting to note that although in all cases the gonads exhibit a predominantly male appearance, many degrees of intersexuality may be recognized. Some of the follicles may possess only a few small ovocytes, while in other follicles they are larger and much more numerous. Quite often such differences are observed in the follicles of the same individual as Coe[5] has reported for the oyster.

In the middle of the summer, when the water temperature reaches the critical point, the ripe spermatozoa are discharged. Soon afterwards two distinct types of individuals become distinguishable, as definitive males and females. In the males a second period of spermatogenesis begins in the autumn and continues at a reduced rate throughout the winter. In the spring, with the increase of water temperature, rapid branching of gonad follicles takes place simultaneously with increased rate of spermatogenesis. The gonads then have the typical male character of the adult. The sperm are discharged later in the summer, when the size of the shell has reached a length of 3 cm or more.

In those young individuals destined to become females the lumen of the follicles remain empty after the spermatozoa are discharged. At the end of the initial male phase the gonad follicles remain distended with only a thin layer of undifferentiated cells and small ovocytes along the inner walls. In many cases numerous phagocytes invade the follicles and devour the pycnotic and degenerated male cells. Ovogenesis begins in early spring. In June and July the follicles contain mature ova. The animals, formerly functioning as males, have now reached the stage of functional females.

The adults are, with few exceptions, of separate sexes. Among several hundred mature clams studied by means of serial sections only two cases of functional hermaphroditism have been observed. Nevertheless, examination of gonads of adult males reveals in almost every instance the presence of small ovocytes somewhere along the walls of the follicles. This may indicate the potentiality of changing the sex even in the adult condition. So far there has been no evidence obtained to warrant such a conclusion. Spermaries of adult males contain mature spermatozoa at all seasons of the year with exception of a short post spawning period. When placed in the sea water, spermatozoa, after 2 to 3 minutes of quiescence, begin to swim actively in their typical spiral way. This simple experiment was tried at bi-weekly intervals throughout the year and always with positive results. The ovaries of adult females also contain large ova at all seasons of the year. In fact, little difference will be noted on superficial examination of samples collected in December and in June. In both cases the follicles are large, distended and filled with large ovocytes. In this respect the quohog differs remarkably from the American oyster, in which only shrunken follicles are found during the autumn and winter.

Thus, in *Venus mercenaria,* as in the other pelecypod mollusks to which reference has been made, the protandric nature of primary gonads has been established. However, the quohog is not exclusively protandric, because a few individuals develop into females without passing through a functional male phase. In this respect there is again a similarity between the quohog and the various species of oysters in which likewise the primary male phase may be omitted or aborted.

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