REACTIONS PRODUCED BY ARTHROPODS DIRECTLY INJURIOUS TO THE SKIN OF MAN*

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During the past few years my colleagues and I have been investigating the reactions shown by the mammalian host to the bites and stings of certain tropical and non-tropical arthropods (Gordon and Crewe, 1948 ; Crewe and Gordon, 1949), and since these reactions are often, although by no means always, confined to the skin we thought it might be of interest to present some of our findings. Before doing so, however, it is necessary to emphasize the fact that we have studied only a few representative species of medically harmful arthropods, and it would therefore be unwise to draw any far-reaching conclusions from such limited data.

Our observations suggest that the pathogenic effects produced by arthropods directly injurious to man fall into certain well-defined groups and can usually be classified in one of four categories: (1) lesions due to mechanical trauma ; (2) lesions due to secondary infections ; (3) lesions due to the injection of substances which are normally harmless, but to which the host has become sensitized as a result of previous exposure ; and (4) lesions due to the injection of directly injurious substances. Although these pathogenic effects are considered separately, they may, and often do, occur in conjunction—a fact which is sometimes overlooked by the clinicians.

Lesions Due to Mechanical Trauma

In the case of the puncture or abrasion made by a blood-sucking arthropod, the extent of the lesion produced will depend on the size and nature of the insect's mouth-parts and the manner in which they are used. Some blood-sucking insects, such as the mosquito, with long and delicate mouth-parts, may feed with the proboscis in the lumen of a capillary ; whereas the proboscis of larger flies, such as the tsetse (*Glossina* sp.), are too bulky to enter the lumen and are used to suck up the blood which results from the repeated laceration of small subcutaneous vessels. It is, of course, obvious that the large and relatively clumsy skin-piercing organs of some of the "horse-flies" or "clegs" (*Tabanidae*) will produce a more extensive wound than will the small and delicate mouth-parts of the midges (*Culicoides*) ; but the difference in the final result is not so great as might be expected, since both insects tend to probe the tissues until a pool of blood, more than sufficient for their purpose, has been produced. From the clinician's point of view, however, it would seem that the uncomplicated trauma produced by any type of blood-sucking arthropod is seldom severe enough to cause any serious disturbance in the host.

When, however, the parasitic arthropod extends its activities from blood-sucking to tissue invasion the resultant trauma may be more extensive. Thus, in the Tropics, myiasis caused by the larvae of certain flies, such as the "Berne fly" (*Dermatobia hominis*), may result in the deep invasion of the subcutaneous tissue by a number of larvae, each of which is more than 1 in. (2.5 cm.) in length, while the invasion of the turbinal mucous membrane, or even of the frontal sinuses, by the so-called "screw-worm" larvae of other flies, such as *Cochliomyia* sp. or *Chrysomyia* sp., may produce even more serious injury: extensive invasions by such large arthropods are obviously not only painful but are bound to interfere seriously with health.

On the other hand, the invasion of the host's tissues by a parasite so minute as *Sarcoptes scabiei*, and one which never penetrates below the stratum corneum, cannot be regarded as causing any serious mechanical trauma, and the extensive lesions sometimes associated with its presence must be ascribed to some other cause. Between these extremes there are a host of tissue-invading parasites, mostly larvae of two-winged flies which in the Tropics and, more rarely, in this country cause varying degrees of mechanical trauma in the tissues of their host.

As already mentioned, a few species of myiasis-causing larvae may produce serious lesions, but with these exceptions, and in the absence of complications, most of the tissue-invading arthropods, so long as they confine themselves to the tissues of their normal host, seldom produce a degree of trauma sufficient to interfere with general health. Occasionally, of course, an invading parasite finds itself in the tissues of the wrong host, as happens in the case of the so-called "larva migrans," and in such instances both parasite and host may behave abnormally. In this case the lesion was probably caused by the larva of an ankylostome normally parasitic in dogs in the Tropics ; but almost precisely similar lesions occur in this country after the penetration of the human skin by the larva of the warble fly (*Hypoderma* sp.), the usual host of which is cattle, or by the larva of the bot-fly (*Gasterophilus* sp.), which is normally parasitic in equines.

Lesions Due to Secondary Infections

It has been shown that the larvae of a few, mainly tropical, species of two-winged flies (Diptera) may produce considerable mechanical trauma. Usually, however, the most serious results of myiasis are those which follow the subsequent invasion by bacteria of the wound previously made by the parasite, and the term "myiasis" generally conjures up a picture of a septic lesion for the cause of which bacteria are more responsible than Diptera.

It sometimes happens that such organisms are introduced by the parasite when piercing the skin, but it seems to be more usual for them to gain access after the abrasion has been made, and such abrasions do not appear to be any more prone to infection than similar lesions caused by other means. In any case, lesions due to secondary infections can scarcely be regarded as being the responsibility of "arthropods directly injurious to the skin of man," and I therefore propose to pass on to my next category.

Lesions Due to Injection of Normally Harmless Substances into a Previously Sensitized Host

The picture which we have just presented of a more or less trivial traumatic injury which may or may not be followed by a more serious bacterial infection is often thought to be further complicated by the injection by the parasite of a substance inimical to the host, the responsible substance usually being thought to be derived from the salivary glands of the parasite, although some workers believe that it originates from some other part of the insect's digestive tract.

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Our own observations do not support this view; they suggest, rather, that only a very limited number of parasitic arthropods secrete a substance of a toxic nature, and when this does occur, as sometimes happens in the case of mosquito bites, the reaction produced is delayed and trivial and never results in the immediate well-marked weal so often associated with the bites of parasitic arthropods.

My colleagues and I have fed a varied assortment of blood-sucking creatures on human volunteers, and, so long as these volunteers have never previously been exposed to the bites of the particular kind of arthropod under investigation, either no reaction has occurred or it has been so slight as to be negligible so far as the clinician is concerned. Of course, it is difficult to ensure that the individual has never previously been exposed to any particular parasite; but this difficulty can be overcome by importing tropical insects, such as the tsetse-fly, and by feeding them on persons who have never visited the Tropics.

As regards the source of the irritating substance, we have been able to show that, in the case of the tsetse-fly at any rate, it must be derived from the salivary glands. This fact has been demonstrated by removing the salivary glands from the living insect and then feeding it on a person who is known to react violently to the bite of the normal insect. In these circumstances the fly feeds to repletion but the host shows no subsequent reaction.

I have just mentioned that persons living in this country and not previously exposed to the bites of the tsetse show no reaction when these insects are fed on them for the first time; the question now arises of what happens if you continue to feed tsetse-flies on such persons. We can answer that question, so far as our observations have gone, by saying that if the flies continue to be fed on such an individual at regular intervals he will remain free from any reaction, but that if the flies are fed at irregular intervals the majority of individuals on whom the flies are fed develop a reaction which may or may not be severe in character.

So far my remarks have been concerned mainly with the tsetse-fly, but we have repeated some of these observations on persons exposed to the bites of mosquitoes, sand-flies (*Phlebotomus* sp.), midges (*Culicoides* sp.), and bed-bugs, and the results obtained have been similar to those following tsetse-fly bites. In addition, we have been able to confirm that these reactions are often highly specific, and that persons who react to one species of insect do not necessarily react in a similar manner when bitten by a different species, although both may be so closely related as to belong to the same genus. These findings may explain why it is not unusual to encounter persons who state that, although they sometimes react violently to flea-bites, at other times they remain unaffected, or that they react to the bites of mosquitoes in one part of the country but not in another.

As regards desensitization, we have not carried out any experiments on the value of antigens prepared from the insects responsible for the reaction, but we have been able to show that, in persons who have become sensitized to the bites of mosquitoes, the reaction diminishes after continued regular exposure, and that this desensitization is usually specific, so that the person who has been desensitized to the bites of one group of mosquitoes, such as the culicines, may still be sensitive to the bites of another group, such as the anophelines.

Perhaps I might summarize the conclusions arrived at by my colleagues and myself concerning parasitic arthropods by saying that, like poor relations, they try to get as much food and shelter as they can from their host, but are scrupulously careful to avoid causing him any unnecessary pain or inconvenience, since the results of such actions are usually detrimental not only to the host but also to the parasite.

It is true that the observations which I have described refer only to a limited number of common parasites; but, so far as those are concerned, it seems reasonable to consider that any immediate and severe reaction associated with their bite or with their invasion of the tissues is due to previous sensitization on the part of the host and not to the injection of any poisonous or toxic substance by the parasite.

Lesions Due to Injection of Directly Injurious Substances

The association between man and arthropod so far considered has been that of host and parasite, and we have shown that, since it is always to the disadvantage of the parasite to cause any serious injury to its host, most of the injuries resulting from this association have been in the nature of accidents caused by secondary infections or following the injection by the parasite of a normally harmless substance into a previously sensitized host. On the other hand, certain arthropods which are non-parasitic and in no way dependent on man for their existence have developed weapons of offence, in the form of secretions which they use to kill or paralyse their prey, while others have developed defensive secretions which they use to protect themselves from interference. These offensive and defensive secretions resemble each other in many respects, and in some instances are used for dual purposes; but generally they differ in their virulence.

In the case of arthropods, such as scorpions and spiders, which have developed predatory habits and which secrete poison that is to be used to kill or paralyse their normal prey, the venom secreted is usually of a high virulence and when injected into man may produce serious general as well as local effects. In the case of other venomous arthropods, such as bees, which have not developed predatory habits, the venom secreted is not intended to kill but merely to produce a sufficiently quick and painful reaction to deter the intruder from any further interference; and in such instances the poison, although quick-acting, is usually of a milder character, the reaction produced tending to remain localized. It must not be forgotten, however, that the stings or bites of usually only moderately poisonous arthropods may take on a serious aspect if inflicted on a previously sensitized person, in whom the result of even a single sting may be followed by severe and sometimes fatal consequences.

The literature concerning the venom of scorpions and bees contains a great number—in the case of bee-venom one might term it a vast number—of papers dealing with the chemical structure and physiological effect of these poisons, together with an almost equally large literature describing the clinical manifestations which have been observed to follow the stings of these creatures; but there seems to be no account of the histological lesions produced. As my colleagues and I wished to compare these lesions with those produced by blood-sucking insects, we undertook a limited number of experiments in which a scorpion or bee was allowed to sting a guinea-pig, the tissues being removed from different animals at various times after the infliction of the sting and then sectioned and examined.

The results of this investigation showed, as might be expected, that, whereas the uncomplicated bites of blood-sucking insects never cause any inflammation and are comparable to the injury which might result from the probing of a surgical needle beneath the skin, the stings of scorpions and of bees result in a very marked inflammation. In the case of the bee, the sections showed oedema, marked cellular infiltration, and some necrosis of the underlying muscle layer, which was followed within 24 hours by a walling-off of the damaged tissue by a palisade of inflammatory cells. In the case of the scorpion sting, the reaction was somewhat similar, though more severe, and was associated with an extensive coagulative necrosis of the underlying muscle.

"Immunity"

There remains one aspect of the association between the skin-piercing arthropod and its host to which, so far, no reference has been made. It is not unusual to encounter individuals who declare that a particular venomous arthropod, such as a bee, will not sting them, or that certain blood-sucking fleas or flies do not bite them. The first group of persons seem to depend for their immunity on their power to handle particular arthropods—in this case bees—without alarming them. The second group is more difficult to explain; unquestionably there are persons who are not so attractive to lice or mosquitoes as their less fortunate fellows, but in our experience such cases are rare, and we have not yet encountered a case of complete immunity.

Pepys—you may remember—declared that while at Portsmouth he shared a bed with a certain Dr. Clarke, and that the fleas bit the doctor but not the diarist, a happening which seems to have pleased the latter "mightily." Pepys's statement can never now be substantiated, but we have carried out a number of experiments in which persons who stated that they were seldom bitten by mosquitoes, together with controls claiming no such privilege, introduced their hands and forearms into a large cage containing many hungry mosquitoes. The cage was arranged in such a way that, though the observer could see what was going on inside, the persons volunteering for the experiment could not. Under these conditions the results of individual experiments were always similar; the persons claiming immunity continued to maintain that they were not being bitten, but the impartial observer recorded in his notebook that the mosquitoes were unimpressed by such an assertion and were biting the "immunes" as readily as the "non-immunes."

It would seem, therefore, that the majority of individuals who believe that they are relatively immune from the bites of a particular species of insect are mistaken, and that their apparent immunity is the result of their failure to notice the insect during the time that it is biting. This failure is due either to the individual's not having become sensitized to the species in question, or because, although previously sensitized, he has become desensitized as a result of regular and prolonged exposure.

Summary

The pathological effects produced by arthropods directly injurious to man—as distinct from those which as transmitters of diseases are regarded as indirectly injurious—can usually be classified in one of four categories.

1. Lesions due to mechanical trauma, in which the damage done is usually severe only when it is caused by certain of the larger species of myiasis-producing larvae or when an abnormal host is attacked.

2. Lesions due to secondary infections—these include the more serious effects of myiasis which follow the infection by bacteria of wounds previously made by invading arthropods.

3. Lesions due to the injection of substances which are normally harmless but to which the host has become sensitized as a result of previous exposure. Recent research suggests that any immediate and severe reaction associated with the bite of parasitic arthropods or with their invasion of the tissues is due to previous sensitization of the host. Such reactions are usually highly specific.

4. Lesions due to injection of directly injurious substances. Certain predatory arthropods, such as scorpions and spiders, secrete venom usually of high virulence which, when injected into mammals, causes both generalized symptoms and an extensive coagulative necrosis of the underlying muscle. In the case of non-predatory insects, such as bees, the reaction tends to be mild and to remain localized.

REFERENCES

Crewe, W., and Gordon, R. M. (1949). *Ann. trop. med. Parasit.*, **43**, 341.

Gordon, R. M., and Crewe, W. (1948). Ibid., **42**, 334.

DIVISION OF POPLITEAL VEIN IN THE TREATMENT OF SO-CALLED VARICOSE ULCERATION*

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Non-specific ulcers of the lower leg have for a long time been termed varicose ulcers, evidently because varices of the subcutaneous veins were thought to be the cause of the ulcer formation. To-day, however, we know that this is only part of the truth and that the root of this evil goes much deeper. Knowledge of the normal and pathological physiology of the veins of the lower extremity has made very considerable progress during the past decade. Modern investigation tends to regard the entire vascular system of the leg as one system, similar to a U-shaped communicating glass vessel. The aorta and the large arteries form one branch of the vessel, the capillaries the bottom, and the large vein trunks and the vena cava the other branch. Being completely filled with fluid, this system is in perfect hydrostatic equilibrium. If a quantity of blood is introduced into one side of the system, as is the case each time the heart stroke pours blood into the aorta, an equal amount of blood flows out of the other end of the system, from the vena cava into the right side of the heart. This explains how the venous blood is made to return from the lower extremity irrespective of the body's position.

However, when the body is brought into the vertical position another factor is added. It is a well-known fact that in this position, because of the action of gravity, a large quantity of blood assembles in the lower parts of the leg. To explain this it is necessary to remember that the human U-shapel vessel, unlike those made of glass, does not have rigid and impermeable walls. Instead, the blood vessels, especially the veins, have elastic coats which are apt to give way under high pressure. The lumen widens and an ever-increasing amount of blood can accumulate. After some time a condition of pronounced venous stasis is created.

To get rid of this surplus of blood the healthy human being is in possession of a highly efficient auxiliary

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