PARARAMA, A DISEASE CAUSED BY MOTH LARVAE: EXPERIMENTAL FINDINGS[1]

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Contact with hairs (setae) from larvae of the moth Premolis semirufa *is known to have painful or crippling effects on the fingers of Brazilian rubber workers. Research on mice exposed to these setae, reported here, provides new information about how this occurs.*

A caterpiller called "pararama," larva of the moth *Premolis semirufa*, has previously been reported by Vianna and Azevedo (*1*) to have affected at least 24 rubber workers at a plantation named *Granja Marathon* (Marathon Farm) in the municipality of São Francisco, which is located in Brazil's north-central state of Pará. These authors have termed the delayed clinical manifestations of the condition "pararama," using the caterpiller's local name. (The larvae are also frequently referred to simply as *lagartas*–caterpillers.)

The presence of these larvae has been noted for many years at another location as well, the rubber plantations of Belterra in the Pará municipality of Santarém.

The lesions frequently observed after accidental contact with the larvae of certain lepidoptera, their cocoons, or their adult forms are itching, blistered, pruriginous processes involving allergic and toxic manifestations. Both isolated cases and epidemics have been reported (Gusmão, *et al.*,–*2*); more recently, such lesions have also been considered an occupational disease (Katzenellenbogen–*3*).

Contact with a pararama causes immediate intense itching (pruritus), hyperemia, and local edema. It also gives rise to chronic manifestations later on, and these sometimes deprive the patient of the use of one or more fingers, presenting a clinical picture corresponding to ankylosis.

Martins (*4*) and Dias (*5*) have confirmed observations in Belterra, where Machado (*6*) says that the proportion of rubber plantation workers affected by this disease has been as high as 40 per cent. Macêdo (*7*), in a radiological study, found no alterations on the surface of finger joints, but noted periarticular, edematous and fibrous alterations of underlying tissues.

Lacking further data of this type, we undertook experimental research on mice, using the larvae indicated by rubber workers as the cause of their lesions, to investigate development of the articular injuries cited in these clinical and radiological reports.

Materials and Methods

Well-developed larvae (Picture 2) collected from the trunks of rubber trees (*Hevea brasiliensis*) on Granja Marathon were brought to the laboratory in screened boxes, where they were kept, and were fed with leaves from the same trees. Several of them formed cocoons during the first 24 to 48 hours and molted a few days later.

Some adult forms were mounted and sent to Professor Lauro Travassos Filho at the São Paulo State Agriculture Ministry's Zoology Department; there the species was identified as *Premolis semirufa* (Walker, 1856; Hampson, 1901) a moth of the superfamily *Noctuoidea*, Family *Arctiidae* (see photograph). In addition,

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some mature larvae were subjected to macroscopic and histologic examination. Three types of surface hairs (setae) were macroscopically isolated; these have been classified as large, medium, and small (Picture 2). The large ones, measuring up to 3 cm in length, are located chiefly on the lateral surfaces of the thoracic and abdominal segments, emerging from small protuberances. The medium-length ones are about 1 cm long and are located on the dorsal surfaces of the first and seventh abdominal segments, there being two tufts of setae on each segment. The small ones, measuring 1.5 to 2 mm in length, are also dorsally situated, and are found on abdominal segments two through eight; they occur in two pairs of tufts on each segment.

The various types of setae are also woven into the pararama's dun-colored cocoon, which is shaped like a spindle (except that one of the sides is flattened where the cocoon is attached to a surface). The small setae are erect and disposed perpendicularly about the outer surface, giving the cocoon a velvety appearance (Picture 3).

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To prepare slides for histologic examination (Pictures 4 and 5) larval segments were sliced transversely, fixed in formaldehyde, and treated with paraffin.

Dead larvae were dried in an oven at 37°C and were stored for later use in the experiments reported here.

Experiments

Preliminary Test

Setae from living larvae, dead and dried larvae, and cocoons were placed on the shaved abdomens of adult mice and affixed with adhesive tape. Each kind of seta from each type of source was tested on two animals, so that 18 mice were used in all.

When these mice were sacrificed 24 and 48 hours later, it was observed that only the small setae had inflicted injury, which occurred regardless of whether they came from living larvae, dead and dried larvae, or cocoons. Therefore, subsequent experiments used only dried larvae from which the large and medium setae had been removed.

Experiment A:

Five three-day-old mice were put in a glass container with some dried larvae and kept there for five minutes. The container was shaken four times, using circular and lateral movements to increase the animals' contact with the larvae. One mouse was sacrificed two hours later, two were sacrificed 24 hours after exposure, and the last two were sacrificed 48 hours after exposure.

Experiment B:

Eight seven-day-old mice were exposed to larvae as in Experiment A; in addition, before adding the mice the inside of the container was sprayed with small setae extracted from another larva. The animals were exposed for 10 minutes and the receptacle was shaken six times. Four animals were sacrificed 24 hours later and the others were sacrificed on the fourth day after exposure.

Experiment C:

Five full-grown mice were exposed as in Experiment B. Three were sacrificed after 24 hours and the other two on the fourth day after exposure.

Experiment D:

Four full-grown mice were exposed as in Experiment B on four separate occasions, at intervals of four days. They were then sacrificed 18, 25, 32, and 39 days after the last exposure.

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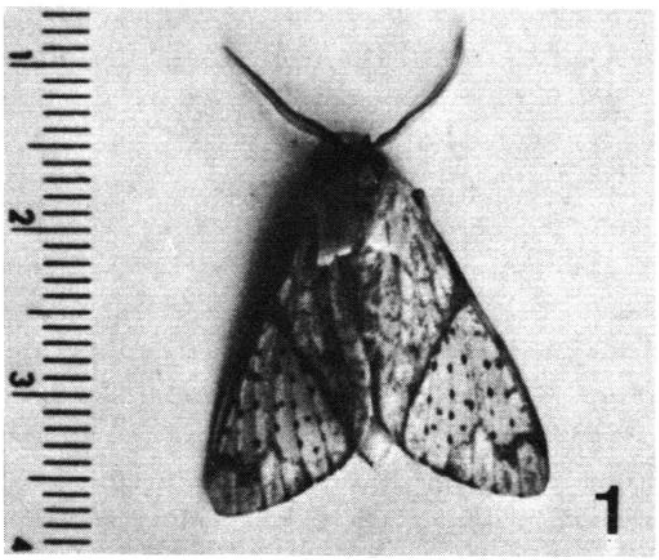

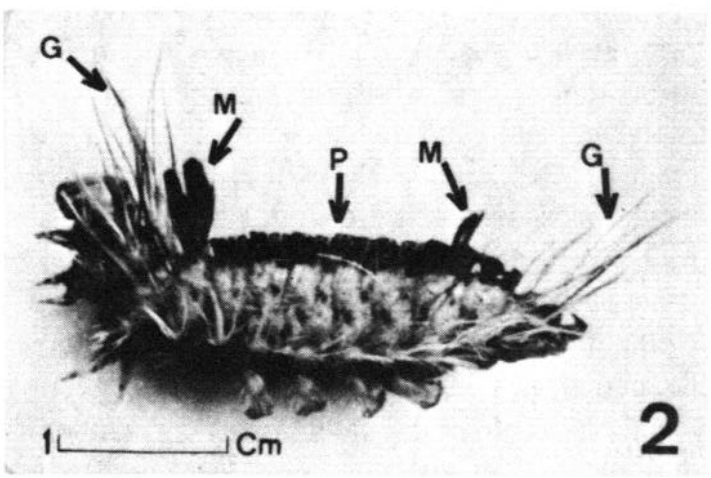

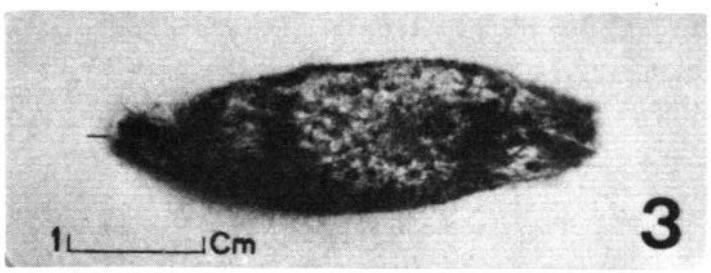

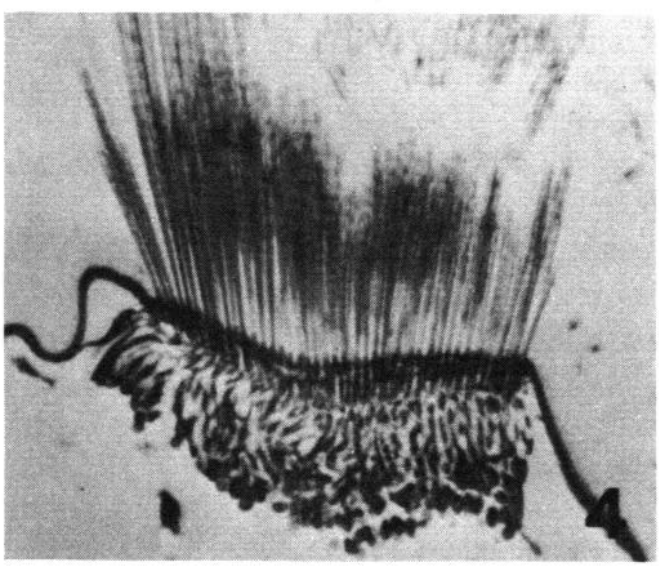

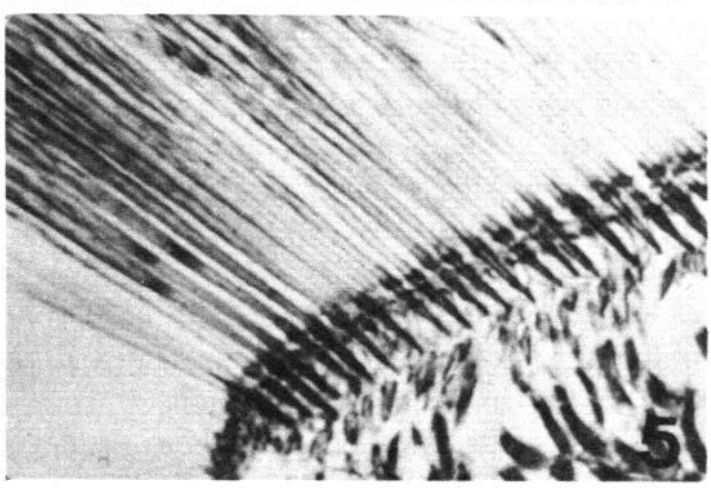

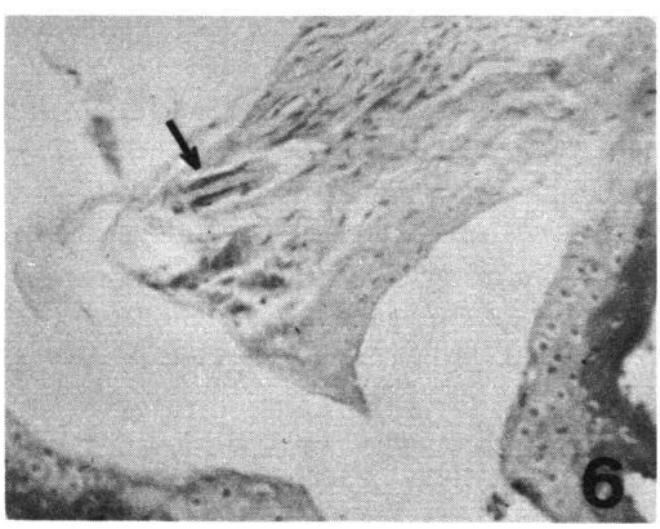

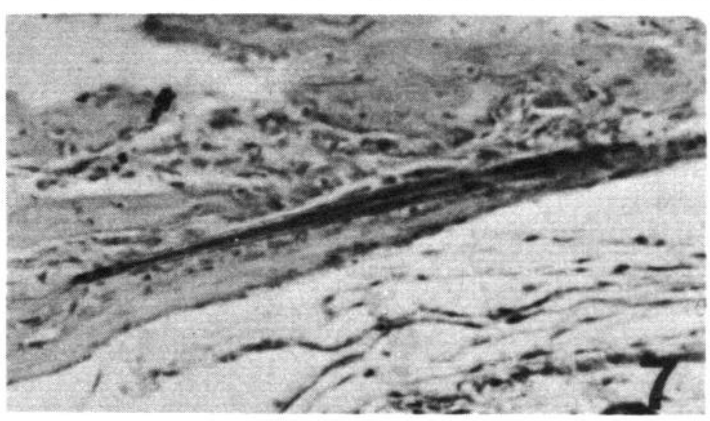

(1) Adult form of the moth *Premolis semirufa.*

(2) The larva *pararama,* after being fixed in formaldehyde. Arrows indicate the large (G), medium (M), and small (P) setae.

(3) Pararama's spindle-shaped cocoon. The surface is covered with small setae.

(4) Tissue slide made from a tuft of small setae; secretory cellular elements may be seen under the cuticle. (Carbol-fuchsin light green solution, approximately 50X.)

(5) Detail of a tuft, showing the tubular nature of the small setae and their sharp tips. (Carbol-fuchsin light green solution, approximately 120X.)

(6) Section of a mouse foot 18 days after exposure, showing part of a seta in a synovial bursa evidencing a fibrous and slightly granulomatous response. (Hematoxylin-eosin, approximately 250X.)

(7) Section of a mouse foot 25 days after exposure, showing a seta under the periosteum accompanied by a fibrous, histiocyte-producing reaction. (Carbol-fuchsin light green solution, approximately 250X.)

All the animals were anesthetized with ether prior to being sacrificed. The newborn animals were then fixed whole, after their cranial, thoracic, and abdominal cavities had been opened. To examine the adult animals, slides were made from portions of the abdominal wall, snout, perianal tissue, hind feet and lungs. A 10 per cent formaldehyde solution was used to fix the samples. After fixation, the feet were decalcified in an aqueous solution of 5 per cent formic acid. Standard techniques for embedding in paraffin and sectioning were used; the resulting 6-micron sections were stained with hematoxylin-eosin and carbol-fuchsin light green solution.

Results

There was virtually no evidence of large or medium setae in the tissues of mice exposed to these types in the preliminary tests. There was just one case—that of a mouse that had been sacrificed 24 hours after exposure to medium setae—in which we found two reactive dermal-epidermal foci with very superficial leukocytic infiltration. However, the small setae did penetrate the tissues of the exposed animals, being found later at the opening of sebaceous glands, throughout the epidermis, at various levels of the dermis, sometimes in the abdominal muscles, and less frequently in the subperitoneal tissue. The presence of setae in the connective tissue was accompanied by neutrophilic leukocyte inflitrations and by edema, the latter being less intense in the animals sacrificed after 48 hours.

In Experiment A, the animal sacrificed two hours after exposure had small setae at various levels of its epidermis and dermis, and occasionally in its cutaneous muscles; some edema was observed, but there was no evidence of leukocytic infiltration. In the animals killed after 24 and 48 hours, several setae were found in the dermis of various parts of the body—including the snout—and in the periostea of some ribs, the jaws, and other bones. The presence of these setae was marked by leukocytic infiltration and edema. Occasional hemorrhagic foci were also observed in the lungs, although no setae were observed in the lung tissue samples examined.

Similar results were observed in the Experiment B mice sacrificed 24 hours after exposure. In addition, setae were found in the deep tissues of the feet, in the corium of the mucosa of the mouth and tongue, and frequently in the corium of the snout. The mice sacrificed after four days also showed setae in these areas, there having meanwhile been changes in the local reaction, with partial replacement of neutrophilic elements by histiocytes, giving the appearance of a granulomatous reaction to foreign bodies.

Experiment C animals sacrificed 24 hours after exposure showed some setae within the abdominal wall, in the perianal tissue, in the dermis of the snout, and in the feet. The local changes previously mentioned (neutrophilic infiltration and edema) were observed. The two animals sacrificed after four days showed results similar to those obtained in the Experiment B mice sacrificed after four days. Setae were found in the same tissues, accompanied by a similar granulomatous response. In one animal a granuloma in the pulmonary parenchyma was found to have formed around a seta.

In Experiment D, only the hind feet of the animals were examined. Lesions were found in the dermis, tendon sheaths, periostea (Picture 7), bone marrow, and less frequently in synovial bursae (Picture 6); setae were found at the center of foreign body granulomas. Little variation in cellular composition or fibrous tendency of the lesions was observed in the Experiment D animals kept alive a relatively longer time.

Discussion

During the preliminary tests, as well as in the other experiments, exposure to small setae produced extreme restlessness in the exposed animals almost at once, indicating the setae in their tissues caused itching similar to that experienced by accidentally exposed humans.

In man, itching and edema are the initial acute manifestations normally encountered (along with hyperemia); these tend to disappear after a few hours, or after a week at the most. In some patients, however, the edema or swelling of the joints persists, along with immobility of the affected fingers, these symptoms characterizing chronic cases of pararama (*7*).

Histopathologic examination of mice sacrificed two hours after exposure to small setae showed only edema, but this was accompanied by neutrophilic infiltration in animals sacrificed after 24 and 48 hours. The mice sacrificed four or more days after exposure showed steady replacement of their acute reaction processes by a chronic granulomatous response to the presence of setae in the tissues. Thirty-nine days after exposure the setae still persisted in the tissues, and were accompanied by well-defined foreign body granulomas with fibrous proliferation of the peripheral connective tissue.

These results show that the small setae's marked penetration ability permitted them to reach the tendon sheaths, periostea, and synovial bursae of the exposed mice. This in turn leads to the supposition that the setae can reach the same sites in the hands of exposed rubber workers, though up to now there has been no direct proof of such natural pathologic behavior. At the same time, the ability of setae to persist in tissues for over 30 days without showing any signs of absorption supports the theory of chronic pararama evolution in man.

The clinical progress of affected patients and the histopathologic changes observed experimentally lead us to suppose that more than one factor is responsible for the lesions. As is true of other lepidoptera setae, the pararama's hollow setae intimately linked to glandular elements presumably carry chemical substances—which in this case are assumed to cause the immediate itching, edematous reaction, and neutrophilic infiltration that occur in the first phase of the disease. The physical persistence of these setae—in probable conjunction with their chemical make-up—provokes the chronic granulomatous and fibrous response. The number of setae involved and the particular circumstances prevailing in each case may be cited to explain why the chronic form of the condition has been experienced by only a small portion of the affected rubber workers.

There is little published literature on occupational hazards, such as those referred to here, involving lepidoptera larvae. Katzenellenbogen (*3*) refers to a dermatitis caused by caterpillers of *Thaumetopoea pinivora* (*wilkinsoni*), among forest workers in Jerusalem. The setae of dead larvae were shown by experiment to cause dermatitis, and histologic examination revealed acute inflammation; but setae from these larvae were not found to have penetrated tissue to which they were exposed.

In the last analysis, the presence of setae from *Premolis semirufa* larvae in the soft tissues of mouse paws, and in perichondria, periostea, tendon sheaths, and synovial bursae of the experimental animals—accompanied by formation of foreign body granulomas and a tendency toward fibrosis—provides a parallel to the clinical manifestations and radiological findings in chronic human cases of pararama.

SUMMARY

Pararama is an occupational disease of Brazilian rubber workers apparently caused by contact with caterpillers of the moth species *Premolis semirufa*. The chronic form of the condition involves long-term disability in the fingers of affected persons.

Until now, however, little was actually known about the disease process itself. The experimental research on mice, reported here, sheds new light on this matter.

On penetrating the skin of laboratory mice, the larva's small dorsal hairs (setae) almost

immediately cause acute edemous inflammation. Infiltration by neutrophilic leukocytes follows, and this stage in turn is superceded by fibrosis and formation of foreign body granulomas. Lesions caused by the setae have been found in the animals' skin, tendon sheaths, periostea, bone marrow, and other tissues.

The presence of lesions in the peripheral connective tissues of the joints parallels the clinical and radiological picture associated with pararama cases affecting the fingers of workers who tap latex from the rubber tree *Hevea brasiliensis.*

REFERENCES

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WORLD SMALLPOX SURVEILLANCE

A total of 96,951 smallpox cases had been reported to the World Health Organization by 19 September 1973, approximately twice the number reported by that date last year. The sharp increase was attributable to major smallpox epidemics in the three remaining endemic countries of Asia: Bangladesh, India, and Pakistan. This year all three countries will record their highest total number of cases since 1967, the first year of the global eradication program. While smallpox incidence did show its expected seasonal decline, the number of cases recorded during August in each of these countries remained well above the levels recorded in August 1971 and August 1972.

Ethiopia is still the only African country where smallpox is known to be endemic. Smallpox incidence in Ethiopia is now 73 per cent below what it was at this time last year and is continuing to decline; less than 100 cases per week were reported over the past 12 weeks. However, the eastern province of Harar was the source of two cases imported last July into the French Territory of the Afars and the Issas. [*Weekly Epidemiological Record* of the World Health Organization, Vol. 48, Nos. 32 and 38, pp. 316 and 370.]