

DERMATOZOONOSIS BY *CULICOIDES*' BITE
(DIPTERA, CERATOPOGONIDAE) IN SALVADOR,
STATE OF BAHIA, BRAZIL

IV — *A Clinical Study* *

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(With 8 text-figures)

The sensitivity of human tegument to insect bites and arachnid stings, as well as to the infestation of the skin by those arthropods, or worms, sometimes induces cutaneous reactions that are called Dermatozoonosis.

The pathogenic action is evidenced by either an early or delayed reaction or both, depending on the degree of the organism sensitivity, or the nature of injurious or both.

The dermatozoonosis by *Culicoides*' bite shows polymorphic cutaneous aspects. For this reason the etiologic diagnosis becomes, sometimes, difficult chiefly because the *Culicoides* are not always noticed during the bite, due to its small size. However, there seems to be no doubt that only those Dermatozoonosis cases caused by *Culicoides* bite are being studied here, as we have pointed out in a previous paper (9).

MATERIAL AND METHODS

From 1954 to 1961, 244 patients, with skin lesions due to *Culicoides*' bite, were seen in the Dermatological Clinic of the "Hospital das Clinicas da Universidade da Bahia". A review of their records and a personal observation of some of them provide the data that are now being presented. Skin biopsies were obtained from five cases on which we made the histopathologic study.

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RESULTS AND COMMENTS

Pathogenesis of the lesion

Each individual has different reactions to *Culicoides*' bites, ranging from an insensible to a highly sensitive one. Fortunately, among us the hypersensitive persons are the minority.

We could observe that, among persons equally exposed to *Culicoides*' bites, only some reacted to them, while others were totally unharmed. It is obvious that it is not the substance inoculated by the insect alone which provokes the dermic lesion. Two factors are needed: a) the allergenic substance inoculated by *Culicoides*; b) the individual's allergic response.

a) — *Substance inoculated by Culicoides' bite* — ROCKWELL (1952) injected into patients extracts from different parts of the bodies of mosquitoes, and the intensity of the reactions obtained was the same for all types of inoculum. He concluded that the allergen was all over the body of the mosquito.

The injection of the extract of our *Culicoides* species, into our Dermatozoonosis patients, caused cutaneous reactions of high intensity, similar to the ones caused by the diptera bite. However, no definite conclusions can be drawn, as we did not employ adequate techniques. However, there seems to be no doubt that the substances proceed from the salivary glands of the diptera.

According to WIGGLESWORTH (1959), in the salivary glands of some hematophagous diptera, it may be found free amino-acids and several enzymes, such as: proteinases, lipases, collagenases. HERMAN & SCHULTZ (1962) showed that blisters can be formed by enzymatic process of proteolytic, lipasic or glycolytic nature. Therefore, enzymes inoculated by *Culicoides*, through biting, could have the same effect.

On the other hand, GUIMARÃES & OLIVEIRA ROCHA (1959) try to explain how the lesion is formed, as follows. It is possible that the Histidin found in the hemolymph of several species of *Nematocera* and which becomes Histamin through decarboxilation may also exist in the *Culicoides* secretions. It seems that this second theory has a far greater possibility of being the true one.

b) — *The individual's allergic response* — The great majority of our patients showed propensity to other allergic diseases or had already suffered from some of them. As an illustration, we mention here the case of one of our patients who had allergic reaction to aspirin. what immediately provoked a facial edema. When she was bitten by *C. paraensis*, on the spot of the bite appeared a small erythematous papule, that soon developed into a vesicle.

According to GUIMARÃES & OLIVEIRA ROCHA (1959), helminthic infection seem to increase the organism sensitivity to several antigenic stimuli. Because it is so frequent among us, probably contributes to the exarcebation of the lesion. Stool examination for many patients showed, in almost of them, the presence of eggs of several helminthes,

or cysts of protozoa. We call the attention to this fact because one of the first measures taken in the treatment of Dermatozoonosis by *Culicoides*' bite at the Dermatological Clinic, consists in eliminating the intestinal worms of patients.

ROCKWELL (1952) remarked that rabbits previously bitten by *Aedes aegypti* (Lin) reacted fairly well to new mosquito bites. This is not the case with our patients. They always presented cutaneous reactions of similar intensity, on the different times they were bitten by *Culicoides*.

In addition to what has been discussed, we can say that the pathogenesis of the cutaneous lesion is not clear yet; more accurate studies are necessary. Perhaps when the mechanism of the reaction has been identified, it will be possible to treat Dermatozoonosis more efficiently.

Dermatological study of the lesion

The lesion acquires polymorphous cutaneous aspects and simulates the Prurigo, Scabies, Lichenoid lesions, or the Follicular Impetigo. It can also become a real Eczematization.

ROCKWELL (1952) observed in supersensitive persons three kinds of allergic reactions to mosquito bites: urticarian, tuberculinic and eczematous. These reactions are also seen on hypersensitive patients bitten by *Culicoides*. The lesions, depending on the stage of evolution or their intensity, can give the affected region the following cutaneous features: micropapular lesions (Fig. 1); vesicular lesions (Fig. 2); crust-ulcers (Fig. 3); desquamatory lesion (Fig. 1); exzematous lesions (Fig. 5); and hyperpigmented or hypopigmented scars (Fig. 6).

After the *Culicoides*' bite, there is an almost immediate formation of a small erythematous plaque which soon becomes papule. Within a certain period of time, which varies from second to hours, the papule develops into a vesicle. When the vesicle breaks open, it tears up the skin surface that later scales off. As a consequence, there may occur a secondary infection and the formation of pustules. When the reaction is more intense, the whole picture resemble an actual eczematization.

In some patients a small and transient erythematous spot can be seen. In others, the local erythema can develop into papule. Still in others, the lesion goes as far as eczematization. After the lesions are healed, they leave small scars generally hyperpigmented but sometimes hypopigmented, that can spot the whole area of the injured limb, depending on the number of bites.

From what has been said, we can deduce that the cutaneous condition is characterized by stages in the following order: erythematous plaques, papules, vesicle, pustules, eruptions, scales, crusts, and hyperpigmented scars. On certain areas, the polymorphic aspect can be easily noticed, due to new bites on places where lesions already existed.



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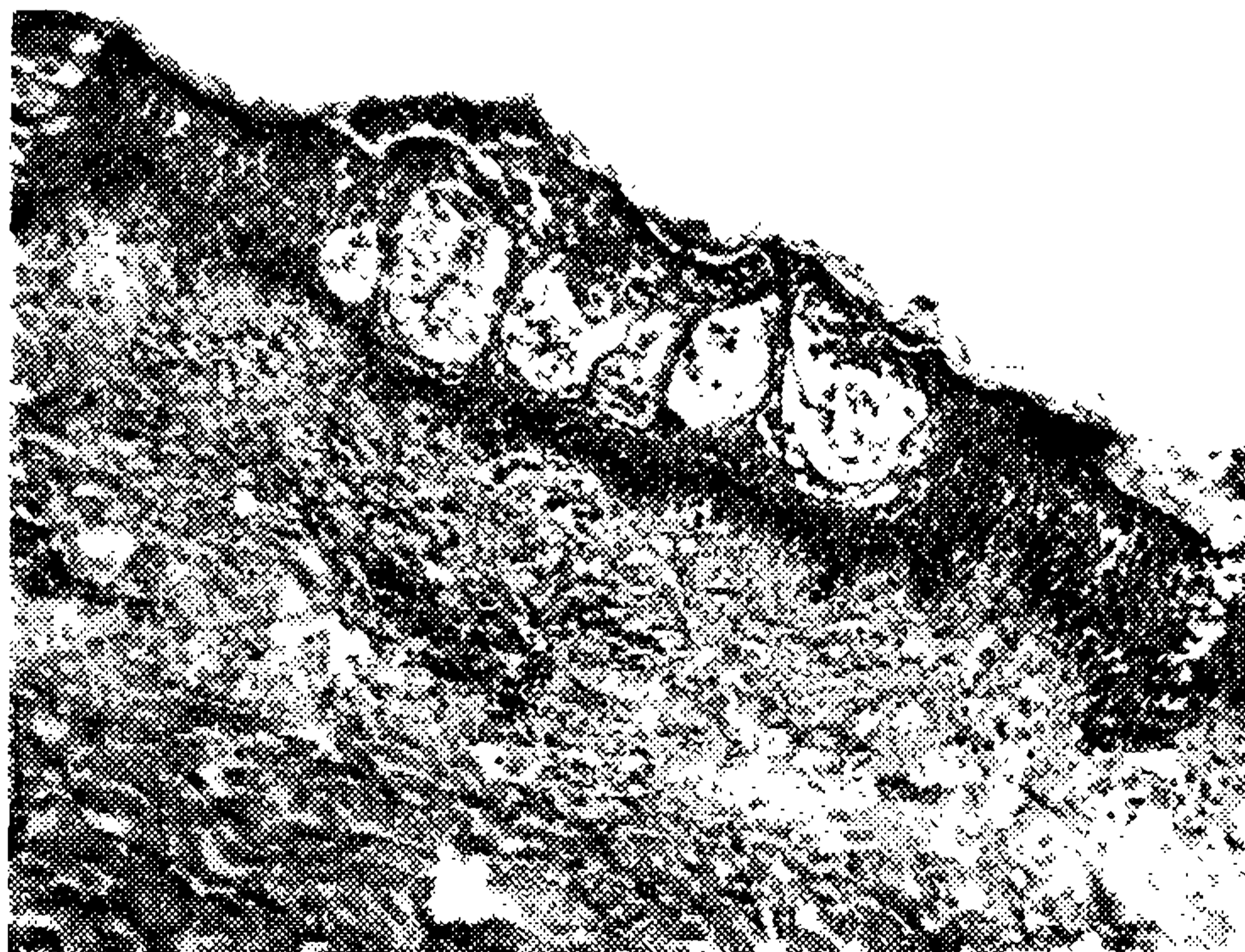
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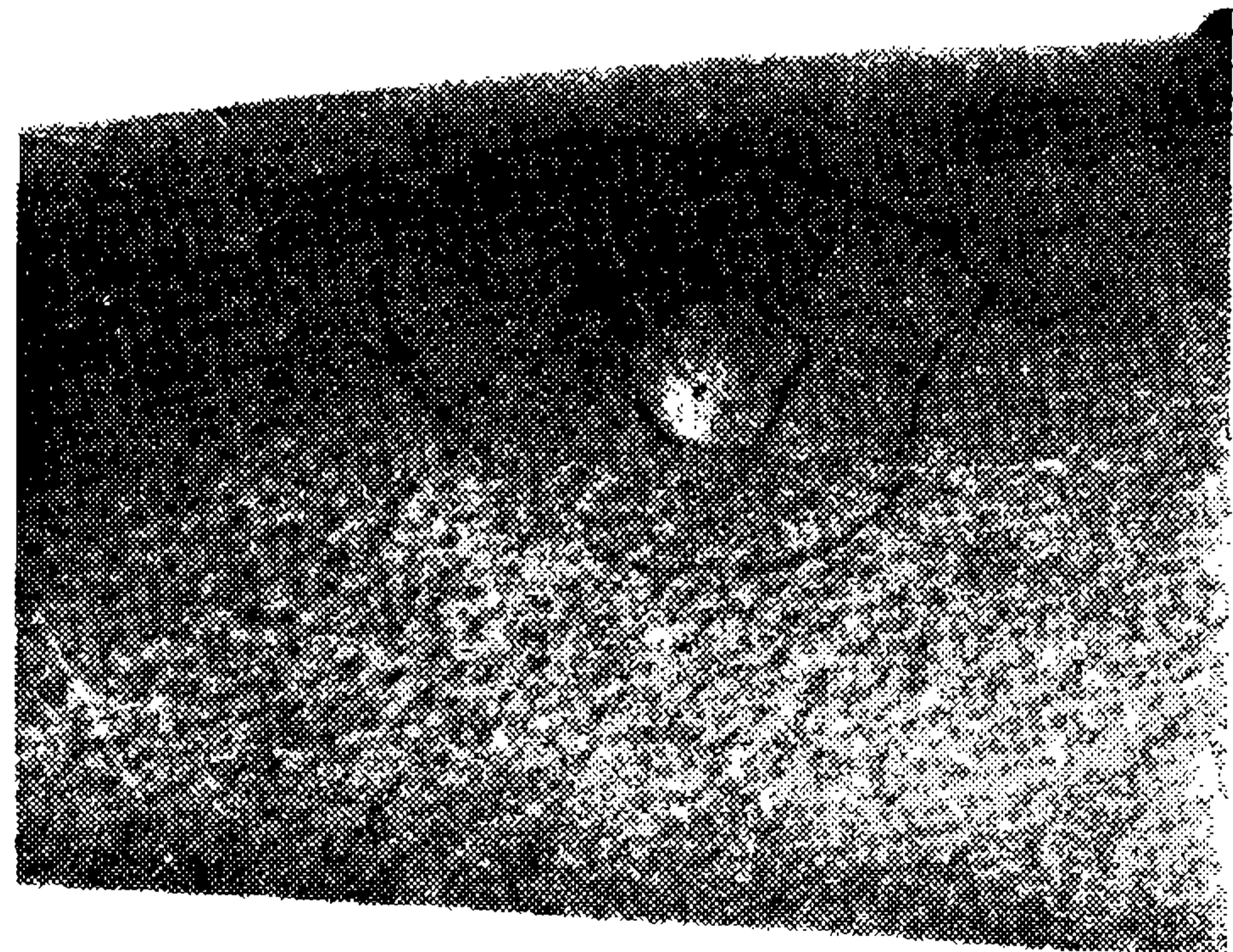
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Fig. 1 — Dermatozoonosis with microspapular lesions.
 Fig. 2 — Dermatozoonosis with vesicular and pustular lesions.
 Fig. 3 — Dermatozoonosis with crust ulcers.
 Fig. 4 — Dermatozoonosis with desquamatory aspect.
 Fig. 5 — Dermatozoonosis with eczematous aspect.
 Fig. 6 — Dermatozoonosis with hyperpigmented scars.
 Fig. 7 — Histopathologic aspect of the lesion of Dermatozoonosis by *Culicoides*' bite (After GUIMARÃES & OLIVEIRA ROCHA, 1959).
 Fig. 8 — Intradermal Test with antigen of *Culicoides* in a patient with Dermatozoonosis: internal ciclo — papule; external ciclo — erythema.

Histopathological study of the lesion

The lesion does not have characteristics of its own. It is similar to that of eczema, showing vesiculation and spongiosis, as it can be seen in Figure 7. The following studies of biopsies is a good illustration of what we emphasized.

Observation 1 — Biopsy of a leg lesion

Epidermis — It presents a discreet hyperkeratosis and acanthosis and granulosis on restricted areas. There is a slim prolongation of the interpapular cones. Dermis — The papilar and subpapilar connective tissue are homogeneous and finely split at some points. It is clearly acidophilic on its preliminary stage of hyalinization. There are lympho-fibro-histiocytic infiltration predominantly adventitial and periadventitial. The vessels are generally enlarged. The infiltrating process throughout reaches the skin appendages and nervous filaments. The PAS reaction (MacManus' Method) shows the blade of mucopolysaccharides, sometimes fine and dented and other times pierced, split or disorganized; one or the other point is very thick, presenting a PAS positive lively net surrounding the wall of the vessels. Fibrinoid necrosis can also be seen.

Observation 2 — Biopsy of the arm lesion

We are dealing with a two month duration eruptive process, that determines the formation of erythematopapular elements, of a confluent pattern, which are later covered with scales or thin crusts resulting from desquamation and which finally pigmented.

Epidermis — The skin presents parakeratosis and a pronounced acanthosis with papillomatosis. Throughout the dermis, there is edema and slight lympho-histiocytic infiltration surrounding the vessels.

Observation 3 — Biopsy of a right foot lesion

Epidermis — It presents the cells of the granulosa layer going deeply into the chorion. Dermis — We can clearly observe a reactional chronic inflammatory process, with an infiltration of lymphocytes beside several fibroblasts, fibrocytes and histiocytes surrounding the vessels. Their walls are swollen and presents ectasia and desquamation of the endothelium. Hypodermis — There is a certain quantity of mastocytes, chiefly surrounding the blood vessels. The PAS reaction showed focus of fibrinoid degeneration at the level of the blood vessels.

Lesions' localization

The lesions caused by *Culicoides* bite are mostly located on the legs. However, they may also appear on all regions of the body that are not protected by clothes. The study of 211 patients that were checked at the "Hospital das Clínicas", shows that the lesions are more frequently located on the following spots:

Region of the body	Number of patients	Percentage
Legs	211	100%
Thighs	54	26%
Arms and forearms	160	76%
Face	30	14%
Body	43	20%
Total number of patients:	211	

As we remarked in a previous paper, a series of factors are responsible for the location of the sores mostly on the legs. Besides a specific characteristic of *C. paraensis*, there are other favorable factors such as greater exposure of legs to bites, and they are more frequently protected against light and wind.

Children are specially affected in other region than the legs, perhaps because of the habit of going naked.

Subjectives symptoms and signals

All patients had intensive pruritus, chiefly nocturnal. If the clinical picture is more intense, one can observe insonmia, anorexia, and nervous irritability. The majority of patients presented swelling of the crural lymph nodes.

Laboratory Examinations

Test with Culicoides antigen

In the preparation of the antigen, we used *C. paraensis* specimens collected in nature. Only the females that had no blood in their abdomens were used. Ten specimens were smashed in 0.5 ml of saline and centrifugated. For the test we injected 0.01 ml of the floating liquid through the dermis with a tuberculin syringe.

The test was read fifteen minutes after the injection, and the persons who had positive reactions presented a papule about one centimeter wide, surrounded by an erythematous halo three centimeters wide (Fig. 8).

The test was made in ten healthy persons and in twenty six Dermatozoonosis patients. As we can see on Table I, nine healthy persons presented negative results while 24 patients had positive ones. When the result was positive, fifteen minutes after the injection, the reaction was already formed with the mentioned dimensions. Two of the patients only showed reaction twenty minutes after the injection of the antigen. The majority of positive patients stopped having the reaction twelve hours after the test; in only one patient we could observe a more delayed reaction. After 24 hours, no patients presented the reaction.

Summing up, we can say that the method seems to be valuable in the ethiologic diagnosis of Dermatozoonosis.

TABLE I
Intradermal test with *Culicoides* antigen in healthy persons and patients with Dermatozoonosis

TYPE OF PERSONS	N.º of persons tested	N.º of persons with positives results	N.º of persons with negative results	Total number of persons	Percentage of positives
Healthy.....	10	1	9	10	10
With Dermatozoonosis.	26	24	2	26	92
TOTAL.....	36	25	11	36	70

Blood Examination

Generally speaking, erythrocytes examination presented normal figures in 41 patients, except for the fact that six patients had rates of circulatory hemoglobin inferior to 11 gram per cent, what could be explained by verminosis in those patients.

The leucocytes examination in 51 patients showed, in the total counting of leucocytes, leucophilia in 45 per cent, a normal result in 41 per cent, and moderate leucocytosis in 14 per cent of patients, according to the data on Table II.

TABLE II
Total counting of leucocytes in 51 patients with Dermatozoonosis

TOTAL NUMBER OF LEUCOCYTES PER MM ³	Number of patients	Percentage
3,000 to 4,000.....	5	10
4,000 to 5,000.....	9	18
5,000 to 6,000.....	9	18
6,000 to 7,000.....	7	14
7,000 to 8,000.....	9	18
8,000 to 9,000.....	5	10
9,000 to 10,000.....	0	0
10,000 to 15,000.....	7	14
TOTAL.....	51	100

The differential counting of leucocytes did not show any deviations, but it revealed a marked eosinophilia from 5 to 30 per cent of eosinophiles per mm³ in 71 per cent out of the 51 patients (Table III). The eosinophilia, however, cannot give us a sure indication of the allergic nature of the process, since it is a well known fact that intestinal parasitism by worms increases the number of eosinophiles, and all our patients suffered from it.

TABLE III
Eosinophile counting in 51 patients with Dermatozoonosis

PERCENTAGE OF EOSINOPHILES PER MM ³	Number of patients	Percentage
1 to 5%.....	15	29
5 to 10%.....	10	20
10 to 15%.....	14	27
15 to 20%.....	4	8
20 to 25%.....	6	12
25 to 30%.....	2	4
TOTAL.....	51	100

Sixty seven per cent of the patients showed lymphocytosis, some of them with an averages of 40 to 50 per cent of lymphocytes per mm³ (Table IV) .

A close analysis of the data lead us to think of a cronic inflammatory process in the generality of cases, with a probable allergic nature.

TABLE IV
Counting of lymphocytes in 51 patients with Dermatozoonosis

PERCENTAGE OF LIMPHOCYTES PER MM ³	Number of patients	Percentage of patients
2 to 5%.....	1	2
6 to 10%.....	1	2
11 to 15%.....	0	0
16 to 20%.....	7	14
21 to 25%.....	8	16
26 to 30%.....	7	14
31 to 35%.....	4	8
36 to 40%.....	10	20
41 to 45%.....	9	18
46 to 50%.....	2	4
More than 50%.....	2	4
TOTAL.....	51	100

Stool Examination

According to GUIMARÃES & OLIVEIRA ROCHA, intestinal parasitosis seems to exert a deep influence in the exarcebation of the reaction to *Culicoides*' bite. In the 181 patients who made stool exams, several species of intestinal parasites were found, as we can see on Table V. It is possible that due to this fact the great majority of ours patients had exarcebated lesions.

TABLE V
Stool examination for 181 patients with Dermatozoonosis

SPECIES OF PARASITES	Number of patients	Percentage
<i>Ascaris lumbricoides</i>	46	25
<i>Ancilostomidae</i>	20	11
<i>Trichocephalus trichiurus</i>	55	30
<i>Schistosoma mansoni</i>	19	10
<i>Endolimax nana</i>	6	3
<i>Giardia lamblia</i>	4	2
<i>Entamoeba coli</i>	25	14
<i>Entamoeba histolytica</i>	3	2
<i>Iodamoeba butischilii</i>	3	2
TOTAL	181	100

Urine analysis

The urine examinations presented normal results in 57 patients with Dermatozoonosis.

TREATMENT

Dermatozoonosis presents a relative resistence to treatment and for this reason several measures were taken for its therapeutics.

The disensibilization of patients was tried by some Authors. ROCWELL (1952) injected into patientes, 0.05 ml of extract from *Aedes aegypti* (Lin.), starting with water dilution at 1:10,000,000, with three or five-day intervals until a bearable maximum dosage was reached. Reactions on those individuals became less severe as they were subsequently bitten by the mosquito. He stresses that the process is valuable in the treatment of Dermatozoonosis, but if the extract is applied in high concentrations one can get hypersensitiveness instead

of protection. GOLDMAN (1952) observed a certain inhibition of the cutaneous reaction by the use of a compound "F", which was probably obtained from smashed insects. SHAFFER et al. (1952) registered successfully the local use of DDT in 46 patients with Dermatozoonosis, who were healed within two weeks by the continuous use of that substance.

Such processes have not yet been used among us. However, good results were obtained in a great majority of cases where the therapeutic scheme by NEWTON GUIMARÃES was employed.

Since symptoms are mainly determined by *Culicoides*' bite, it is easy to understand that the principal aim is to avoid the attack of sensitive individuals by the insect. For this reason, among us, patients were told to protect the regions left exposed to the insect bite, by using proper clothing or repellent substances.

On the other hand, we tried to eliminate the intestinal parasites, for, as we have already pointed out, it seems to be one of the factors capable of intervening in determination of symptoms. The treatment was followed by the use of oral antihistaminics and the local application of unctio taking as basis zinc, sulphur, menthol, camphor and cade oil. The complications of eczematization and impetigo were treated by the classical processes.

Unfortunately, the majority of patients left the Clinic before a pre-established time, thus we did not have a complete follow up of patients or definite data about their cures.

Last but not least, we want to mention GUIMARÃES & OLIVEIRA ROCHA (1959) who believe that a local treatment with corticosteroids ointment possibly presented better results in the treatment of Dermatozoonosis. We did not use such substances, mainly because their price was very high.

RESUMO

A observação de 211 pacientes com reação intensa à picada do *Culicoides*, que procuraram tratamento na Clínica Dermatológica do Hospital das Clínicas da Universidade da Bahia, durante os anos de 1959 a 1962, permitiu o estudo clínico dessa Dermatozoonose, cujos dados são aqui apresentados.

A lesão parece ser de natureza alérgica e devido ao aspecto polimorfo pelo qual se apresenta, essa Dermatose pode lembrar o Prurigo, a Escabiose, as Lesões liquenoides; quando a manifestação é mais intensa torna-se uma verdadeira eczematização; quando há infecção secundária, lembra o impetigo folicular.

O estudo histológico da lesão revelou ser ela a de uma inflamação crônica, com vascularites e perivascularites dermo-epidérmica, provavelmente de natureza alérgica.

Para que haja a formação da lesão, são necessários: a substância inoculada pelo inseto e o componente alérgico do indivíduo. Não se

conhece a natureza da substância inoculada pelo inseto e as seguintes hipóteses são apresentadas para explicá-la: substâncias enzimáticas ou a histamina existentes nas glândulas salivares do *Culicoides*.

Após a picada do *Culicoides* forma-se no local uma pequena área eritematosa que logo após se transforma em pápula; as pápulas podem desaparecer ou transformarem-se em vesículas; estas ao se romperem dilaceram a superfície cutânea, descamam-na ou pode advir uma infecção secundária e transformam-se em pústulas.

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