

CUTANEOUS ALLERGIC REACTIONS TO
TRITOMA INFESTANS AFTER XENODIAGNOSIS

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We determined the frequency of cutaneous allergic reactions to bites of Triatoma infestans during xenodiagnosis in a rural community where Panstrongylus megistus is the only domestic vector of Trypanosoma cruzi. Localized urticaria or more intense cutaneous allergic reactions at 48 and 72 hours were observed in 86.7% and 82.1% respectively of the individuals in our study. Urticaria was more severe in children and older adults and in women than in men. The high frequency of reactions suggests either cutaneous reactivity to T. infestans without prior sensitization or cross reactivity between P. megistus and T. infestans. A single application of topical corticosteroid or antihistamine medication did not reduce the cutaneous reactions.

More than 60 years ago, xenodiagnosis was introduced for diagnosis of *Trypanosoma cruzi* infection (Brumpt, 1914). In the absence of sophisticated laboratory facilities in endemic areas this simple technique became widely accepted. Brumpt (1914) considered this procedure innocuous and noted no untoward local or generalized effects on the subjects. Since that time, local cutaneous allergic manifestations to triatomine bites have been observed (Arnold & Bell, 1944).

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Cutaneous and, in some cases, generalized allergic reactions to the bites of almost all species of triatomine bugs including the vectors of Chagas' disease have been recorded. However, reports have been limited to individual cases or selected groups. A systematic study of cutaneous allergic manifestations of triatomine bites in a defined population has not been reported.

The objective of our study was to determine the frequency and intensity of cutaneous allergic manifestations to *T. infestans* during xenodiagnosis in a rural population in the State of Bahia where *Panstrongylus megistus* is the only domestic vector of Chagas' disease (Sherlock & Serafim, 1974). The effectiveness of topical antihistamine and corticosteroid medications for reduction of cutaneous allergic reactions to *T. infestans* bites was also evaluated.

MATERIALS AND METHODS

Population: The study was conducted on a "fazenda" (estate) in the "município" (county) of Castro Alves of the State of Bahia, Brazil. The study area in tropical agricultural region of the "Recôncavo Baiano" was located adjacent to the site of a larger epidemiologic study (Mott et al., 1976). The estate had 26 houses and 122 residents in a census completed in April 1976. In June 1976, 116 residents participated in a study to determine the relationship between *T. cruzi* parasitemia and seroreactivity to *T. cruzi* (Hoff et al., 1979). A venous blood specimen, electrocardiogram, and *T. infestans* xenodiagnosis was obtained as previously mentioned (Hoff et al., 1979).

Xenodiagnosis: Xenodiagnosis was performed with laboratory bred fifth instar *T. infestans* nymphs which had fed on pigeons at weekly intervals until four weeks prior to our study. We utilized five *T. infestans* in each of two boxes which were placed on each forearm of adults or thighs of infants for 30 minutes. After the boxes were removed and the skin cleaned with alcohol, coded topical creams were then applied over the xenodiagnosis sites by the double blind method, recorded, and covered with plastic foil. A control cream of Vitamin A and D ointment(1) was applied to one arm and on the other arm either a corticosteroid cream (2) or an antihistamine cream (3) was applied. The participants were instructed to remove the plastic foil after 12 hours and wash the xenodiagnosis site with water. Systematic recording of immediate allergic reactions was not done.

Observations of the xenodiagnosis sites were independently recorded by two other investigators at 24, 48, 72 hours and 7 days. At least one observation of the xenodiagnosis site was made on 111 persons. Over 90% of these individuals were observed at 24, 48 hours and 7 days. At 72 hours, 75.6% of the study group were observed. The cutaneous allergic reactions to *T. infestans* were classified as: 0) no reaction, 1) papules (without erythema), 2) localized erythema, 3) localized urticaria, 4) confluent urticaria, 5) hemorrhage of vesicles, 6) necrosis or anaphylaxis.

RESULTS

Immediate reactions: During the course of removing the xenodiagnosis box about 20% of persons were observed to have localized urticaria.

Delayed reactions: Almost 90% of persons experienced localized urticaria or a more intense cutaneous allergic reaction to *T. infestans* bites.

(1) Hipoglós Pomada, Laboratories Andromaco, S.A., São Paulo.

(2) Creme Drenison 1/4, Eli Lilly do Brasil, Ltda., São Paulo.

(3) Andantol, Labofarma, S.A., São Paulo.

Effect of age: At 24 hours, the most intense reactions occurred in the youngest and oldest age groups (Table I) although at 72 hours the frequency of severe reactions in the 0-4 year age group had diminished. Urticaria was most frequent at 48 hours in the study group. Hemorrhagic lesions were only observed in children below five years of age. At seven days most of the intense reactions had regressed.

Effect of sex: At 24(4) and 72(5) hours women had a significantly greater frequency of these reactions than men (Table II). At 48(6) hours and 7(7) days the frequency of intense reactions was not significantly different between men and women. We did not record subjective reactions.

Effect of topical medication: Throughout the study, the observers could note no visual difference between the cutaneous reactions at the xenodiagnosis sites treated with control, corticosteroid or antihistamine creams.

DISCUSSION

In this study, most persons experienced localized urticaria or a more severe cutaneous allergic reaction after *Triatoma infestans* bites. The high frequency of reactions may be explained by 1) cross reactivity between *T. infestans* and local triatomine vector, *P. megistus*, or 2) cutaneous allergic reactions independent of prior exposure.

Cross reactivity between *P. megistus* and *T. infestans* as well as between *Rhodnius prolixus* and *T. infestans* has been reported in three volunteers in whom Romana's sign (unilateral bipalpebral edema) was experimentally produced by the bites of noninfected bugs (Lumbreras et al., 1959). However, on a population basis, information on cutaneous cross reactivity between species is lacking. The cutaneous allergic reactions to *T. infestans* bites are well documented (Salgado et al., 1963) due to their frequent use for xenodiagnosis in Brazil (Perlowagora-Szumlewicka et al., 1973). However, no correlation with prior exposure was made. In contrast to *P. megistus*, *T. infestans* domestic infestations are often intense (Sherlock & Serafim, 1974) and therefore exposure may be greater. Cutaneous sensitization or even desensitization due to the frequent bites may occur in such endemic areas.

The specificity cutaneous allergic reactions to bites of triatomine species is controversial (Feingold et al., 1968). In Costa Rica and Venezuela no immediate reactions to the bites of triatomine bugs other than indigenous vectors of Chagas' disease have been reported (Maekelt, 1974; Zeledon, 1953). No observations on the frequency of delayed reactions (after 24 hours) in three areas is available. In general, immediate hypersensitivity reaction to arthropod bites is dependent on prior exposure to the same species (Gaafar, 1972); however, as we have observed, this may not be true for triatomine bites.

Severe cutaneous allergic reactions including generalized anaphylaxis to bites of *R. prolixus* have been reported in Venezuela (Maekelt, 1974; Torrealba, 1958). Due to such severe reactions, it has been recommended that xenodiagnosis with species not be used in field surveys for *T. cruzi* parasitemia (Maekelt, 1966). Serial xenodiagnosis with *T. infestans* has been utilized for evaluation of chemotherapy for *T. cruzi* infection without the occurrence of severe reactions (Salgado, 1976). However, repeated exposure of a human volunteer to *T. infestans* resulted in generalized anaphylaxis (Balazuc, 1950).

(4) Chi-square test, $\chi^2 = 5.00$ df = 1 < .05 p > .02

(5) Chi-square test, $\chi^2 = 4.39$ df = 1 < .05 p > .02

(6) Chi-square test, $\chi^2 = 1.99$ df = 1 p > .5

(7) Chi-square test, $\chi^2 = .77$ df = 1 p > .5

TABLE I

Rate of individuals with localized urticaria or more intense allergic cutaneous reactions to *T. infestans* according to age

Age (years)	No. in Study	24 Hours		48 Hours		72 Hours		7 Days	
		Examined	% with reactions	Examined	% with reactions	Examined	% with reactions	Examined	% with reactions
0-4	21	20	90.0	21	95.0	21	76.2	21	23.8
5-9	21	20	90.0	21	95.0	20	90.0	21	9.5
10-24	27	24	83.3	24	79.2	17	82.4	26	22.2
25-44	20	18	55.6	19	89.5	12	91.7	19	21.0
45-64	18	16	56.3	16	68.8	12	67.0	15	0
65+	4	3	100.0	4	100.0	2	100.0	4	25.0
Total	111	101	77.2	105	86.7	84	82.1	106	16.9

TABLE II
 Rate of individuals with localized urticaria or more intense allergic cutaneous reactions to *T. infestans* according to sex

Age (years)	Time after xeno:	No. in Study	24 Hours		48 Hours		72 Hours		7 Days	
			Examined	% with reactions	Examined	% with reactions	Examined	% with reactions	Examined	% with reactions
Men		58	54	68.5	56	82.1	41	73.2	54	13.0
Women		53	47	87.2	49	91.8	43	90.7	52	19.2
Total		111	101	77.2	105	86.7	84	82.1	106	16.9

Some antigens injected with the triatomine saliva may be derived from the vertebrate blood meal sources necessarily used to rear the bugs in the laboratory (Dias, 1940). For example, the salivary glands of *R. prolixus*, but not of *T. infestans*, contain pigments derived from hemoglobin (Wigglesworth, 1943). Although circulating precipitating antibodies specific to *R. prolixus* have been demonstrated in experimental animals after repeated exposures (Fox & Bayona, 1968), their relationship to the cutaneous allergic response is unknown.

The host immune response to the triatomine bite may affect *T. cruzi* transmission (Kartman, 1964). The bite provokes an inflammatory response by intradermal inoculation of saliva containing undefined antigens and histamine (Harrington, 1956; Pick, 1954).

Allergic reactions are well documented to bites of triatomine species known to be important vectors of Chagas' disease, including *Triatoma infestans* (Dias, 1968; Laviopierre et al., 1959; Lumbreras et al., 1959; Silva, 1964-1965), *Triatoma dimidiata* (Feingold et al., 1968), *Rhodnius prolixus* (Dias, 1968; Laviopierre et al., 1959; Silva, 1964-1965; Torrealba, 1958; Zeledon, 1953), and *Panstrongylus megistus* (Dias, 1968). Triatomine species which participate in a sylvatic cycle, occasionally have been reported to cause allergic reaction in man; these include *Triatoma rubrofasciata* (Africa, 1934; Arnold & Bell, 1944; Teo & Cheah, 1973), *Triatoma protracta* (complex) (Swezey, 1963; Wood, 1942, 1953, 1957), and *Triatoma sanguisuga* (Goldman, 1971).

We observed a higher frequency of early (24 hour) and late (72 hour) severe cutaneous reactions in women than in men. No sex difference in skin reactivity to intradermal antigens has been reported. Estradiol, a sex hormone, is a strong attractant to arthropod vectors (Bos & Laarman, 1975). Thus, greater exposure to bites could lead to greater sensitization in women. However, there are no epidemiological data to suggest that women in this rural community are more exposed to triatomines than men.

Topical corticosteroid or antihistamine creams did not effect the rate or intensity of reactions to xenodiagnosis. On the other hand, Dias (1968) has reported reduction of cutaneous reactions to xenodiagnosis with varied medical creams. However, since the effect of a control topical medication was not reported, the results of his study are difficult to interpret. We did not evaluate the efficacy of topical medication for reducing symptoms or the immediate hypersensitivity reactions.

Our findings suggest that there may be common antigens between *T. infestans* and *P. megistus*. Cutaneous allergic reactions of the delayed type occur with *T. infestans* xenodiagnosis and its use in mass surveys should be undertaken with caution. In population studies, alternative methods of detection of *T. cruzi* parasitemia such as blood culture (Hoff et al., 1979) or artificial xenodiagnosis (Laviopierre et al., 1959) should be considered.

RESUMO

Reações Cutâneas Alérgicas ao Triatoma Infestans após Xenodiagnóstico

A frequência de reações cutâneas alérgicas às picadas de *Triatoma infestans* após xenodiagnóstico foi determinada numa comunidade rural na qual *Panstrongylus megistus* é o único vetor doméstico. Urticária focal ou reações cutâneas alérgicas mais intensas foram observadas em 86.7% e em 82.1% dos participantes estudados, respectivamente às 48 e às 72 horas. A urticária foi mais severa em crianças e adultos idosos e mais severa em mulheres do que em homens. A alta frequência das reações sugere a existência de reativi-

dade cutânea ao *T. infestans*, sem prévia sensibilização, ou uma reatividade cruzada entre *P. megistus* e *T. infestans*. A aplicação tópica de pomada de corticosteróide ou de anti-histamínico não reduziu as reações cutâneas alérgicas.

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