Table 1. Three indices used as mimicry indicators.

| Index | 0.00000000 | <i>eira rica</i> netic) | Castianeira alba (nonmimetiz) | | |
|-----------------------------|----------------|----------------------------|----------------------------------|----------------|--|
| | Male | Fe- male | Male | Fe- male | |
| Carapace | 55-58 | 57-61 | 69-72 | 69-75 | |
| Leg thickness Abdomen | 15–19 33–38 | 22–23 46–64* | 29–31 52–58 | 30–32 62–63 | |

* High values are for gravid females.

dorsal scutum; the abdomen is distinctly constricted, the legs are thin, and the hind femora extend high above the abdomen. Castianeira alba is not antlike, either morphologically or behaviorally. It runs, never walks, from under one leaf to under another.

Ants have much thinner legs and longer, thinner bodies than do most clubionid spiders, so the degree of morphological resemblance to ants can be quantified by means of several indices that express the extent of elongation: the carapace index (carapace width/ carapace length \times 100), the leg thickness index (femur IV width/femur IV length \times 100), and the abdomen index (abdomen width/abdomen length \times 100). These indices are useful as mimicry indicators, low values indicating mimetic adaptation (Table 1).

Castianeira rica exhibits several mimetic forms which result from three different factors: (i) sexual dimorphism, (ii) a wide variation in color in adult females, and (iii) developmental changes. The two sexes differ markedly in color and form. The female is red-brown to maroon-black with a moderately narrow carapace and abdomen, whereas the male is bright red-orange with a very thin carapace and abdomen and with thinner legs than the female (Table 1). The male resembles species of Atta and Odontomachus, whereas the female is a more general mimic, resembling moderately large ponerine ants within the spiders' color range.

Castianeira rica achieves adult form in six molts after hatching. The developing spiders resemble ant models of equivalent size. Instars II and III (instar I is spent in the egg sac) are small, black, and shiny, and mimic small myrmicine ants; instars IV and V are yellow-orange and resemble medium-sized attine ants. A similar case involving the development of the salticid ant mimic, Myrmarachne plataleoides, was reported from India by Mathew (2), and he

coined the term "transformational mimicry" for this phenomenon.

The mimetic complex in C. rica thus contains at least five forms-two from sexual dimorphism, an additional one from color variation in the female, and at least two more from transformational mimicry. Castianeira alba has developmental changes in size, but exhibits little sexual dimorphism (Table 1); it has one basic, disruptive, black and white pattern for all instars and both sexes.

The only relationship between mimetic C. rica and its model ants appears to be their occurrence in the same microhabitat-heavily shaded leaf litter. Castianeira alba is found nearby in sunny, drier, more open areas devoid of most ants (3).

The obvious protection from predators resulting from ant mimicry is enhanced by two specific advantages of the described mimetic complex: (i) the mimic maximizes its protection at every stage by resembling available models of a similar size and, (ii) the mimic uses various models, even in one general size class, increasing the repertoire of models, and thereby making the system potentially more stable.

This latter advantage is also the result of the generalized character of the individual mimics. Castianeira rica is a mimic of subfamilial and tribal taxa of ants and is not species-specific (4). JONATHAN REISKIND

Department of Zoology, University of Florida, Gainesville 32601

References and Notes

- 1. J. Reiskind, Bull. Mus. Comp. Zool. 138, 163
- (1969). 2. A. P. Mathew, J. Bombay Natur. Hist. Soc. 37, 369 (1934).
- 3. In captivity C. rica can rarely live more than 24 hours without the presence of liquid water or water-saturated cotton. Under similar conditions C. alba can survive about a week.
- 4. A related species *Myrmecotypus rettenmeyeri*, found in Panama, is a species-specific mimic of a dominant neotropical ant Camponotus sereceiventris [J. Reiskind, Psyche 74, 20 (1966)], whereas most mimetic *Castianeira* of North America are more generalized than North
- 5. Field work supported by a grant from the Evolutionary Biology Committee of the Depart-ment of Biology, Harvard University. I thank ment of Biology, Harvard University, I thank the Instituto Interamericano de Ciencias Agri-colas in Turrialba, Costa Rica, and Mr. J. Erickson, the assistant director at that time, for aid in this investigation. This study is part of one presented in partial fulfillment of the requirements for the degree of Doctor of Phi-losophy, Harvard University, and was sup-ported by graduate fellowships from NSF and Harvard University Harvard University.

4 June 1970

LSD: No Teratogenic Action in Rats, Mice, and Hamsters

Abstract. Lysergic acid diethylamide tartrate was given to 98 pregnant rats, 67 mice, and 22 hamsters as a single dose of 5 to 500 micrograms per kilogram of body weight per day either at the beginning of gestation or during the period of organogenesis. Examination of the 1003 rat fetuses, 521 mouse fetuses, and 189 hamster fetuses obtained failed to prove any abortifacient, teratogenic, or growthdepressing effects.

Whether LSD is a teratogen is still an open question. A teratogenic action for LSD has been reported several times. In rats, the number of stillborn and stunted fetuses was increased after subcutaneous administration of 5 μ g/ kg to pregnant rats on the 4th day of gestation (1). However, this experiment was performed on only ten rats; five rats were treated later in gestation without effect. In certain strains of mice a high incidence (57 percent) of brain malformations was reported after administration of LSD on day 7 of pregnancy (2). Lens anomalies have been described in the mouse treated with LSD (3). When LSD was given to 37 pregnant hamsters at dosages varying from 0.084 μ g/kg to 0.24 μ g/kg, it provoked 5 to 8 percent malformation (anencephaly, exencephaly, spina bifida, hy-

drocephaly, localized or generalized edema) (4). Some fetuses had several malformations. However, the percentage of malformed fetuses was not specified. In the same article, a similar action of mescaline and of bromolysergic acid was reported. In the case of mothers taking LSD, two babies born with limb deformities are known (5, 6). Nevertheless, two observations can hardly be considered as evidence of the teratogenic action of LSD in man. On the other hand, no teratogenic effect from LSD was found in 55 litters of rats, the 508 fetuses examined all being normally developed (7). Similar negative results have been reported for the rabbit (8), mice and hamsters (9), and man (10, 11).

In respect to the possible causal relationship between chromosomal dam-

age and teratogenesis, chromosome aberrations due to LSD have often been noted, in both experimental and clinical conditions. But negative data have also been reported, and in spite of numerous works the possible chromosome toxicity from LSD is still questioned.

Lysergic acid diethylamide tartrate (12), in amounts from 5 to 500 μ g/kg per day, was given subcutaneously to Wistar rats, either from the 4th to the 10th day, or from the 7th to the 13th day of gestation (the day of appearance of spermatozoa in the vagina is taken as the 1st day of gestation). In the rat, implantation occurs on the 7th day, and organogenesis is over on the 14th day. In order to repeat the experiment of Alexander et al. (1), we gave some pregnant rats one dose of 5 μ g/ kg on either the 4th or the 7th day of gestation (Table 1).

A total of 98 litters was obtained, comprising 1003 fetuses. These were taken and examined on the 21st day of gestation, 1 day before the delivery. No increase in fetal mortality was found for any group of experimental animals. The mean weight of the fetuses on the 21st day was normal.

Some fetal malformations were found. In the group of rats receiving 5 $\mu g/kg$ on the 4th day of gestation (99) fetuses), there were six edematous fetuses of which one had a cleft palate. In the group of animals receiving 50 μ g/kg from the 4th day to the 10th day (117 fetuses), we observed four cataracts, all in one litter. In the group of animals which received the highest dosage (500 μ g/kg from the 7th day to the 13th day), we dissected 48 fetuses out of 124 and did not observe any malformations of thoracic and abdominal viscera. The low rate of malformed fetuses is obviously not significant.

Three doses of LSD (5 μ g/kg per day, 50 μ g/kg per day, or 500 μ g/kg per day) were given subcutaneously to Swiss mice either from the 4th to the 10th day or from the 6th to the 14th day. In mice implantation occurs on the 6th day, and organogenesis is over on the 14th day (Table 1).

A total of 67 litters was studied, amounting to 521 fetuses. These were taken and examined on the 19th day of gestation, 1 day before the delivery. There was no significant increase in fetal mortality in any group of animals. The mean weight of the fetuses was not significantly modified. No external malformations were observed. In the group

7 AUGUST 1970

Table 1. Effect of prenatal treatment with LSD. Fetal mortality includes dead fetuses and partial and total resorptions. It is expressed in absolute number. It must be noted that the fetal mortality in controls is high for rats, but this value varies in our animals from 10 percent through 20 percent; this must be kept in mind in evaluating the significance of the number in the treated animals.

| LSD (µg/ kg) | Treat- ment (days) | Litters (No.) | Living fetuses (No.) | Fetal mortality (No.) | Mean weight per fetus (g) | Mal- formed fetus (No.) |
|--------------------|--------------------------|------------------|----------------------------|-----------------------------|------------------------------------|----------------------------------|
| | r. | | Rats | | | |
| 5 | 4th-10th | 10 | 117 | 8 | 3.73 | 0 |
| 5 | 7th-13th | 12 | 115 | 28 | 3.24 | 0 |
| 50 | 4th-10th | 10 | 117 | 16 | 3.0 | 4 |
| 50 | 7th-13th | 11 | 101 | 11 | 2.92 | 0 |
| 250 | 4th-10th | 11 | 113 | 19 | 3.32 | 0 |
| 250 | 7th-13th | 12 | 118 | 16 | 3.47 | 0 |
| 500 | 7th-13th | 11 | 124 | 17 | 3.43 | 0 |
| 5 | 4th | 11 | 99 | 20 | 3.21 | 6 |
| 5 | 7th | 10 | 99 | 15 | 3.50 | 1 |
| 0 | | 20 | 203 | 52 | 3.40 | 0 |
| | | | Swiss mice | | | |
| 5 | 4th-10th | 10 | 82 | 14 | 1.30 | 0 |
| 5 | 6th-13th | 10 | 81 | 12 | 1.14 | 0 |
| 50 | 4th-10th | 15 | 126 | 28 | 1.16 | 0 |
| 50 | 6th-13th | 16 | 119 | 34 | 1.15 | Ū. |
| 500 | 6th-13th | 16 | 113 | 20 | 1.15 | Ŭ, |
| 0 | | 10 | 70 | 25 | 1.21 | Ō |
| | | | Hamsters | | | |
| 50 | 7th-13th | 14 | 122 | 44 | 1.49 | 0 |
| 500 | 4th-12th | 8 | 67 | 15 | 1.50 | ů 0 |
| 0 | | 18 | 170 | 38 | 1.68 | Ŏ |

treated with the highest amount (500 μ g/kg per day from the 6th to the 14th day of gestation), 50 fetuses out of 113 were dissected. No malformations of thoracic and abdominal viscera were observed.

Two doses of LSD, either 50 μ g/kg per day from the 7th to the 13th day of gestation or 500 μ g/kg per day from the 4th to the 12th day of gestation, were given to hamsters (Table 1). Implantation occurs on the 6th day; organogenesis is over on the 13th day.

Altogether 22 litters were examined, totaling 189 fetuses. These were taken and examined on the 15th day of gestation, 1 day before birth.

The fetal mortality and the mean live young per litter were comparable to those of the controls. The mean fetus weight on the 15th day of the gestation was also normal. No external malformations were observed. In the group treated with the highest amounts, we dissected 30 fetuses out of 67 and found no visceral malformations.

Thus, in these three species (rat, mouse, and hamster), no abortifacient, teratogenic, or embryonic growth-depressing effects were observed after treatment with LSD, even though some animals received enormous doses of the drug.

Of course it is impossible to conclude from these experimental data that LSD may not be teratogenic in man. The difficulty of such extrapolations from species to species is well known. Only extensive clinical observations will provide specific information with respect to man.

> C. Roux **R.** DUPUIS M. AUBRY

Laboratoire d'Embryologie Faculté de Médecine,

St-Antoine, Paris, France

References and Notes

- G. J. Alexander, B. E. Miles, G. M. Gold, R. B. Alexander, *Science* 157, 459 (1967).
 R. Auerbach and J. A. Rugowski, *ibid.*, p.
- 1325.

- 1325.
 J. K. Hanaway, *ibid.* 164, 574 (1969).
 W. F. Geber, *ibid.* 158, 265 (1967).
 F. Hecht, R. K. Beals, M. H. Lees, H. Jolly, P. Roberts, *Lancet* 1968-II, 1087 (1968).
 H. Zellweger, J. S. McDonald, G. Abbo, *ibid.* 1967-II, 1066 (1967).
 J. Warkany and E. Takacs, *Science* 159, 731 (1968). 7. J. Warkan 731 (1968).
- 8. S. Fabro and S. M. Sieber, Lancet 1968-II, 639 (1968).
- J. A. Dipaolo, H. M. Givelber, H. Erwin, Nature 220, 490 (1968).
 M. Hulten, J. Lindsten, L. Lidberg, H.
- Ekelund, Ann. Génét. 11, 201 (1968).
- H. Sato and E. Pergament, Lancet 1968-II, 639 (1968).
- 12. We thank the Sandoz Laboratories which provided LSD for our experiments, with the authorization of the Ministère des Affaires Sociales, Paris, France.

26 June 1970