

COLLECTIVE ASTHMA, SIMULATING AN EPIDEMIC, PROVOKED BY CASTOR-BEAN DUST

ERNESTO MENDES, M.D.,* AND A. ULHÔA CINTRA, M.D.,** SÃO PAULO, BRAZIL

ON Aug. 11, 1952, the Public Health Department of the State of São Paulo was notified that in Baurú, a town of 60,000 inhabitants, in São Paulo, Brazil, there had appeared an odd type of asthma, apparently of an epidemic nature inasmuch as in a few days 150 cases were registered, with 9 deaths attributed to that illness. The symptomatology consisted of extremely violent dyspnea of the asthmatic type which started suddenly. On account of its apparently epidemic character and seriousness from a clinical viewpoint, the illness was at first attributed to a pneumotropic virus. Subsequent investigation showed that these were cases of bronchial asthma provoked by castor-bean dust. The origin of this allergen was found in a large castor-bean crushing mill which exists in the town of Baurú.

The term "epidemic asthma" has been improperly used to designate the collective asthmogenic action of an allergen in the form of an epidemic. Ancona, in 1923, published a paper on "epidemic asthma" brought about by a cereal parasite: *Pediculoides ventricosus*.

As far as the castor bean (*Ricinus communis*) is concerned, cases of asthma of an epidemic character have been described by Figley and Elrod in 1928 and by Grimm in Germany in 1928. In the 30 cases of asthma described by Figley and Elrod in Toledo, Ohio, it was proved that the allergen was the dust from the castor-bean dust, and in 55 cases there were quite evident indications that the etiology was the same. In Grimm's description 30 cases were studied in which scratch tests made with dust from castor beans gave strongly positive reactions.

MATERIAL, METHODS, AND RESULTS

Thirty patients were studied: 9 in the Hospital das Clínicas of the University of São Paulo, 4 in the town of Baurú, and 17 in Agudos, a small town 15 kilometers from Baurú.

The following methods of etiologic diagnosis were used: (1) cutaneous tests; (2) local passive transfer of antibodies; and (3) experimental provocation of symptomatology.

1. *Cutaneous Tests*.—The selection of extracts for cutaneous tests was made by choosing possibly allergenic substances in the industrial field and in the cereal warehouses of the town of Barurú where there are important oil mills, principally pressing cotton seed, peanut, and castor bean. Twelve extracts for cutaneous reactions were prepared with the following origins: seven

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*Assistant of Department of Microbiology and Immunology of the Faculty of Medicine of the São Paulo University. (Professor Carlos da Silva Lacaz.) Experimental Allergy section.

**Professor of Clinical Medicine, University of São Paulo Medical School.

extracts composed of the principal forms through which cotton seed and linters go; three kinds of dust from cereals; one sample from castor-bean dust which is known as castor-bean pomace.

The extracts were prepared with coea solution, dialyzed, filtered through the Seitz filter, and diluted 1:10, 1:100 and 1:1,000 for use in intracutaneous tests.

The group of 9 patients brought to the Hospital das Clínicas was tested with all the extracts; at first with a scratch test using extracts diluted 1:10 and 1:100 and thereafter with intracutaneous tests using extracts diluted 1:1,000. All the patients responded with strongly positive scratch tests to the castor-bean pomace extracts. Four of these patients also presented positive intracutaneous tests with extracts of cotton seed and cereal dust. These patients had been suffering from rhinitis and asthma for several years.

The other 21 patients observed in Baurú and Agudos were tested exclusively by scratch test with the use of only three extracts: castor-bean pomace diluted 1:100; a mixture of cotton seed dusts at 1:10 and a mixture of cereal dusts. Of these 21 patients, 19 showed cutaneous reactions strongly positive to castor-bean extract. Four patients, asthmatic for a long time, also presented positive cutaneous reactions to other inhalants.

On two patients the scratch test with castor bean was negative. One of these patients was an old asthmatic individual, but the other patient was probably a misdiagnosed case for she complained only of shortness of breath and showed no other symptoms of asthma.

2. *Local Passive Transfer of Antibodies.*—At the Hospital das Clínicas, the local passive transfer of reagins was made with the sera of 9 patients. The patients' sera were filtered through the Seitz filter and a volume of 0.05 ml. was injected intracutaneously in the dorsal region of two nonallergic patients. Twenty-four hours later 0.03 ml. of castor-bean extract diluted 1:1,000 was injected in the same site, previously prepared with the serum. Comparative test injections were made only with the extract.

The sera of all of the 9 patients provoked strongly positive Prausnitz-Küstner reactions.

3. *Experimental Reproduction of Symptomatology.*—Four of the patients admitted to the Hospital das Clínicas were selected to be submitted to experimental asthma provoked by the inhalation of extract of castor-bean pomace. Two of these patients were already suffering from asthma before the epidemic; one already had allergic rhinitis and the other had already suffered from asthma or allergic rhinitis up to the time the collective type of asthma broke out.

As the allergen was used, an extract was made in the usual way, in coea solution, dialyzed and filtered, with 1,240 gammas of protein nitrogen per milliliter.

In a 36-cubic-meter carefully calked room were placed four No. 40 DeVilbiss nebulizers, one at each corner and 2 meters high. The four nebu-

lizers were connected with rubber tubes to the air injector of a vacuum pump. In each of the four nebulizers were placed 3 ml. of extract of castor-bean pomace. The nebulizers were operated for an hour.

The four patients were previously examined and did not show either symptoms or signs of asthma during a period of over 15 days. In order to remove psychological factors, the patients were not informed of the experiment and were directed to the room on the excuse of a radiologic examination.

The following were the results: after one minute had elapsed one of the patients already showed allergic nasal and eye symptoms and after two minutes she was withdrawn from the room and had developed a typical attack of asthma. The other three patients began to show symptoms after three minutes characterized by sneezes, pruritus of the eyelids, cough, and accentuated dyspnea which called for their withdrawal from the room.

TABLE I. PRINCIPAL DATA GATHERED FROM OBSERVATIONS

CASE	SEX	AGE	P.A.H.	F.A.A.	C.R. TO CASTOR BEAN	C.R. TO OTHER ALLERGENS	P.K.	EXPERI- MENTAL ASTHMA
1	F.	25	Asthma and rhinitis	-	+	+	+	+
2	F.	63	—	-	+	-	+	+
3	F.	24	Asthma	-	+	-	+	+
4	F.	20	Rhinitis	-	+	+	+	+
5	M.	33	Rhinitis	+	+	+	+	
6	M.	20	—	-	+	-	+	
7	M.	70	—	-	+	-	+	
8	M.	18	Rhinitis	+	+	-	+	
9	M.	17	Asthma and rhinitis	-	+	+	+	
10	M.	36	Asthma	+	+	-		
11	M.	9	Asthma and rhinitis	+	+	+		
12	F.	8	—	-	+	+		
13	F.	28	Rhinitis	-	+	-		
14	F.	25	Rhinitis	-	+	-		
15	F.	38	—	-	-	-		
16	M.	20	Asthma and rhinitis	+	+	+		
17	F.	35	Asthma	+	+	-		
18	M.	43	Asthma	+	+	+		
19	M.	12	—	+	+	-		
20	M.	34	—	-	+	-		
21	M.	9	—	-	+	-		
22	F.	54	Asthma	-	+	-		
23	M.	54	Asthma	-	+	+		
24	M.	20	—	-	+	-		
25	M.	39	Asthma	+	-	+		
26	F.	45	—	-	+	-		
27	M.	30	Asthma	-	+	-		
28	M.	3	Asthma	+	+	+		
29	M.	32	—	-	+	-		
30	M.	38	—	-	+	-		

P.A.H. = Personal allergic history.

F.A.A. = Familial allergic antecedents.

C.R. = Cutaneous reaction.

P.K. = Prausnitz-Küstner reaction.

The four patients had serious attacks of bronchial asthma which, in spite of the administration of epinephrine, aminophylline, cortisone and oxygen, lasted about two hours. At the end of the experiment the four patients affirmed that the symptoms had been identical with the symptoms observed in

the town of Baurú. Three physicians and two nurses who took part in the experiment and were submitted therefore to the inhalation of castor-bean extract did not show any symptoms.

DATA OBTAINED FROM HISTORY

Sex.—There were twelve female and eighteen male patients.

Age.—The youngest patient was three years, and the oldest was seventy years old. The following are the age groups of our patients.

0-10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years
6 cases	4 cases	6 cases	8 cases	2 cases	1 case	2 cases

Allergic History.—The history disclosed the following:

- a. 12 patients already suffered from asthma before Aug. 11.
- b. 6 patients suffered previously from allergic rhinitis.
- c. 16 patients had asthma for the first time between Aug. 11 and 16.
- d. 7 patients showed hereditary allergic histories.
- e. In 10 patients the asthmatic symptoms were followed and sometimes preceded by rhinitis, conjunctivitis, and pruritus of the ears, nose, palate, and eyelids.
- f. The majority of the patients rid themselves of the symptoms when they left the town of Baurú, for which reason 17 of the sick transferred themselves to the town of Agudos, 15 kilometers away. In this latter town the patients exclusively allergic to castor bean did not suffer any symptoms.
- g. The symptoms appeared again when the patients returned to Baurú. There were patients who made from four to five attempts to return, but every time they did so they had violent attacks of asthma.
- h. According to observations made by some patients, whenever it rained the symptoms disappeared or decreased in intensity. The direction of the wind also influenced it, in the opinion of the nurses and physicians of the Hospital of Baurú.
- i. The symptoms disappeared in all patients allergic solely to castor bean when the crushing mill ceased to work.
- j. A new episode, again of an epidemic nature, took place one month after the crushing mill resumed work.

DISCUSSION

The clinical data along with the cutaneous tests, the passive transfer of antibodies and the experimental reproduction of the symptomatology were sufficiently suggestive to prove we were dealing with patients who had allergic manifestations of the respiratory tract, with predominating asthmatic symptoms whose etiologic agent was the dust from the castor bean. As a matter of fact some patients (Cases 12 and 20) made three attempts to return to the town of Baurú and every time they had attacks of asthma which compelled them to return to the town of Agudos, situated at a distance of 15 kilometers. The direction of the wind and rain seemed to interfere, since some patients in the local hospital showed no symptoms on rainy days while

others became worse when the wind blew in a certain direction. This observation had already been made by Grimm in Germany, inasmuch as according to the direction of the wind the attacks took place in certain districts.

With reference to the allergen of castor-bean dust, the following points should be stressed:

1. The great capacity of sensibilization is noted, a fact already known by other authors such as Ratner with experiments on animals. The allergen is extremely potent and sensibilizes with certain facility, since in our observations 38.5 per cent of the patients had no previous allergic manifestations.

2. The allergenic source being found in the bean dust and not in the oil explains the manner in which the allergen spread itself in the atmosphere of Baurú. In that locality there is a large castor oil mill which has been operating for several years. In order to secure a better yield of oil, at the time of the epidemic outbreak the mill started a new process of extraction which consists of treating castor-bean pomace with hexane. After this treatment the cake is thrown into the grinder and thence into a "cyclone" preparatory to sacking the castor-bean pomace. During the period of sacking the ground castor-bean pomace an atmosphere loaded with dust from castor-bean residues is formed. Through ventilators this powder is in a large part transferred to the outside of the mill. This new method has probably contributed to render the allergen more diffused in the atmosphere and under more suitable conditions to sensitize. In this way it can be explained that the cases of collective asthma of an epidemic nature occurred one day after the changes made in the method of extracting castor oil.

3. The active allergenic principle studied by Barnard is soluble in water and precipitated by alcohol and is not destroyed by heat. Based on these properties of the allergen, the mill changed the method of extraction by causing the castor-bean dust to pass through water receptacles in order to retain the allergen and keep it from concentrating in the atmosphere. With this new method the mill resumed work two months ago after having been inactive for one year.

4. Two patients who had not been to Baurú for a long time had attacks of asthma a few hours after their arrival. One of them (Case 24) had not been to Baurú for six months and upon arriving in that town had an attack of asthma. This patient worked with fertilizers, including castor bean, in the town where he lived and must have thus become allergic to it. Allergy from castor-bean fertilizers is well known, and Vaughan published three cases.

Some patients continued to have asthma in spite of leaving Baurú (Case 16), owing to their being old asthmatic persons with other sensitizations. These patients, allergic to various substances, continued to have their usual attacks even during the time the mill was closed, but not with the severity observed during the so-called epidemic period.

The patients suffering from asthma exclusively from castor-bean pomace had no further attacks after the factory was closed and adopted the new protective measures.

Recently, on studying allergy to castor seed fertilizers, Small stated that scientific proof can be obtained by making the patient inhale the allergen under certain conditions, but this was not encouraged for the castor bean is an extremely potent allergen. We succeeded in the experimental reproduction of asthma on human beings provoked by castor bean (Cases 1, 2, 3, and 4) with a method that is close to natural conditions, inasmuch as the nebulization was not made with the apparatus in direct contact with the patient, and the psychic factors of suggestion were removed.

With the greater industrial development, we are convinced that identical episodes will be observed not only with castor bean, but with other potent allergens such as those derived from cotton seed, etc. It is also likely that in the vicinity of the castor oil or cotton seed oil mills there is a greater incidence of allergic manifestations, principally of the respiratory tract, than in the population in general.

SUMMARY

In August, 1952, in Baurú, a city of 60,000 inhabitants, in the State of São Paulo, Brazil, the Public Health Service was notified within a few days of 150 cases of a particular type of bronchial asthma, and nine deaths were attributed to it. The illness simulated an epidemic.

Allergic studies in 30 cases revealed that they were cases of bronchial asthma and other allergic manifestations of the upper respiratory tract brought about by allergy to castor-bean (*Ricinus communis*) dust.

The etiologic proof was made by history; strongly positive cutaneous tests; passive transfer of the skin-sensitizing antibodies, and by experimental provocation of symptoms.

The experimental reproduction of the symptoms was possible by placing 4 patients in a room in which had been nebulized for an hour a 1:10 solution of the allergen. The four patients had extremely severe attacks of asthma, one to three minutes after they went into the room.

The cases of collective asthma coincided with the changes made in the method of extraction of castor-bean oil by hexane, which occurred one day before at the large mill operating for some years in the city of Baurú.

A new outbreak of collective asthma identical with the first one was observed about a month later when the mill resumed work after a period of inactivity and observation demanded by the physicians of the Public Health Service.

With the closing down of the mill for a year no new cases of asthma of a collective nature were observed.

The mill is now working again using a method of catching the dusts in a water reservoir, based on the fact that the allergen is soluble in water and precipitated by alcohol.

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