

AN OUTBREAK OF ACUTE TOXICITY CAUSED BY EATING FOOD CONTAMINATED WITH DATURA STRAMONIUM

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ABSTRACT: We report methods used to characterize an outbreak of food-borne acute toxicity among the labour force of a cotton plantation in Middle Awash Agricultural Development Enterprise in July and August 1984. Among 1492 patients seen at the Enterprise and Ministry of Health clinics during this period, 688 (46.1%) exhibited unusual sign and symptoms. Thirty three patients required hospitalization for intensive medical care while nine patients were reported to have died due to this condition. Contamination of corn flour with pesticides was initially suspected and laboratory animal tests were carried out which failed to show any signs of acute toxicity. Investigation of the source of the corn and its processing was simultaneously conducted and revealed the contamination of the corn with seeds of an indigenous plant identified as *Daturastramoniwn*, an antimuscarinic alkaloid. These alkaloids contain hyoscyne and hyoscyamine which is known to have toxic effect on the exocrine glands, heart, and the autonomic nervous system in man. Signs and symptoms observed in the patients and preventive measures implemented are discussed.

INTRODUCTION

Middle Awash Agricultural Development Enterprise is located in western Hararghe region, eastern Ethiopia about 255 km away from Addis Ababa. The Enterprise is mainly engaged in cotton plantation in a wide area of Middle Awash plains. The work force of the Enterprise reaches about 20,000 during cotton picking and weeding seasons. Food to the workers is supplied by the Enterprise in a form of ration mainly comprising corn flour, rarely wheat flour, when supplied in excess is sold to the local town people and merchants who in turn export to the places in the neighbouring regions.

In August 1984, the Awash Agricultural Development Corporation who manages the Middle Awash Agricultural Development Enterprise requested the Ministry of Health to take measure on an illness afflicting the labour force of the Enterprise for which no description was given except suspecting food-borne toxicity. Samples of corn flour were sent to the National Research Institute of Health laboratory for food toxicity testing but all of them were reported negative. The Ministry of Health took initiative to investigate and control this illness with no further description.

Case Definition. The team which was formed by the Ministry of Health arrived at Middle A wash Agricultural Development Enterprise on August 10, 1984. The team observed few cases and went through the registers of 5 health units. After this observation, cases commonly showed dryness of mouth and throat, blurred vision, dry and flushed skin, and some neurologic abnormalities such as restlessness, confusion, talkativeness, delirium, etc. after ingestion of bread and 'tella' prepared from corn flour distributed few days ago by the Enterprise. Hence a case was defined as the occurrence of one or more of the following symptoms-dryness of mouth and throat; difficulty in swallowing; hot, dry, and flushed skin; blurred vision -within 30 minutes after the consumption of food or 'tella' prepared from corn flour distributed by the Middle Awash Agricultural Development Enterprise between July 18 and August 5, 1984, or at least one of the following neurologic symptoms or signs within 24 hours after the consumption of the corn flour -mania, talkativeness, restlessness, confusion, delirium, or other serious signs or symptoms such as seizures or coma.

This report of illness was clearly different from intoxication with food contaminated with pesticides, ergot fungus, and lathyrus peas that have occurred in Ethiopia in the past (13,14).

The team of investigators immediately started its function with the following objectives:

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- 1) to characterize the illness under question and possibly find the etiologic agent,
- 2) to recommend methods of preventing future occurrence of such illness.

CASE FINDING, MATERIALS AND METHODS

The immediate task of the investigators was to suspend the distribution of corn flour originated from the same source (main store of the Enterprise at Nazareth) and advise the Enterprise management to find other sources for their regular ration supply to the labour force. The next task was to establish a committee composed of various professions with responsibility to the local administration. The main duty of the committee was to help trace the source of the suspected corn flour. The third task was to disseminate the available information of the acute toxicity to the health authorities, storekeepers, bakery owners, farm management, cereal retailers, and the labour force.

To identify the potential cases, health records were reviewed from July 17 to August 10, 1984 for all persons who met our case definition. In addition, fifty postcases were interviewed to determine the interval between ingestion of the suspected corn flour and onset of the illness.

To confirm the outbreak was due to eight samples of the suspected corn flour obtained from stores of the Enterprise and labelled from F-100 to F-107. Part of the samples were to be fed to a batch of mice and to be observed for at least 15 days. The rest of the samples were to be tested for potential toxic agents including bacteria, fungus, yeasts, chemical residues and indigenous plants. The assay was considered positive for toxin if the mice demonstrated restlessness within 30 minutes of feeding except that the period of observation was extended to 15 days to determine the prolonged effect. All these were performed at the Central Laboratory and Research Institute (now called National Research Institute of Health), Addis Ababa. Tests were performed using thin-layer chromatography (TLC) for both identification and quantification of toxin. Each sample was analyzed and quantified according to the methods recommended by the British Pharmacopoeia (15) for known indigenous plants. Test for possible contamination with pesticides was performed using UV spectrophotometer. Bacteriologic examination was carried out for possible pathogenic organisms as recommended elsewhere by the standard methods used by the Bacteriology Division of the Institute.

RESULTS

Source of corn consumed by patients

After thorough and arduous investigation of the source of the suspected corn, the committee came up with the following report. The corn was cultivated by the southern Agricultural Development Corporation, Awassa branch, and sold to the Awash Agricultural Development Corporation few months before the outbreak. The purchased corn contained impurities such as seeds of stramonium (locally known as 'atse faris'). The corn was stored at the central store of the Enterprise, Nazareth, from where it has to go to two flour mills who have contactual relationship with the Enterprise. Owners of the flour mills have agreement to sieve any impurities found in any cereal they powder. Grain stores are occasionally fumigated with malathion by unskilled persons. The indigenous plant which was later identified as *Datura stramonium*, naturally grows in the cultivation fields. Harvesting was performed with combiners mixing the plant's seeds and leaves with the grain. The corn was sold without further processing. The committee, however, could not confirm whether sieving was regularly performed or not at the flour mills.

Description of cases

The reviewed cases (1942) and 9 deaths from registers and charts of the health units participated in the management of the outbreak showed that 688 patients met our case definition. The rest of the cased failed to include any symptoms presented other than food intoxication as the diagnosis. The majority of cases were from Amibara and Gewane farm units (538 of 688). Almost all patients complained dryness of the mouth and throat and difficulty in wallowing (647 and 688 respectively). Eighty eight percent of the patients (609 of 688) complained blurred vision. Flushed face and dry skin were among the chief complaints (426 of 688). Mania, talkativeness were more frequent neurologic symptoms (table 1).

Table 1. Symptoms of illness among 668 patients after consultation of the suspected corn-flour,

Sign & symptoms	Present	
	No. (688)	%
Dryness of mouth & throat*	647	94.04
Blurred vision with or without loss of accommodation**	609	88.62
Difficulty in swallowing**	605	87.94
Abdominal distention/discanfort	187	26.45
Vomitting	27	3.92
Dry and flushed skin**	426	61.92
Palpitation**	495	71.95
Mania**	144	20.93
Talkativeness**	323	46.95
Restlessness**	344	50.00
Deliriun**	371	53.92
Depression**	14	2.03
Exhaustion**	19	2.96
Coma**	11	1.59

* Source: Registers & charts of 3 hospitals, 4 health centres and 5 health stations.

** Criterion for inclusion as a case.

Exhaustion, depression and coma were symptoms observed relatively in only few cases, this shows that the illness was dose dependent as there was variation of dose among the cases. The most affected age group was 15-39 for both sexes which may be due to the domination of this age group in the labour force. The sex ratio was 3.3:1 which again may be due to the large number of males in the work force. The average interval between distribution of the suspected corn flour and onset of the outbreak was about 3 and a half days (table 4) whereas the average interval between consumption of the suspected flour and onset illness for the fifty postcases was about 30 minutes (data not shown). The case fatality rate was 1.31% in the cases reviewed.

Table 2. Age & sex distribution among 688 persons affected by food contaminated with *Datura stramonium*, Middle Awash, July-August, 1984.

Age in year	Male		Female		Total	
	No.	%	No.	%	No.	%
5	-	-	-	-	-	-
5-14	3	0.57	1	0.63	4	0.58
15-24	94	17.80	32	20.00	126	18.31
25-34	223	42.23	115	71.87	338	49.13
35-39	158	29.92	12	7.50	170	24.71
40-44	29	5.49	-	-	29	4.21
45-49	13	2.46	-	-	13	1.89
50-54	8	1.53	-	-	8	1.16
55+	-		-	-	-	-
Total	528	100	160	100	688	100

Among the 33 cases referred to hospitals, Addis Ababa and Metahara, the diagnosis of only 3 was known as postintoxication hysteria (Dejazmatch Balcha Soviet Red Cross Hospital). The postmortem examination performed at Menilik II Hospital did not indicate the etiology but asphyxia was recorded as the pathological finding which could be due to respiratory depression.

Laboratory Studies

After observation of presence of seeds of stramonium in the suspected corn, the laboratory investigation was geared towards identifying and analyzing the toxic content of the indigenous plant. The standard solution was prepared from the wildy growing *Datura stramonium* seeds collected alongside the road near Middle Awash. The extraction performed revealed 0.3% total alkaloids, hyoscyamine, hyoscine, and traces of atropine in 6 of 8 samples (table 3). The amount of stramonium in each sample ranged from 30 to 200 mg/kg flour which means 0.09 to 0.06 gm alkaloid/kg flour (table 3).

Table 3. Estimated content of alkaloid in eight samples of corn-flour by place of collection during the outbreak of acute food intoxication.

Samples	Content of stramonium in mg/kg flour	Content of alkaloid in gm/kg flour	Content of alkaloid in mg/150 gm bread	Place of store where samples were collected
F-100	200	0.60	90.00	Amibara I
F-101	150	0.45	67.50	Amibara II
F-102	50	0.15	22.50	Melka Werer I
F-103	-	-	-	Amibara I*
F-104	30	0.09	13.50	Mekla Werer II
F-105	100	0.30	45.00	Gewane
F-106	40	0.12	18.00	Nazareth flourmill
F-107	-	-	-	Dophen- Bolhaboo**

* This sample of flour was wheat in nature, purchased from Debre Zeit Flour Mill Factory and was used as control.

**This farm unit has its won flour mill, did not share the corn-flour distributed during the outbreak. This was also used as a control sample.

The laboratory studies for bacterial, yeast and fungal contamination revealed presence of spoilage bacteria, mould, and yeast in 6 of 8 samples. However, the bioassay failed to indicate presence of any acute toxicity even after feeding several batches of mice with the sample flour for 15 days. Traces of pesticide, malathion was detected in all samples.

Estimates of total alkaloid ingested by the patients was found difficult to quantify due to lack of information on the amount of alkaloid ingested. However, we based our estimation on rationing information given by the storekeepers. Thus, single bread was assumed to contain about 150 gm corn flour. Taking this assumption into consideration, the amount of alkaloid ingested per meal ranges between 13 and 90 mg per person, an extremely high dose for human.

When extracts of stramonium at the dose of 75 mg per kg body weight was injected into mice, restlessness was observed after 15 minutes; the mice recovered in 24 hours.

DISCUSSION

This report describes an outbreak of poisoning characterized by dryness of mucus membranes, flushed and dry skin, blurred vision, and neurological manifestations. Severely affected patients had signs of severe neurological manifestations-seizures, depression, and coma

Epidemiological and environmental investigations indicated that the illness followed the consumption of corn cultivated near Awassa, Sidamo Region. The corn flour was found to contain *Datura stramonium*, an indigenous plant that wildly grows in cereal cultivation fields. *Datura stramonium* is a solanaceous plant containing alkaloids; hyoscyamine, hyoscyne, and atropine, the sympatholytic compounds mainly affecting the exocrine glands, heart, and the autonomic nervous system (1,2,6). The marked neurologic changes observed in this outbreak were cognitive and transient except in the terminal cases.

The evidence seems to support the hypothesis that the poisoning was caused by consumption of corn flour contaminated with stramonium seeds. Hyoscine and hyoscyamine are the only toxins found in a proportion above the normal dose for therapeutic use of these compounds.

Another factor in favour of hyoscyamine and hyoscine as the responsible agents is the observation that patient's signs and symptoms were compatible with their pharmacological properties. Hyoscyamine or hyoscine (scopolamine) have similar properties of atropine. If given above clinical doses, they cause dryness of mouth and throat, thirst, blurred vision, dry and flushed skin, disturbed speech, ataxia, restless-ness, hallucinations, delirium, depression, and coma (1,3,4,10).

Extracts of stramonium has long been used as mydriatic drops. Finely powdered leaf of the plant has been used in tobaccos for relief of respiratory symptoms (2,3,9). In old days, the plant was used in arrow heads by primitive societies to poison their preys (8).

In Ethiopia, leaves of stramonium has been frequently used by priest school students who

Table 4: Pattern distribution of the suspected corn-flour and illness among 688 patients, middle Awash, July and August, 1984

Farm unit	Date of distribution	Qty. Distributed	No. of persons received	Date of illness/ingestion	No. of cases	No. of deaths	A.H.
Gewane	18.7.84	119	595	23.7.84	207	3	6
Amibara	1.8.84	179	895	4.8.84	331	6	3
Melka Werer	5.8.84	104	520	5.8.84	16	-	-
Melka Sadi*	-	-	-	19.8.84	10	-	-
Dophen-Bolhabo	-	-	-	-	-	-	-
Metahara Sugar Factory	7	7	7	2.8.84	124	-	24

* No official distribution was made but history of drinking home-made beer 'tella' was confirmed. Source: Distribution slip of Middle Awash store.

* Home-made bread was eaten prior to illness, patients were among the labour force of the Sugar Cane Plantation & Factory. The flour was purchased from

an open market smuggled from Middle Awash Cotton Plantation. Source* Metahara Hospital.

A.H. = Admission to Hospital.

believed that when the juice of the plant is taken it makes them brilliant at their oral education, a medication known as 'abisho' in Amharic. Users of this plant turn to be maniac after ingestion of alcohol even in a small quantity (Bedru, 1990).

Recent occasional poisoning due to accidental ingestion of stramonium seeds or leaves especially in children have been reported (1,4,5), however, no massive outbreak similar to the one we are reporting is so far reported.

Several authors have proved that rodents and marsupials are very tolerant to these alkaloids. In white rats, small doses (13 mg/kg body weight) is slightly sedative and analgetic, but never hypnotic. Doses between 65 and 130 mg per kg body weight were purely excitant (5). The mechanism of tolerance has been described by several authors long ago. The levoisomers the potent form of these alkaloids is rapidly hydrolysed by an esterase found in sera of rabbits and

rodents (3,4,5). The liver in situ in cats, rats, and rabbits rapidly inactivates large amount of atropine, scopolamine, and hyoscyamine. The toxicity of atropine in rats is increased by injuring the liver with carbon tetrachloride (3,4,5). We thus assumed that the quantity of alkaloids found in the incriminated corn flour samples was too small to show acute toxicity in the laboratory mice. However, we suggest further investigation to confirm this association.

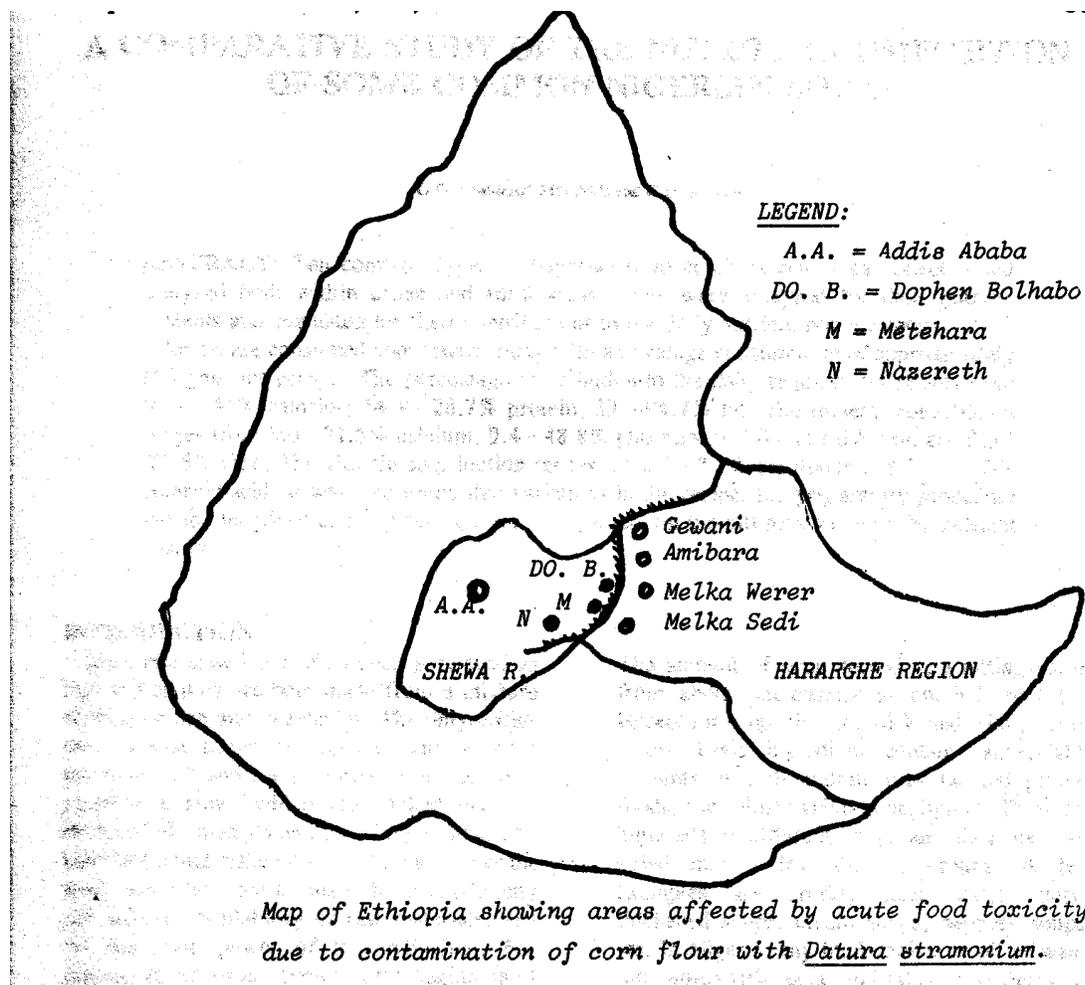
It has been described elsewhere that seeds of *Datura stramonium* contains 0.16 to 0.5% total alkaloids whereas the leaf contains 0.2 to 0.7% which is similar to our finding (0.3%) (2,9).

There are several limitations to our study. As in other explosive outbreaks with important public health implications, we chose not to undertake an analytic study to confirm our primary hypothesis -that corn flour was the source of the illness observed. The unusual nature of the illness its explosiveness, the high number of population at risk, and the fact that cases spread to different regions through smuggled corn flour, and that patients shared no common exposure other than the consumption of corn flour, and the result of tests on stramonium extracts persuaded us of this. We thus chose to undertake immediate control measures and to investigate the mechanism by which corn flour caused the epidemic. Moreover, failure of the attending health workers to record the presenting symptoms of most of the cases was the cause for eliminating 1254 cases which could have most probably been true cases. The desperate conditions observed during the management of the outbreak must have contributed to the failure. In this context, the investigation of cases could not be completed in a rigorous fashion for all reported illnesses.

Another fact is that some of the health workers who participated in the outbreak management prior to the arrival of the investigators administered atropine as an antidote for suspected food intoxication. This might have further complicated the situation.

One of the most important outcomes of this study was that without epidemiological and clinical description of an outbreak of illnesses, laboratory tests alone may not help in finding the etiology. This has been proved by certifying the corn flour samples as negative for acute toxicity by the same laboratory we used for our study.

In Middle Awash and regions afflicted with the outbreak, steps have been taken to prevent recurrence of poisoning due to *Datura stramonium*. Tons of corn flour contaminated with this plant were dumped and another tons of unpowdered corn mixed with the plant were advised to be sieved before powdering into flour. Weeding away the plant from the corn cultivation field is advised. Treatment of cases with atropine as an antidote to be discouraged, physostigmine to be used instead to reverse the action of the alkaloids. Finally, we suggest further laboratory study on extracts of stramonium leaves and seeds on animal models to determine the cause of tolerance. No new outbreak of stramonium poisoning due to consumption of corn flour have been reported in Middle Awash since August 1984.



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