

# Organophosphate Poisoning Associated with Fetal Death:

## A Case Study

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### Abstract

The increasing use of organophosphorus insecticides in agriculture and inside homes and schools, as well as its widespread existence in the environment, poses a potential health hazard. As the use of these agents increases, acute and chronic exposure has become more common. As with other organophosphates, chlorpyrifos kills insects and other animals, including human beings, because of its toxicity to the nervous system. Exposure of pregnant women to organophosphates is an important clinical entity because of its effects on two organisms—mother and fetus. There are few reports about fetal toxicity of organophosphates in the literature because of the relatively few cases reported. In this paper we report a case of intoxication from chlorpyrifos, an organophosphorus compound, during pregnancy, causing fetal death.

**Key Words:** Abortion, chlorpyrifos, organophosphates, poisoning, pregnancy.

### Introduction

ORGANOPHOSPHATE COMPOUNDS used as pesticides in agriculture are toxic not only to pests, but also to humans, whether through unintentional exposure or, especially, in suicide attempts.

Despite the widespread use of pesticides, and the fact that studies have investigated the mechanism, clinical findings, diagnosis, treatment and prognosis of the poisoning, little is known about potentially adverse effects *in utero* resulting from exposure of pregnant women to pesticides (1) due to the relatively few reports in the literature and the prohibition on evaluating the disease experimentally in pregnancy. The data found in the literature include few case reports of intoxicated pregnant women and limited animal studies. This case study covers intoxication from chlorpyrifos, an organophosphate compound, causing the death of a

fetus because of delay in therapy of the mother (who was treated successfully).

### Case

A 23-year-old primigravida female was brought to the emergency department (ED) after taking an excessive amount of chlorpyrifos-ethyl (Sarban 2 dust<sup>®</sup>) in an attempted suicide 12 hours previously. She had been taken to a rural hospital at first because she could not feel her baby's movements in the second hour after ingestion of the substance. She was hospitalized for 8 hours after gastric lavage. Then she was transported to our center after being diagnosed by fetal ultrasonography, with *in-utero* death of the fetus at gestation age of 19 weeks. (Her relatives had brought the bottle of the chemical to the hospital.) Her medical history revealed nothing significant. Her initial vital signs were as follows: blood pressure, 120/90 mm Hg; pulse, 120 beats/min; respiratory rate, 15 breaths/min; and axillary temperature, 36.7°C. Physical examination revealed a palpable uterus 2 cm under the umbilicus, fasciculation at her tongue, and miosis. There was no lacrimation, excessive urination, emesis, or bradycardia. Other systems examined were normal. Her laboratory tests were as fol-

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lows: white blood cell, 6,700  $\mu\text{L}$  (normal range: 4,300–10,300 $\mu\text{L}$ ); Hgb, 10.2 g/dL (13.6–17.2 g/dL); Hct, 30.3% (39.53–50.33%); platelets, 240,000/ $\mu\text{L}$  (156,000–373,300/ $\mu\text{L}$ ); plasma cholinesterase, 39 U/L (5,500–12,000 U/L); glucose, 78 mg/dL (70–105 mg/dL); BUN, 7 mg/mL (8–25 mg/mL); creatinine, 0.5 mg/dL (0.8–1.2 mg/dL); Na, 139 mmol/L (135–145 mmol/L); K, 3.5 mmol/L (3.5–5.1 mmol/L); ALT, 28 U/L (<41 U/L); AST, 30 U/L (5–40 U/L); LDH, 475 U/L (160–500 U/L); creatine kinase, 39 U/L (<170 U/L); and amylase, 43 U/L (28–100 U/L). A 12-lead electrocardiogram revealed sinus tachycardia.

As soon as the patient was admitted to the ED, two 18-gauge catheters were inserted and supplemental oxygen was administered at the rate of 4 L/min. Cardiac and pulse oxymetric monitoring were also initiated. Fluid replacement was initiated as 3,000 mL/m<sup>2</sup>/day. After intravenous (IV) 10 mg metoclopramide administration, gastric lavage was performed and charcoal was given through a nasogastric (NG) tube, at a dose of 1 g/kg. Atropine sulfate 10 mg IV bolus following 60 mg infusion/day was started. Simultaneously, IV 2 gr 2-PAM (pralidoxime) was given for 20 minutes in the other arm. An Obstetrics and Gynecology Department consultation was obtained for the patient's pregnancy and fetal condition. Obstetric ultrasonographic results revealed no cardiac activity of the fetus, whose biparietal diameter matched gestational age of 18 weeks 5 days. At the advice of the obstetrician, 200 mg of misoprostol was given intravaginally. Twelve hours later, she delivered the fetus by normal vaginal route. A curettage was performed for placenta residue. Autopsy and histopathological examinations were performed.

The follow-up of the patient was done by our clinic in the observation unit. Atropine infusion therapy continued for four days, and daily plasma pseudocholinesterase levels were monitored for enzyme regeneration. Her plasma pseudocholinesterase levels were not remarkably elevated (day 2: 42 U/L, day 3: 31 U/L, day 4: 51 U/L, discharge day 7: 52 U/L); no cholinergic symptoms were detected and atropine infusion was gradually stopped. She was given 2 packages of erythrocyte suspension because of vaginal bleeding after curettage (resulting in a decrease in hematocrit level) on the second day of hospitalization. On the fifth day of hospitalization, she had fever with a bad odorous vaginal discharge. Endometritis was diagnosed and proper antibiotherapy was initiated. She did not have any symptoms of toxicity, and so she was started on oral feeding. The patient was discharged 7 days after admission. One week later, she was referred for gynecologic and psychiatric therapy.

The body measurements of the fetus, with male external genitalia, according to the autopsy report, were as follows: body length, 25.5 cm; weight, 410 grams; head circumference, 17.5 cm; chest circumference, 14.5 cm; abdominal circumference, 14 cm; and length of the foot basis, 3 cm. The autopsy report listed the fetus as having an estimated gestational age of 19 weeks, based on anthropological measurements. The fetus had traumatic lesions, tool wounds or morphological defects. A blood sample of the fetus was analyzed with the Agilent GC/MS device (Hewlett Packard, with liquid-liquid extraction method). The result revealed the presence of a chemical, 264 ppb chlorpyrifos, which is an organophosphate insecticide.

## Discussion

Organophosphates, a widely used class of insecticidal compounds, have been shown to cross the placental barrier and thus potentially affect the developing fetus (2). The toxicological effect of chlorpyrifos has been studied extensively. According to Environmental Protection Agency (EPA) guidelines of the United States, chlorpyrifos has been shown not to be mutagenic (3), carcinogenic (4) or teratogenic (5). Breslin et al. evaluated its potential to produce developmental and reproductive toxicity in rats and showed that oral administration of chlorpyrifos to pregnant rats at parentally toxic dose levels was not embryolethal, embryo-fetotoxic, or teratogenic, and did not adversely affect fertility or the function or the structure of the reproductive organs (6).

In tests conducted by Dow Chemical, feeding chlorpyrifos at high doses to pregnant mice caused them to give birth to small pups with an increased incidence of skeletal abnormalities. At a lower dose, the same study found an increase in skull defects that allowed the brain to be exposed (7). In 1993, chlorpyrifos was claimed to cause neurologic disorders in humans, with *in utero* exposure, when a family had two babies with similar neurologic problems such as cerebral palsy, cataracts and seizures. It was learned that the parents were using a chlorpyrifos-containing pesticide to kill ticks to protect their first baby from Lyme disease. When their second and third babies were born with neurologic abnormalities, the doctors agreed that *in utero* exposure might have affected the mother and caused the diseases (8). Chlorpyrifos was detected in cervical mucus, sperm fluid, and human milk by German researchers, findings that suggest its serious effects on human reproduction (9).

Our patient's report of not feeling her baby's movements 2 hours after ingestion of the toxic

substance, plus the autopsy findings of suppressed maternal serum pseudocholinesterase levels, high levels of chlorpyrifos detection in fetal blood and lack of any macroscopic anomalies, lead us to conclude that chlorpyrifos is fetotoxic and that it may have been the cause of fetal death in this case. Based on our experience with the follow-ups of other pregnant intoxicated patients, we conclude that early recognition and treatment of organophosphate intoxication in pregnant women can be managed successfully without any abortion or fetal death, and that healthy babies can be delivered. We have had three other pregnant patients with organophosphate intoxication in the last five years, all of whom received medical therapy immediately after admission. One of the fetuses was in the 20th week of gestation, the other two were near term. All three women gave birth to healthy babies. The follow-ups of the babies were also normal and the oldest one is a healthy 4-year old girl today. We could not determine the name of the organophosphate compounds of those previous intoxications and of course chlorpyrifos may not have been the toxic substance. But we think that for this patient, late admission to a medical center and delay in medical therapy (2-PAM and atropine) may have been the reasons for fetal loss. The mechanism of the fetal death may have been fetal bradycardia and/or placental insufficiency because of maternal bradycardia. These sugges-

tions should be investigated and new experimental studies need to be designed.

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