

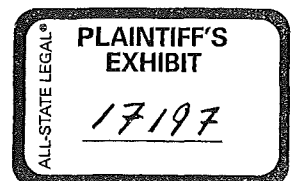
HUMAN HEALTH PROBLEMS
WITH THE HERBICIDE PARAQUAT
IN CALIFORNIA - 1965 THROUGH 1974

By

Keith T. Maddy, Staff Toxicologist

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California Department of Food and Agriculture
Division of Pest Management, Environmental
Protection and Worker Safety
Worker Health and Safety Branch
1220 N Street, Sacramento, California 95814



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Keith T. Maddy, D.V.M., M.P.H.
Staff Toxicologist
Agricultural Chemicals and Feed
California Department of Food and Agriculture

INTRODUCTION

The herbicide Ortho Paraquat CL, containing 29.1 percent by weight of paraquat dichloride (1,1'-Dimethyl-4,4'-bipyridinium dichloride), hereafter referred to as, paraquat, was first registered in California in 1965. The registrant is the Ortho Division, Chevron Chemical Company, of the Standard Oil Company. Paraquat's usage in California has increased since its introduction until in 1973, 374,009 pounds were reported applied to 822,769 acres of land. Its largest single use is as a cotton defoliant; in 1973, 161,289 pounds were reported applied for this purpose to 423,914 acres of cotton. Prior to mid-1974, many of the uses of paraquat were not reportable so the above figures understate the actual usage.

Paraquat is effective when applied as a contact desiccant. If application is not done with extreme care, the effects of any drift are soon apparent on nearby non-target plants as spotting or other plant injury symptoms.

Since registration of paraquat in California, there have been at least seven human deaths, a number of disabling injuries, and numerous illnesses due to exposure to paraquat. The deaths have been primarily due to accidental ingestion; the injuries have been primarily eye, skin, and systemic exposures of users of paraquat.

There have been human health problems with paraquat since its development in the British Commonwealth Countries in 1962. An article prepared by the editors of the British medical publication, Lancet, in 1971 stated that by that date information had been collected on 124 cases of fatal poisoning from this agent throughout the world. Based on comparisons of cases that have been diagnosed, reported in medical literature, and collected by official agencies and manufacturers as compared to those that actually occur without being so reported, it can reasonably be estimated that several hundred persons have died from paraquat poisoning world-wide in the past twelve years. Some of the cases are reported as suicides, others usually follow accidental drinking of paraquat. There is no way of determining the number of misdiagnosed and undiagnosed fatalities due to exposure to this herbicide.

The Environmental Protection Agency Bibliography, No. 72-30, has a good list of references of human exposures to diquat and paraquat. (See Attachment One.)

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FATAL CASES

To our knowledge, none of the seven fatal cases of paraquat poisoning in California that have come to the attention of the California Department of Food and Agriculture since 1965 have been reported in the medical literature.

Fatal Case No. 1: Riverside County, 1966. A 47 year old male farm worker who was applying paraquat carried two jugs on the tractor fender, one containing paraquat, the other one water. He thought he was going to drink water but took paraquat into his mouth instead. He spit it out and immediately sought medical attention. He died two weeks later of lung fibrosis in spite of all medical efforts to save him.

Fatal Case No. 2: Marin County, 1972. A pesticide applicator, being aware how effective paraquat was, poured some into a soft drink bottle without adding a new label and took it to his brother's home for weed control. He set the bottle down within handy reach of a four-year old nephew who assumed the material was something to drink. The child sipped from the bottle, spit it out, and then began to vomit severely. The vomiting continued for 12 hours. The boy complained of how bitter the paraquat tasted. The boy was under medical attention within one hour of ingestion. Paraquat levels in the urine were ranging between 290 and 460 ug/l, seven to ten days after ingestion. Thirteen days after ingestion the typical pulmonary symptoms began, also with the development of bilateral pneumothoraces. Respiration became progressively more difficult, and in spite of all possible medical efforts, he died of suffocation and cardiac arrest on the nineteenth day after ingestion of the poison. At post mortem, the lungs were found to be extensively filled with fibrous tissue.

Fatal Case No. 3: Santa Clara County, 1972. A short-term county jail inmate, reported to be a thirty-three year old male with a wife and seven children, was working as a trustee in a park. In a tool shed he noticed an unlabeled, colored liquor bottle containing what he thought was wine or whiskey. He sipped some, spit it out, and immediately sought and received medical attention. The exposure was considered so minimal that he was released from medical care to return to previous duties. Two days later, he began to experience breathing difficulties and he was returned for more medical attention. Seven days after the exposure, he died of suffocation due to hemorrhagic consolidation of the lungs, proliferative alveolitis, foci of fibrinous exudate in the septae, and early evidence of fibrosis. Grossly, the lungs were unusually heavy and firm. At postmortem, 1.6 ppm paraquat was found in the blood and 2.4 ppm in the liver.

Fatal Case No. 4: Del Norte County, 1972. A pesticide applicator according to associates handled and applied paraquat in a careless manner for two days. The application was at the rate of one and one-half quarts per acre. The third day he experienced flu-like symptoms and he sought medical attention. He had a variety of symptoms, including dizziness, chest pains, and bleeding within

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the intestinal tract. He died of cardiopulmonary failure fifteen days after applying paraquat. At postmortem, pulmonary fibrosis was not mentioned in the report. The exact cause of death in this case was not confirmed as due to paraquat; body tissues or fluids were not submitted for laboratory analysis for paraquat.

Fatal Case No. 5: Los Angeles County, 1974. A 16-year old male saw what he later said he thought was a soft drink in an open unlabeled bottle on a school official's desk. He sipped some and then spit it out. He rinsed his mouth out with water. He was taken to a hospital and received extensive medical care. He died twenty-one days later of suffocation due to lung fibrosis. Paraquat was found in the urine and valiant medical efforts were made to save this boy's life, including the importation of some experimental drugs from England. A school employee had poured a small amount of paraquat from the original one-gallon pesticide container into a small bottle which was not relabeled.

Fatal Case No. 6: Orange County, 1974. A 16-year old male who was reported despondent drank some paraquat with suicidal intent. He said he spit it all out immediately. He died of suffocation 21 days later due to lung fibrosis. Equally strenuous efforts were employed to save this boy's life, to no avail. This paraquat had been purchased six years before by the father and had been kept in the garage.

Fatal Case No. 7: Orange County, 1974. A 54 year old male with suicidal intent drank about one cup of paraquat. He died 20 hours later despite immediate medical attention.

Other diagnosed fatalities may have occurred and were not brought to the attention of the Department of Food and Agriculture. There have also been some suspect fatal cases but the death was recorded only as a poisoning. One such case occurred in Los Angeles involving a fifty year old male gardener in August 1970. The man had considerable exposure to paraquat as an applicator prior to going through a syndrome of symptoms typical of paraquat poisoning. The physician reported the case as poisoning, possibly food poisoning.

NONFATAL CASES

Nonfatal cases range in severity from cases of mild inflammation of the eye or skin to near fatal outcomes. Fisher, et al, in 1971 reported a case cared for in San Francisco of a forty-nine-year-old man who sipped about ten ml. of paraquat by mistake. He developed the typical syndrome seen in these cases: burning discomfort in the mouth, pharynx and esophagus, severe nausea and vomiting, and extreme headache. He had some loose stools. He became well enough by day three that he returned to work but then symptoms of kidney failure began. Forced diuresis was instituted and peritoneal dialysis was also used. Significant amounts of paraquat were found in the urine and dialysate through day thirteen, but most was gone by day twenty-one. Fine pulmonary rales were heard from days ten through twenty-one and chest roentgenograms showed the gradual accumulation of small bilateral effusions between

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days twelve and seventeen. An area of pulmonary atelectasis developed, diffusing capacity for carbon dioxide by the single breath technique remained low. Surprisingly, in spite of extensive lung injury, this patient survived.

Each year since paraquat has been registered about 10 to 20 cases of illness due to paraquat exposure have been reported by California physicians on Doctor's First Report of Work Injury Forms to the Department of Industrial Relations and then to the State Department of Health. Recently, some details of these reports have been shared with California Department of Food and Agriculture. There also have been a disturbing number of work injury reports revealing symptoms similar to paraquat exposure, but which give the cause as "herbicide" or "weed killer". In 1973 and this year, we have been following up a number of these cases and have in fact determined a few of them to have been paraquat exposure cases.

Early in 1974, the Department of Health summarized symptoms reported on Doctor's First Report Work Injury Forms of 19 of the paraquat exposure cases reported in 1973 (see attachment). We now find this report, if misunderstood, can be misleading as inferring that all of these cases were mild and that recovery was probably an uneventful outcome.

For example, in the State Department of Health report, the case listed as "age unknown" was found upon our follow-up investigation to be a Tulare County adult male farm worker who for some reason had not given his age. With a hand held spray nozzle, he was spraying paraquat mixed at the rate of one quart in one hundred gallons of water on weeds in a walnut grove. He did not mix or load this pesticide. He only worked with the dilute spray. He said he did not wear special protective suiting, a respirator, or a face shield. After working at this one week, he became quite ill and went to a doctor, exhibiting symptoms of vomiting, weakness, severe headaches and shortness of breath. When an agricultural inspector first interviewed him three weeks after the exposure, he was still quite weak and short of breath. His physician stated that his X-ray revealed an emphysema-condition. He had been in good health with no breathing problems prior to this incident. Unfortunately, urine samples were not analyzed for paraquat content. He remained too ill to work for six months, and two years later, he was still experiencing severe breathing difficulty and was unable to work when last interviewed.

As another example, four of the reported cases occurred to Los Angeles city and county employees and our follow-up investigations revealed more extended illnesses beyond those suggested in the first report. The four affected employees said several other employees became quite ill while handling paraquat. The four affected employees reported early symptoms of headache, bitter taste in the mouth, and dizziness. Sometimes, these symptoms would be followed by a stuffy feeling in the nose, a sore throat, and a tightness in the chest.

Our Department followed one of these cases in detail. This adult male was still unable to work for two years after exposure to paraquat when last interviewed and he had great difficulty during this period arranging for support of a wife and two boys. Prior to the onset of his illness he had regularly applied paraquat to grass and weeds with a

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back-pack Hudson Sprayer. He had several episodes of what he thought was flu. He suffered headaches, dizziness, bronchitis, kidney pain, bleeding into the intestinal tract, muscle spasms, blurred vision, a bitter taste in the mouth, difficult breathing, a tightening sensation in the throat, swelling of cervical lymph nodes, and painful urination. He continued to work for several weeks while having these symptoms and he was referred to several physicians without a definite diagnosis being made. Then after spraying paraquat for five consecutive days, he became quite sick. He fainted and was taken to the hospital in a coma. He was treated in the hospital for six weeks before his urine was collected and tested for paraquat content. A physician sent the urine in for paraquat analysis and 2 ppm of paraquat were found. He received extensive treatment for pulmonary, liver, and kidney problems. Two years later he still had only 50 percent of his lung capacity, had blurred vision, lacked coordination, complained of headaches, and a burning sensation when he urinated. He was unable to work and reportedly had suicidal intentions. At the time of preparing this report, this man still remained under a physician's care because of the poor condition of his lungs and liver and was again in a hospital.

During 1974 I gave numerous talks on pesticide safe handling practices throughout the state to farmers and pesticide applicators. In each of these talks I listed the pesticides with major human safety problems, such as parathion, phosdrin, methyl bromide, and paraquat, and safer ways to handle them. In questions, comments, and conversations after these meetings, I became concerned by the frequency with which persons who had applied paraquat mentioned problems of severe headaches, dizziness, shortness of breath, nose bleedings, and of how few of these persons said they sought a physician's attention after experiencing these symptoms.

When paraquat is applied, there are often drift problems to nearby crops. Drift to spinach and other crops soon to be eaten by man are of concern. An example of this type of problem occurred in 1973 in San Joaquin County. Paraquat was being applied by helicopter at the quite concentrated rate of one quart in ten gallons of water in a field 200 yards from a home and garden site. In making a procedural turn at the end of the field the helicopter passed directly over the house and garden and the lady resident noticed that spray drops were falling from the nozzles, but she gave no thought to it at the time. The next day fresh broccoli, chard and chicory were brought in from the garden and prepared for a meal that was eaten by two adult males and two adult females. Upon eating the meal, all four experienced a severe burning sensation in the throat and all complained about a bitter taste to the food. Previously, the vegetables from this garden had tasted quite good. The two women developed lesions in their mouths and placed themselves in the care of two different physicians. Five days after the application, our Department heard about the situation and agricultural inspectors collected samples of the garden plants. Between 1.2 and 1.5 ppm of paraquat was found on the plant leaves by our laboratory.

Besides Ortho Paraquat CL, we also have registered in California another product, Ortho Spot Weed and Grass Killer, which is 0.44 percent, by weight, paraquat dichloride. This product is widely available in garden supply stores and grocery stores throughout the state. This is a

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small foam spray pressurized can that contains paraquat in a ready-to-use dilution at a concentration also commonly used when Ortho Paraquat CL is diluted. We have concerns about the safe use of this Ortho Spot Weed and Grass Killer. It is widely used to kill grass around homes, in cracks in sidewalks, in rock borders, and in other non-crop areas around houses and schools. These are favorite play areas for children.

A problem of this type was brought to our attention in May 1974 in Sacramento. A gardener for an apartment house had made an illegal (conflict with label) application of Ortho Paraquat CL to weeds and grass in a rock border beside a sidewalk in front of an apartment. Two days later a four-year-old girl was playing on the sidewalk and she picked up a rock and put it in her mouth. This set off a vomiting syndrome that lasted for six hours. Medical attention began one hour after onset. On hearing of the case four days later, I advised the physician of a source for laboratory analysis of urine for paraquat content. A urine sample was collected and found to be negative for paraquat. The child was checked for pulmonary changes by clinical examination and by X-ray; no changes have been observed to date. We collected rock samples four days after application but because of soil contamination our laboratory considered the sample unsuitable for assay. Then, nine days after application, grass samples were collected from the same spot the child played and a level of 29 ppm of paraquat was found. Had the gardener made the application with the Ortho Spot Weed and Grass Killer, it would have been legal but the same amount of paraquat dichloride probably would have been applied to the area and the hazard to children would have been just as great. The Ortho Paraquat CL takes note of the hazard to children and prohibits by its label the use of this material where children or pets will contact the sprayed vegetation.

We can take little comfort in the fact that we've received few reports of problems with the Ortho Spot product. Our Department receives few of the reports of human exposures to pesticides that occur in urban areas. For example, in 1973, the Poison Control Center in Los Angeles received 27,705 calls, primarily from physicians, each handling a poison exposure case most of which were ingestion cases. Over 3,000 of these were economic poisons and technically were pesticides and about 100 of these pesticide cases dealt with herbicides. The kind of herbicide was not recorded in any of these cases.

A large unstudied area of concern is the cotton harvest. Much of the cotton of the state is sprayed with paraquat just prior to harvest. Cotton gin trash often contains up to 5 ppm of paraquat. We don't know the nature of the hazard to the driver of the cotton picker working in the cotton-harvester dust which at times is very heavy. Likewise, there may be a hazard to the tractor driver hauling the harvested cotton to the gin, and particularly there may be a hazard to the workers in the gin.

In my previous position as Chief of the Pulmonary Diseases Branch, National Heart and Lung Institute of the National Institute of Health, I became aware of the recent major research efforts of that Institute and the National Institute of Occupational Safety and Health being undertaken to determine the reasons for the high incidence of serious lung disease in cotton gin workers. The National Institute of Occupational Safety

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and Health recently reported that the health hazards to gin workers were of a major order of magnitude, needing immediate correction to prevent damage to workers' lungs. Although the irritant effect of pieces of the cotton plant are considered as the primary problem, the possible role of paraquat in the problem has been given little consideration.

EXPERIMENTAL DATA

A question can be asked, "Why did the Department register this pesticide in 1965 if it leads to so many problems?" In looking at the rather sketchy data that was submitted at that time, there was little hint of problems that subsequently developed. The oral toxicity to rats was then calculated and reported on a single dose exposure in the range of 120 to 150 mg. ion/kg body weight. Kimbrough and Gains have more recently determined that a ninety-day oral dose LD₅₀ in female rats is 21 mg/kg with a chronicity factor of 2. More recent work has shown a wide range (ten fold difference) of toxicities of paraquat for animals. It now appears that man is among the more susceptible to poisoning. Only 10 to 15 ml. of the commercially available paraquat (with paraquat dichloride content commonly 20 percent in the British formulations and 29 percent in the formulations in the United States) has been found to be fatal in a human adult by ingestion. Dermal toxicity values on an mg/kg basis are almost the same as the oral toxicity values.

A number of early animal toxicology studies were quite short term and did not reveal injuries or deaths that developed later. For example, the data presented by the registrant at the time of initial registration stated that a 25 percent solution of technical paraquat dichloride in the rabbit's eye showed a normal eye at three days. Sinow and Wei at the University of California in 1973 reported "Exposure of the eye of rabbits to 0.2 ml of paraquat at concentrations ranging from 6.25 percent to 100 percent of the Ortho Paraquat CL (242 mg/ml) resulted in a dose-related toxicity to the eye. Maximum effect was observed nine days after administration. At the 6.25 and 12.5 percent concentrations, severe conjunctival reactions were observed, with some instances of slight corneal damage at the 12.5 percent level. The iris became congested and swollen, corneal opacification increased, and a pannus reaction occurred at concentrations of 25 and 50 percent." An unexpected finding was the death within six days of all of the animals that had received the 100 percent concentration in at least one eye and the animal that had received the 50 percent concentration in both eyes.

Concerning worker health problems as the registrant predicted them in 1965, their data stated in summary "There should be few worker hazard problems."

In 1974 when we notified the registrant that the worker hazards of this product were serious and of concern, they sent us the summary of Swan's work conducted in Malaya that concludes surprisingly with the statement that ordinary care in personal hygiene is sufficient to prevent any hazard from surface injury or from systemic absorption. We have obtained the original paper and must conclude that while the exposures and injuries encountered in this study which the author minimizes, may have been acceptable at one time in Malaya; they would not be acceptable

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for uses of the product in California.

In the Malaya study, in order to separate mixing and loading exposure from applicator exposure, the foreman did the mixing and loading of the worker's back-pack sprayer equipment. The foreman suffered sufficient airborne exposure that he developed hemorrhage from the nose. In two separate studies, workers were divided according to the use of no protective clothing and various combinations of protective clothing. The studies covered twelve weeks. There were pre, mid, and post physical examinations. Chest films were taken, but no pulmonary function studies were done. Paraquat was found in the urine of 50 percent of the workers when working in dense foliage without protective clothing. However, even when working in short foliage and wearing protective clothing, seven percent of the workers were found to have paraquat in their urine. In the first study, one man suffered skin damage of the scrotum and was hospitalized for 14 days, and he continued to have further skin problems when he was returned to work. In the second study, in the normal clothing group, three had skin irritations, one on the genitalia. In the two groups wearing protective clothing, there were four cases of skin problems lasting up to a week. One man developed epistaxis. None of the applicators in Swan's study were exposed to any dilution stronger than 1 to 400 of the paraquat formulation sold there. It consists of 20 percent technical paraquat dichloride. This is not a good safety record to be so widely quoted in summary form as a demonstration of the safety of paraquat for applicators. In California, it is common practice for ground applicators to mix and load the paraquat into their own spray equipment; as a result, they are exposed to the concentrate as well as to the dilute concentration. Ground applicators are also allowed to handle concentrations of spray solution more concentrated than 1 to 400. A ground applicator may put two quarts of paraquat in 50 gallons of water for application, resulting in a 1 to 100 dilution. Consequently, he uses and is exposed to spray that is more than four times as concentrated as that to which the subjects of Swan's study were exposed.

We register more than 10,000 economic poisons with different labels for use in California. Only about 65 of the toxic chemicals used in these products appear to be repeatedly involved in producing significant human health problems. Paraquat should probably now be considered one of our major health-problem pesticides, along with parathion and phosdrin. The organophosphates are serious problems, but at least there are excellent antidotes (atropine sulfate and 2 P.A.M.) to use to treat persons when they become poisoned. After treatment of organophosphate poisoning, reasonably prompt recovery can be expected. There is as yet no satisfactory treatment for paraquat poisoning and it is difficult to prevent all worker exposure to this product.

We have taken several restrictive actions recently in the handling of Ortho Paraquat CL which has about eliminated its use from the urban areas in particular as well as other areas that may be frequented by people. We have also issued safe handling guidelines for workers. (See Attachment Number Four.)

Kimbrough of EPA recently stated, "More information is also needed on the final fate of patients who have recovered from acute paraquat poisoning. What are their lung functions if followed over a period of

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time? Does long term low level exposure to paraquat affect function in persons exposed occupationally? Studies of this nature are sparse and usually conducted over a brief period of time."

CONCLUSIONS

It is recognized that paraquat is a very useful chemical to destroy unwanted vegetation; however, there are available chemical substitutes for all of its uses, and most of them have negligible toxicity problems. The problems to human health that the continued registration of paraquat poses has led the Department to consider the possible cancellation of the registrations of Ortho Paraquat CL and Ortho Spot Weed and Grass Killer. The Environmental Protection Agency should be encouraged to study the situation nationwide. Certainly this is not just a California problem. EPA officials informed us of two human deaths in Hawaii, one in Missouri, and one in Pennsylvania due to paraquat ingestion in 1974.

Less drastic approaches than cancellation of registration in order to solve the human health problems due to paraquat should be seriously considered. (1) Paraquat could be sold in a far more dilute solution. (2) It could be formulated as a gel or as a high viscosity flowable preparation. (3) It could have a foul odor added. (4) An unappealing color such as black could be added. (5) An emetic could be added. (6) Immediate requirements by regulation for closed-system transfer from the container into a mix tank might eliminate the more serious eye and skin damage cases, finger-nail-loss cases and skin exposures with possible absorption problems that now result from spills of the concentrate. All these actions, plus those recently imposed on severely restricting sales to permit holders only, should minimize the possibilities of accidental ingestion.

The most important potential human health problem has not yet been evaluated. This is the long-term effects of exposure to low levels of paraquat on the human body and particularly the human lung. Even if all back-pack application were stopped and even if tractor-driver and pilot applicators were required to wear appropriate air filtration breathing equipment, regardless of environmental conditions, the problems of exposure of persons not involved in application work by drift of the pesticide aerosol from the target site cannot be solved at this time. The hazard of paraquat residues on plants that man is later exposed to such as during the cotton harvest and cotton ginning has not yet been studied.

Additional studies might lead to safe handling techniques, new formulations, some changes in the basic chemical, the development of an antidote, and the development of effective therapeutic regimens. However, if the registration of products containing paraquat is to be continued, the registrants should be required to initiate a study on long-term effects of exposure of man and other mammals to low dose levels of paraquat. The registrant should also be required to develop safer formulations.

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Case ID: 220300429
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ATTACHMENTS

- EPA, Bibliography Number 72-30. Human Exposures to Diquat and Paraquat. 1972
- (2) California. Department of Health - Illnesses of Employed Persons due to Exposure to Paraquat as Reported by Physicians in California in 1973.
- (3) Swan, A. A. B., Exposure of Spray Operators to Paraquat. Brit. Jr. of Int. Med., Vol. 26, page 322, 1969.
- Information on Personal Safety Precautions on Using Paraquat in a Safe Manner.

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