

# Clinical features and prognosis of paraquat poisoning in French Guiana

## A review of 62 cases

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### Abstract

Paraquat is a nonselective contact herbicide of great toxicological importance, being associated with high mortality rates. Because of its high toxicity, the European Union withdrew it from its market in 2007. The aim of this study is to analyze all cases of paraquat poisoning hospitalized in French Guiana in order to assess their incidence and main characteristics.

Medical records of all paraquat intoxicated patients hospitalized from 2008 until 2015 were reviewed in this retrospective study. Demographics, clinical presentation, and laboratory data were evaluated.

A total of 62 cases were reviewed. The incidence of paraquat poisoning was 3.8/100,000 inhabitants/year. There were 44 adults and 18 children younger than 16 years of age. The median ages were 31 years [18.08–75.25] in adults and 13.4 years [0.75–15.08] in children, respectively. The median duration of hospitalization was longer in children [15.5 days (1–24)] than in adults [2 days (1–30)],  $P < .01$ . The majority of cases was due to self-poisoning (84%).

Children had ingested a lower quantity of paraquat [48.8 mg/kg (10–571.1)] than adults [595.8 mg/kg (6–3636.4)],  $P = .03$ . There were more deaths among adults (65%) than in children (22%),  $P = .004$ . The severity and outcome was determined primarily by the amount of paraquat ingested.

In conclusion, French Guiana has the largest cohort of paraquat poisonings in the European Union. The major factor affecting the prognosis of patients was the ingested amount of paraquat. The administration of activated charcoal or Pemba, in situ, within the first hour after ingestion of paraquat is essential.

**Abbreviations:** AKIN = Acute Kidney Injury Network, CT scan = computerized tomography scanner, NAC = N-acetyl cysteine, NADP = nicotinamide adenine dinucleotide phosphate, NADPH = nicotinamide adenine dinucleotide phosphate hydrogen.

**Keywords:** activated charcoal, French Guiana, high death rate, high incidence, paraquat poisoning, Pemba

## 1. Introduction

Paraquat (1,1'-dimethyl-4,4'-bipyridylum dichloride) is one of the most widely used herbicides, discovered in 1955 and developed in the early 1960s by Imperial Chemical Industries, now Syngenta.<sup>[1,2]</sup> It held the largest share of the global herbicide

market until recently overtaken by glyphosate.<sup>[3]</sup> Paraquat is sold in about 130 countries for use on large and small farms, plantations and estates, and in nonagricultural weed control. It is a quick acting, nonselective herbicide, which destroys green plant tissue on contact and by translocation within the plant.<sup>[4,5]</sup> However, this product is highly toxic for humans and most

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animals. Its ingestion (often for suicide) can cause multiple organ failure, including liver insufficiency and lung fibrosis that can be life-threatening because of respiratory failure. The paraquat inhibits the reduction of nicotinamide adenine dinucleotide phosphate (NADP) to nicotinamide adenine dinucleotide phosphate hydrogen (NADPH), resulting in the overproduction of reactive oxygen and nitrite species that destroy the lipids of cell membranes. As paraquat is taken up against a concentration gradient into the lung, there is inflammation, with leukocyte recruitment and late pulmonary fibrosis, leading to hypoxemia unresponsive to treatment. This is usually confirmed by radiological findings.<sup>[6,7]</sup>

Paraquat poisoning is very serious. Most victims, including those who have ingested a small amount, will die from Paraquat poisoning.<sup>[8–13]</sup> In the majority of cases, the cause of death is pulmonary fibrosis. Because of its high toxicity, the European Union withdrew paraquat from its market in 2007.<sup>[14]</sup> Paraquat is also banned in French Guiana.

French Guiana is an overseas department and region of France, situated on the north-eastern coast of South America (Fig. 1). French Guiana is bounded by the Amapa state of Brazil to the south and east, Suriname to the west, and the Atlantic Ocean to the north-east. The Maroni River forms the French Guiana–Suriname border in the west, and the Oyapock River forms the border with Brazil. The population of Guiana (about 250,000) consists of a majority of mixed African and French ancestry (Creoles), with minorities of metropolitan French, Brazilians, Surinamese, Haitians, and other Caribbeans, Chinese, and Laotians. As a part of France, French Guiana is part of the European Union and the Eurozone. While the sale of paraquat has been banned in French Guiana since 2007, this pesticide remains freely available in neighboring countries (Suriname, Brazil), making it accessible to residents of French Guiana, and

therefore increasing the number of paraquat poisonings reported in French Guiana.<sup>[15–17]</sup>

The aim of this study is to analyze all cases of paraquat poisoning hospitalized in the 3 main hospitals in French Guiana in order to assess their incidence and main characteristics.

## 2. Methods

### 2.1. Inclusion and exclusion criteria

From the 1st of January 2008 to the 31st of December 2015, we included all consecutive patients with paraquat poisoning, admitted in the 3 tertiary referral hospitals in French Guiana, localized in Cayenne, Kourou, and Saint-Laurent-du-Maroni (Fig. 1). The main exclusion criterion was a negative paraquaturia.

### 2.2. Data extraction

We collected information on patient demographics, clinical presentation, hospital course, laboratory findings and outcomes, radiological studies, and clinical follow-up from the medical chart databases using Excel.

### 2.3. Ethical consideration and regulatory

Patients' medical records were retrospectively reviewed, and all data collected were anonymized in standardized forms according to procedures of the Commission Nationale de l'Informatique et Libertés (the French information protection commission). Moreover, the patient anonymity was guaranteed.

### 2.4. Data analysis

We first describe the demographic characteristics, clinical features, laboratory findings, and outcomes. The variables compared between survivors and nonsurvivors are the amount of ingested paraquat, the serum creatinine level, the administered treatment, the timing of such treatment, and the Yamaguchi score and Acute Kidney Injury Network (AKIN) stage (predicting the prognosis for patients with acute paraquat intoxication), and the outcomes.

Data are presented in numbers and percentages for qualitative values, in means, standard deviations, and medians for quantitative values. Data are analyzed using R software (R Core Team 2015). Categorical variables were compared using the  $\chi^2$  test or Fisher exact test (as appropriate) and continuous variables were compared with the Mann–Whitney \*U\* test. *P* values < .05 were considered statistically significant.

## 3. Results

### 3.1. Overall characteristics of patients

The annual incidence of paraquat poisoning was 3.8/100,000 inhabitants/year. There were more cases of paraquat poisoning in 2015 than in 2008 (Fig. 2). Sixty-two patients were included (30 males and 32 females). There were 44 adults and 18 children younger than 16 years. The median ages were 31 years [18.08–75.25] in adults and 13.4 years [0.75–15.08] in children. The median duration of hospitalization was higher in children [15.5 days (1–24)] than in adults [2 days (1–30)], *P* < .01. Regarding the place of residence of the patients, we noted that 67% came from Maroni (Saint Laurent, Papaïchton, and Maripasoula), such as easier access to the chemical due to geographical location,



Figure 1. Map of French Guiana.

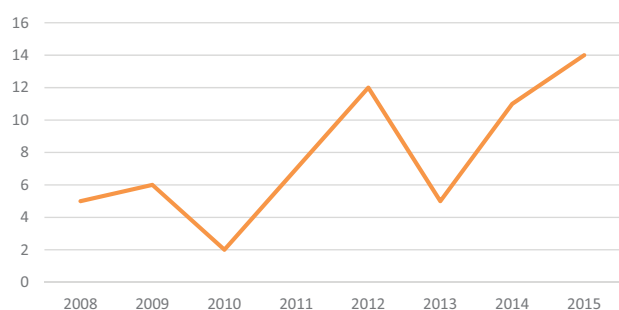


Figure 2. Annual number of paraquat poisonings.

near to the Suriname. No cases occurred in the east (mainly populated by Native Americans). Nearly 84% of children had no psychiatric history.

### 3.2. Clinical and biological manifestations at presentation

All the included patients had vomited before being admitted to the hospital. However, 22 patients (32%) had epigastric pain and

inflammation of the oral mucosa. In 13 patients, paraquat was detected at the same time in gastric fluid and urine. These patients all had lesions on oesogastroduodenal fibroscopy. Fifty-five percent of the patients had a liver cytolysis (Table 1). The mean serum creatinine was significantly higher on admission in the deceased patients ( $81.7 \mu\text{mol/L} \pm 34.4$  vs  $159.7 \mu\text{mol/L} \pm 42.8$ ). Fifty percent of adult patients with creatinine  $> 120 \mu\text{mol/L}$  on admission, died. In 2 patients, we did not have a second creatininemia, but the initial value was very high (737 and  $446 \mu\text{mol/L}$ ).

### 3.3. Emergency management of poisoned patients

The most common gastric decontamination method carried out for the patients was gastric lavage and charcoal in 44 cases (71%). Two patients received a mixture of water and Pemba immediately after ingesting paraquat, while waiting to be taken to hospital.

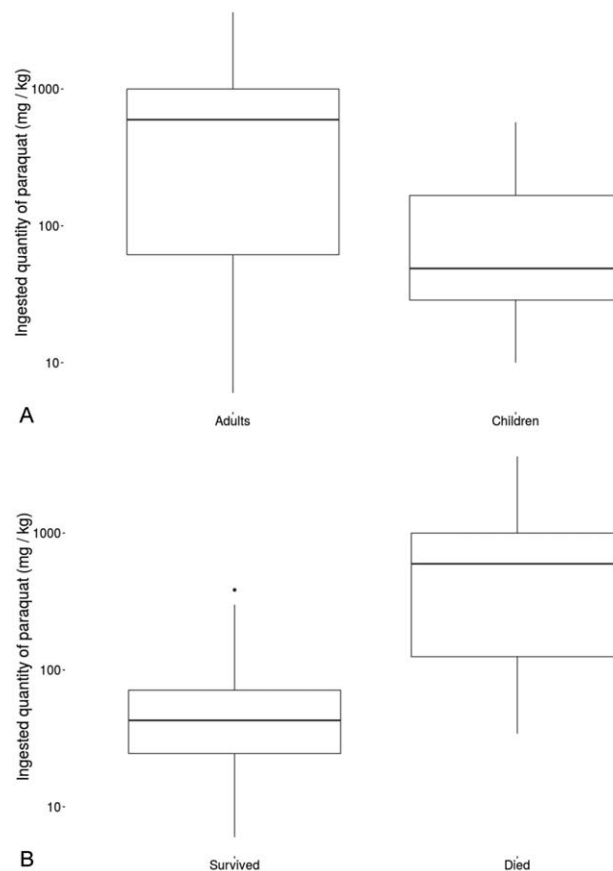
### 3.4. Medical treatments

In 31 cases (50%), treatment was carried out by corticosteroids, by cyclophosphamide in 36 cases (58%), and by N-acetyl cysteine

**Table 1**  
Comparative characteristics: survivors and nonsurvivors.

Characteristics	Number (%) of patients		OR	P
	Survivors	Nonsurvivors		
Admitting hospital			–	.4
Cayenne	15 (60)	10 (40)		
Saint Laurent	11 (37.9)	18 (62.1)		
Kourou	2 (50)	2 (50)		
Flumicil			1.94 (0.53–7.46)	.3
Yes	16 (42.1)	22 (57.9)		
No	10 (58.8)	7 (41.2)		
Solumedrol			0.24 (0.07–0.83)	.01
Yes	18 (64.3)	10 (35.7)		
No	8 (29.6)	19 (70.4)		
Cyclophosphamide			0.50 (0.15–1.66)	.3
Yes	17 (54.8)	14 (45.2)		
No	9 (37.5)	15 (62.5)		
Dexamethasone			0.72 (0.19–2.64)	.7
Yes	9 (52.9)	8 (47.1)		
No	17 (44.7)	21 (55.3)		
Gastric lavage/activated charcoal			2.1 (0.6–7.2)	.3
Yes	17 (43.6)	22 (56.4)		
No	13 (61.9)	8 (38.1)		
Gender			0.9 (0.28–2.81)	1.0
Male	13 (50)	13 (50)		
Female	15 (46.9)	17 (53.1)		
Age			0.16 (0.04–0.7)	.004
Adult	14 (35)	26 (65)		
Child	14 (77.8)	4 (22.2)		
Delay ingestion/first treatment (d, m, r)	2.5 (0.3–23)	1.3 (0.2–22)	–	.07
Amount of paraquat ingested, mL	10 (0.6–100)	20 (0.6–200)		.001
Elevated serum creatinine			4.7 (1–25)	.04
Yes	5 (20.8)	19 (79.2)		
No	9 (56.3)	7 (43.7)		
Yamagushi Score				.01
1	12 (92.3)	1 (7.7)		
2	5 (55.6)	4 (44.4)		
3	4 (17.4)	19 (82.6)		

Delay ingestion/first treatment (d, median, range).  
OR = odds ratio.



**Figure 3.** (A) Comparison of ingested quantity of paraquat between children and adults. (B) Outcome according to the quantity of paraquat ingested ( $P < .01$ ).

(NAC) in 44 cases (71%). No patient has benefited from antioxidant. Only 1 patient was hemodialyzed.

### 3.5. Chest radiographic findings

Pulmonary radiography was performed in all patients. Only 15 patients had a chest computerized tomography scanner (CT scan). There were 4 cases of lung fibrosis, 1 pneumothorax, and 1 interstitial lung disease.

### 3.6. Outcomes

The duration of hospitalization was shorter in adults than in children (Table 1). The majority of cases were due to self-poisoning (84%). Children had ingested a lower quantity of paraquat [48.8 mg/kg (10–571.1)] than adults [595.8 mg/kg (6–3636.4),  $P = .03$ ] (Fig. 3A, B). There was no difference in survival rate according to the given treatment. Among the 3 criminal poisonings, there were 2 children aged 5 and 8 years, whose mother made them drink paraquat before drinking herself. Both children survived and the mother died within 24 hours. The other patient (adult) described a criminal intoxication at work; he died 14 days after consuming the equivalent of 200 mL. We noted more deaths among patients with abnormal liver function during hospitalization. However, 7 patients with a normal liver function died within 24 hours of admission. They did not have a second liver function test performed. There were more deaths among adults (65%) than in children (22%),  $P = .004$ . The severity and

outcome was determined primarily by the amount of paraquat ingested. Ninety-two percent of the patients with Yamaguchi score  $I > 1500$ –399 LogT survived (Fig. 4). Eighty-two percent of the patients with Yamaguchi score  $I < 930$ –399 LogT died. In multivariate analysis, the factor associated with death was the amount of paraquat ingested ( $P = .019$ ).

## 4. Discussion

Our study shows an increase in the annual incidence of paraquat intoxications in French Guiana. There is no recent study on the incidence of paraquat poisoning in neighboring countries. In Korea, the annual number of paraquat poisoning cases has decreased, as well as the incidence of all suicides with pesticides, between 2011 and 2014.<sup>[12]</sup> This was due to the paraquat ban, and suggests that paraquat will not commonly be used for suicide in the future. In countries that continue to authorize the unrestricted sale of paraquat, this incidence may be higher.<sup>[18]</sup> In our review, the median age of patients with paraquat poisoning was 27.4 years and 51.6% were men. This is the same distribution as in the Guianese population pyramid (<https://populationpyramid.net/french-guiana/2016/>). Although the number of deceased patients with abnormal liver function is probably underestimated, these data were consistent with the literature.<sup>[19]</sup> The occurrence of liver cytolysis was comparable in 3 studies (55% in French Guiana, 68% in China, and 66% in Taiwan). Few patients underwent gastroscopy. This investigation can give an indication of the quantity of ingested paraquat. The

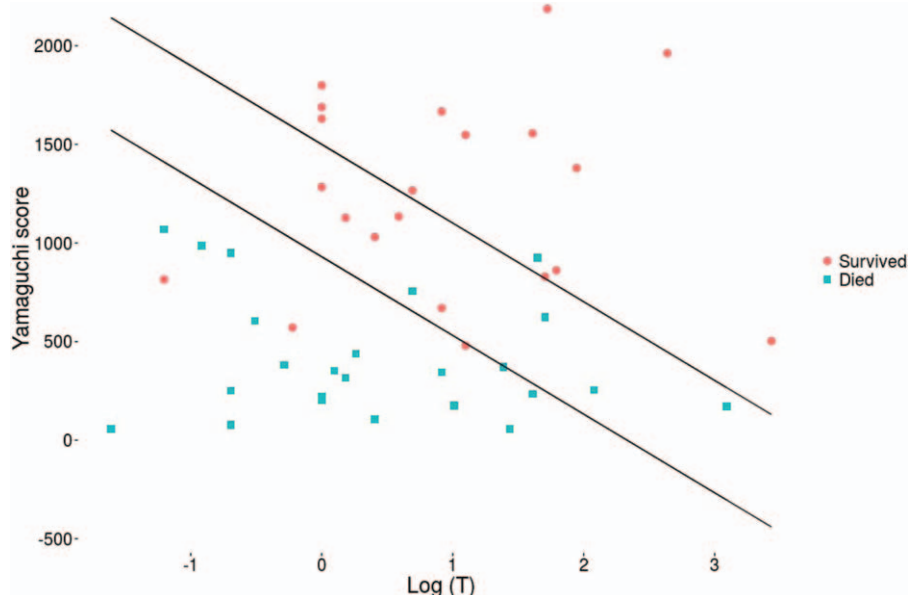


Figure 4. Outcome according to Yamaguchi score.

presence of gastric lesions is associated with ingestion of large amounts of paraquat. The 13 patients who had a positive paraquat gastric fluid also had a positive paraquatemia. We discuss the value of this test, because there is no previous publication looking at paraquat levels in gastric fluid. Overall, the only interest in paraquatemia lies in its prognostic value. In a large prospective cohort study in Sri Lanka, about 451 patients were assessed using 5 methods and predicting outcome in function of the paraquatemia (<https://populationpyramid.net/french-guiana/2016/>). In that study, the surviving patients were followed for 3 months to detect delayed death. All methods underestimated the number of deaths.<sup>[20–22]</sup> The most recent study shows that the paraquatemia is a good marker for survival except when ingested paraquat concentrations were low.<sup>[23]</sup> Furthermore, given the delay in getting the result of this test in French Guiana (technical complex test, done in Mainland France and therefore at a high cost), we can discuss the need to get this test result, unless the test becomes technically feasible in French Guiana. Laboratories performing quantitative analysis of paraquat are few and the results are often known only several days to several weeks after the poisoning (often after death). In 2009, a study was performed to develop an alternative to plasma paraquat dosage.<sup>[24]</sup> It showed that it was sufficient to use the same method for the detection of urinary paraquat, substituting 2 mL of urine for 2-mL plasma. A color change to dark blue was associated with mortality in 100% of cases. There was only a mortality of 50% if the color change was not so pronounced. This method is easy to use and could be implemented in French Guiana.

In our study, 50% of adult patients with creatinine > 120  $\mu\text{mol/L}$  on admission, died. This result was not significant, but there was probably an underestimation of kidney dysfunction on admission. The presence of renal failure on admission carries a poor prognosis.<sup>[25]</sup> A Korean study in 2009 on 278 patients showed that an elevated creatinine level over 120  $\mu\text{mol/L}$  on admission was a significant predictor of mortality ( $P < .01$ ).<sup>[26]</sup> About 51.4% of our patients were in this category. The majority

of poisonings was intentional and this is consistent with literature.<sup>[27–29]</sup> Indeed, self-poisoning has become a response to an increase in emotional distress among young adults.<sup>[28,30]</sup>

There are limited studies of paraquat poisoning in children. A prospective study on 146 Chinese children hospitalized for paraquat poisoning reported similar results to ours.<sup>[8]</sup> In children over 10 years of age, the majority of exposures were intentional. Death rates in children were similar (22% in Guyana, against 22.7% in China, and 33.3% in Taiwan). There were more deaths among patients with renal failure. Similarly, the mean serum creatinine was significantly higher on admission in the deceased patients (81.7  $\mu\text{mol/L} \pm 34.4$  vs 159.7  $\mu\text{mol/L} \pm 42.8$ ). Nearly 84% of children had no psychiatric history. Thus, one can suspect a predominantly impulsive mode of action in our patients, which corroborates a study in Suriname in 2009, showing that 82% of patients hospitalized for suicide attempts committed these on impulse.<sup>[27]</sup> Regarding the Yamaguchi predictive score, 92% of patients having a score  $I > 1500-399$  log have survived, while by definition, the score speaks of 90%. In contrast, 82% of patients with a score  $< 950-399$  log T have died, when the score speaks of a probability of death greater than 95%. So, the SIPP score and paraquatemia are better scores but not achievable in French Guiana.<sup>[31]</sup>

Regarding the place of residence of the patients, we noted that 67% came from Maroni (Saint Laurent, Papaïchton, and Maripasoula) and no cases occurred found in the east (mainly populated by Native Americans who were using another mode of suicide by hanging). It is likely that this poisoning mainly concerned Bushinenge. In Suriname, 70% of patients who committed suicide used a pesticide. In addition, 17% of these patients were Bushinenge (representing 36% of Surinamese mainly from the east of the country against 30% in French Guiana).<sup>[32]</sup>

There is no specific treatment for paraquat poisoning. In our study, we noted the absence of an exact protocol or consistent approach for management of paraquat-intoxicated patients. According to the literature, the use of activated carbon

significantly reduces mortality compared with Earth Foulon or Bentonite. In fact, activated carbon absorbs paraquat best. It is recommended to use it as soon as possible after paraquat ingestion<sup>[33,34]</sup> (within the first hour after ingestion). The number of cases in this study are too small to demonstrate the potential efficacy of digestive decontamination, but the statistical analysis shows a significant trend ( $P=.09$ ). Removing this dangerous product to prevent attempts of suicide and therefore suicidal deaths might result in a reduction in the incidence of paraquat poisoning. Paraquat poisoning and its mortality have disappeared from mainland France and other countries where the sale of the product has been banned.

In some cases, it is difficult to accurately determine the amount ingested. Moreover, the severity and outcome of paraquat poisoning are determined primarily by the amount ingested.<sup>[22,35,36]</sup> Given all these data, how can we reduce suicide attempts by paraquat ingestion in French Guiana? Several studies have attempted to address this increasingly common problem.<sup>[29]</sup> The pesticide industry has set up educational campaigns for safer use of pesticides.<sup>[37]</sup> Thus, the ban on paraquat in Suriname would be an essential measure to decrease cases of paraquat poisoning in French Guiana and Suriname. What role is there for the use of Pemba? Two patients received a mixture of water and pemba immediately after ingesting paraquat, while waiting to be taken to hospital. Obviously, we lack information on this decision and it is difficult to establish a causal relationship between intake of pemba and survival, as there are many confounding factors (lower ingested amount, for example). Pemba is local clay, otherwise known as kaolin, often used by Bushinenge in western French Guiana. It is prepared in a traditional way and is sold as balls of different sizes. Recently, a more addictive and dangerous use of Pamba in pregnant women was studied, and its anti-reflux properties were assessed.<sup>[38]</sup> In fact, regular use causes anemia due to iron deficiency. In 1968, a study showed that 80% of paraquat was absorbed by Kaolin in the environment.<sup>[39]</sup> It would be interesting to assess the paraquat absorbing capacity of Pemba in a laboratory setting. If these tests were conclusive, we could consider providing the rural health centers with Pemba, or simply inform people that in case of paraquat poisoning and pending medical evacuation, Pemba could be used in secondary prevention, to reduce intestinal paraquat absorption.

This study has some limitations. First, it cannot be considered as an exhaustive evaluation of paraquat poisoning in French Guiana, because it is based only on reports from hospitalized patients. As the records from the rural health centers were not computerized, it was very difficult to gather all the necessary information. While most patients seen at these centers were then transferred to 1 of the 3 hospitals and therefore included in this study, we cannot exclude that some patients have remained on site, because transferring them was impossible or they refused. Finally, the large area of French Guiana makes it plausible that some patients have died of poisoning at home, without timely transfer to a health center. A significant number of patients were excluded from the study because of a lack of laboratory diagnosis. Although the number of paraquat poisoning cases is underestimated, this data analysis allowed drawing a composite sketch of this problem in French Guiana.

## 5. Conclusion

With an incidence rate of at least 3.8 cases/100,000 inhabitants/year, French Guiana has the largest rate of paraquat poisoning in

the European Union, with a high mortality rate of 52%. The major factor affecting the prognosis of patients was the ingested amount of paraquat. No treatment has proven its effectiveness on mortality. The preventive administration of activated charcoal or Pemba, in situ, within the first hour after ingestion of paraquat is essential. Extensive pharmacological research on pemba may be needed. An outright ban on the sale of Paraquat in Suriname seems to be the best way to eradicate this scourge from French Guiana.

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