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Main features of *Cortinarius* spp. poisoning: a literature review

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Abstract

Introduction: Cortinarius spp. poisoning is characterized by a delayed acute renal failure. The main features of this severe poisoning are still poorly known and often overlooked. The aim of this literature review is a better description of *Cortinarius* spp. poisoning.

Materials and methods: The main medical databases were searched: Abstracts of Mycology, Current Contents, Medline, Pascal, Micromedex Poisindex, Toxicology abstracts, Toxline. All case reports that included a description of the clinical features of *Cortinarius* spp. poisoning were studied.

Results: 245 cases were collected and 90 cases could be analyzed in details. Gastrointestinal disorders are the main symptoms of the prerenal phase of the poisoning. They appear a few days after the ingestion of the mushrooms (median 3 days). The renal phase is delayed (median 8.5 days). Moderate and transient hepatic abnormalities have been reported. A severe hepatic failure can be ruled out. Muscular lesions are highly questionable. Treatment is supportive. No specific treatment can be recommended. Acute renal failure progressed towards chronic renal failure in half of the cases; intermittent hemodialysis or kidney transplantations were necessary in 70% of those cases.

Conclusion: Cortinarius spp. poisoning is severe. Ingestion of *Cortinarius* species must be systematically suspected whenever tubulo-interstitial nephritis is diagnosed, especially as mushrooms may have been ingested 1–2 weeks before.

Keywords: Mushroom poisoning; *Cortinarius*; Orellanine

Acute renal insufficiency due to mushroom poisoning is occasionally reported; most responsible species belong to the genus *Cortinarius*. This genus comprises 2000–3000 species that were considered as non-toxic until the early 1950s. One hundred and thirty-five poisoning cases attributed to *Cortinarius orellanus* Fries ingestion were observed in Poland from 1953 to 1962 and reported by Grzymala (1965). Since then, other *Cortinarius* spp. have been incriminated and the responsibility of the toxin orellanine has been confirmed (Prast and Pfaller, 1988a; Prast et al., 1988b). Various toxic mechanisms have been proposed (Cantin-Esnault et al., 1998; Oubrahim et al., 1998; Prast and Pfaller, 1988a; Richard et al., 1988; Richard et al., 1991; Richard et al., 1995).

Through a comprehensive study of the case reports published in the medical literature, we propose a description of the main characteristics of *Cortinarius* spp. poisoning.

1. Materials and methods

The following databases were searched: Abstracts of Mycology (Biosis) (1980–1999), Current Contents (ISI) (1989–1999), Medline (NLM) (1977–1999), Pascal (INIST-CNRS) (1987–1999), Micromedex Poisindex (1974–1999), Toxicology Abstracts (CSA) (1982–1999), and Toxline (NLM) (1965–1999). The keywords used were: poisoning, mushrooms, mushroom poisoning, acute renal failure, orellanine, orellanus, and *Cortinarius*. Poisoning case reports related to *Cortinarius* species ingestion that included a description of clinical features and therapy were kept for study. Duplicates were eliminated.

2. Results

Thirty publications were retrieved: 55 individual cases are reported (Andary et al., 1989; Brousse et al., 1981; Calvino et al., 1998; Delpech et al., 1990; Delpech et al.,

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Table 1
Main symptoms of the prerenal phase ($n = 82$)

Symptoms	n	%	Median delay (d)
Vomiting	52	62.7	3
Polydipsia	38	45.8	3
Lumbar pain	30	36.1	5
Nausea	30	36.1	3
Abdominal pain	20	24.1	3
Headache	15	18.1	4
Polyuria	15	18.1	–
Asthenia	14	16.9	3
Diarrhea	14	16.9	3
Anorexia	12	14.5	3
Myalgia	9	10.8	4
Faintness	8	9.6	3
Paresthesia	7	8.4	4
Constipation	5	6.0	–
Chills	5	6.0	–
Somnolence	4	4.8	–
Vertigo	4	4.8	–
Dysgeusia	4	4.8	–
Sweats	3	3.2	–

1991; Eigler et al., 1997; Franz et al., 1996; Gérault, 1981; Grzymala, 1965; Holmdahl et al., 1984; Hölzl et al., 1997; Horn et al., 1997; Kilner et al., 1999; Marichal et al., 1977; Montoli et al., 1999; Nolte et al., 1987; O'Donnell and Fleming, 1997; Rapior et al., 1989; Short et al., 1980) and 190 cases are compiled in different series (Bouget et al., 1990; Busnach et al., 1983; Grzymala, 1965; Holmdahl and Blohmé, 1995; Hulmi et al., 1974; Rohrmoser et al., 1997; Schliessbach et al., 1983; Tidman and Sjöström, 1992). On the whole, 245 cases were collected.

A complete analysis of the main characteristics of *Cortinarius* spp. poisoning was performed from the 90 most-detailed cases, involving 60 men (mean age 28 years) and 26 women (mean age 36 years); sex was unspecified in four cases. The duration of the latent period, clinical features, biological and histopathological analysis, the outcome, and the responsible species are summarized in Tables 1–5.

Table 2
Main biological features of the renal phase ($n = 62$)

Features	*n*	%
Leucocyturia	31	50.0
Hematuria	28	45.2
Albuminuria/proteinuria	19	30.6
Glucosuria	2	3.2
Leucocytosis	12	17.7
Transaminases level increase	5	8.1
Bilirubin level increase	5	8.1
Lactic dehydrogenase level increase	3	4.8
Eosinophilia	2	3.2

Table 3
Biopsies ($n = 36$)

	n	%
First biopsy (median delay = 25 days)	36	100
tubulo-interstitial nephritis diagnosis	10	22.2
tubular damages	28	77.8
tubular lesions	*8*	
tubular necrosis	*17*	
tubular atrophy	*3*	
interstitial edema	20	55.6
inflammatory infiltrates	25	69.4
lymphocytes + neutrophiles	*7*	
lymphocytes + plasmocytes	*8*	
lymphocytes	*3*	
monocytes	*3*	
unspecified	*4*	
fibrosis/sclerosis	14	38.9
Second biopsy (median delay = 75 days)	6	
atrophy/tubular lesions	5	
fibrosis	5	

The other cases brought further information in terms of severity, prognosis and outcome.

In the end, four publications reported some cases supposedly related to *Cortinarius* species ingestion, though imputability was considered doubtful (Bedry et al., 1998; Favre et al., 1976; Leski et al., 1976; Moore et al., 1991). The geographical distribution of the 245 cases is reported in Table 6.

3. Discussion

3.1. Prerenal phase of Cortinarius spp. poisoning

Cortinarius spp. poisoning is characterized by a delayed acute tubulopathy that can progress towards chronic renal insufficiency. It starts by a 'prerenal' gastrointestinal phase. This prerenal phase is well described in 82 cases; symptomatology is summarized in Table 1. Gastrointestinal disorders appear first: vomiting (63%), nausea (36%) and

Table 4
Treatment and outcome of patients with acute renal failure ($n = 62$)

	n	%
Treatment		
hemodialysis/peritoneal dialysis	46	74.2
hemoperfusion	7	
plasmapheresis	2	
N acetylcysteine	2	
Outcome		
death	5	8.1
chronic renal insufficiency (CRI)	32	51.6
hemodialysis/peritoneal dialysis	10	(68.8% of CRI)
kidney transplantation	12	

Table 5
Responsible *Cortinarius* species ($n = 90$)

Cortinarius species	*n*	%
Cortinarius orellanus Fries	53	58.9
Cortinarius speciosissimus Kühner & Romagnesi (= *Cortinarius rubellus* Cooke)	18	20.0
Cortinarius splendens Henry	14	15.6
Cortinarius spp.	5	5.6
Cortinarius cinnamomeus (Linné:Fries) Fries[a]	1	1.1

[a] In combination.

diarrhea (17%); they rarely lead to dehydration and functional renal failure. Abdominal pain (24%) and anorexia (15%) sometimes accompany these symptoms. Constipation may replace diarrhea. The latent period that precedes the occurrence of these symptoms varies from 12 h to 14 days with a median of 3 days. This exceptionally long period of time, unusual in mushroom poisoning, allows repeated intoxication: 18 patients had eaten *Cortinarius* spp. on two to five different occasions.

A burning sensation in the mouth, intense thirst, polydipsia (46%) and polyuria (18%) are more characteristic. In mild intoxications, symptoms resolve spontaneously and the outcome is favorable in a couple of days. In other cases, symptoms may subside or persist; in the latter case, they may be accompanied by headache, chills, night sweats, coldness and asthenia. There is no significant hyperthermia.

Table 6
Geographical distribution of the 245 cases

Countries	*n*	References
Austria	16	Franz et al. (1996), Hölzl et al. (1997), Horn et al. (1997), Rohrmoser et al. (1997)
England	2	Kilner et al. (1999)
Finland	9	Hulmi et al. (1974), Tidman and Sjöström (1992)
France	45	Andary et al. (1989), Bouget et al. (1990), Brousse et al. (1981), Delpech et al. (1990), Delpech et al. (1991), Gérault (1981), Marichal et al. (1977), Rapior et al. (1989)
Germany	2	Eigler et al. (1997)
Ireland	3	O'Donnell and Fleming (1997), Short et al. (1980)
Italy	3	Busnach et al. (1983), Montoli et al. (1999)
Poland	135	Grzymala (1965)
Spain	1	Calvino et al. (1998)
Sweden	26	Holmdahl et al. (1984), Holmdahl and Blohmé (1995)
Switzerland	3	Nolte et al. (1987), Schliessbach et al. (1983)

The patient may think that he has a common virus infection (Schumacher and Hoiland, 1983).

Liver injury was observed at this stage on many occasions, retrospectively in the initial Grzymala's series (Grzymala, 1965) and in some more recent publications (Brousse et al., 1981; Gérault, 1981; Hulmi et al., 1974; Marichal et al., 1977). Increased transaminases and bilirubin levels, hepatomegaly and hepatalgia, may be observed. Histological lesions were observed after autopsy (lipoidosis, necrosis lesions) (Grzymala, 1965).

However, severe liver injury can be ruled out:

- In the three cases reported by Favre et al. (1976); Leski et al. (1976), a mild phalloides syndrome may be evoked, and *Cortinarius* spp. responsibility ruled out, in view of the following data: early gastrointestinal symptoms, a significant transaminases level increase, the description of liver insufficiency, and the questionable way the mushrooms were identified (Schumacher and Hoiland, 1983). Moreover, hepatotoxic species cannot be excluded whenever different mushrooms have been eaten together. This report was not taken into account in our detailed review.
- There were no clinical or biological liver abnormalities in the well-documented series of 26 soldiers who had eaten *C. orellanus*. A liver biopsy was performed in one case; it was normal (Bouget et al., 1990).
- Liver toxicity has not been confirmed in the most recent animal experiment (Prast and Pfaller, 1988a).

Therefore, liver toxicity of *Cortinarius* spp. remains to be proven. If liver injury does exist, it is probably early, limited and transient; it may go unnoticed in the late stages of renal insufficiency. According to Jaeger (1994), the lack of liver injury favors *Cortinarius* spp. poisoning whenever acute renal failure is diagnosed.

Neuromuscular symptoms are observed in 20% of cases: limb paresthesia, muscular cramps and myalgia. They occur near the end of the prerenal phase, in a median period of 4 days, and precede the diagnosis of nephropathy. Creatine kinase level is mentioned by only one team (Bedry et al., 1998). One death was related to massive rhabdomyolysis; seven other people had a mean creatine kinase level of 55,000 UI/l (Bedry et al., 1998). The responsibility of *Cortinarius splendens*, possibly confused with *Tricholoma flavovirens*, as well as doubtful traces of orelline in the renal tissue, are not convincing. This report was not taken into account in our detailed review. Therefore, the possible muscular toxicity of *Cortinarius* spp. remains to be documented.

3.2. *Renal phase of Cortinarius spp. poisoning*

Lumbar and flank pains, oliguria or more rarely polyuria, can appear and combine with the persisting gastrointestinal disorders. A symptom-free interval may also be observed. The period after which acute renal failure is observed is

specified in 52 cases; it varies from 4 to 15 days with a median of 8.5 days. Biological features are specified in 62 cases (Table 2). Leucocyturia (50%), hematuria (45%), and albuminuria (31%) were mainly reported; leucocytosis was noticed in 11 cases (18%).

Renal biopsies were performed in 35 cases (Table 3), 1–9 weeks after the onset of renal failure (median 21 days). They showed tubulo-interstitial nephritis lesions with more or less severe tubular epithelium damages in most cases (atrophy, focal or extended necrosis), interstitial edema (56%) with inflammatory infiltrates (69%) and a beginning interstitial fibrosis (39%). The observation of immune complexes and/or complement deposits as well as eosinophilia in a few cases evoked a possible immuno-allergic mechanism. However, the histological description is much more in favor of a direct cellular toxicity, particularly on the tubular epithelium.

Though no glomerular lesions were generally observed, it was nevertheless reported in one case (Marichal et al., 1977); a mesangial thickening was reported in four cases (Delpech et al., 1991; Gérault, 1981; Short et al., 1980).

A second renal biopsy was performed in seven cases within a time lapse of 35–180 days (median 75 days). These results showed edema decrease, interstitial fibrosis (five cases) and more or less severe tubular lesions.

3.3. Treatment

Treatment is mainly supportive. Hemodialysis or peritoneal dialysis was performed in 74% of cases of acute renal failure. There is currently no specific treatment. At the late stage of severe chronic renal insufficiency, 12 kidney transplantations were carried out within a period of time of 6–30 months (median 10 months) (Bouget et al., 1990; Eigler et al., 1997; Gérault, 1981; Holmdahl et al., 1984; Holmdahl and Blohmé, 1995; Hölzl et al., 1997; Montoli et al., 1999; Nolte et al., 1987; O'Donnell and Fleming, 1997; Short et al., 1980).

The small number of cases, the important inter-individual variability, and the different possible outcomes make any assessment of the various elimination techniques or specific therapeutics difficult. In an attempt to eliminate the toxin from the body, hemoperfusion has been combined with hemodialysis; but it did not prevent the evolution towards terminal chronic renal insufficiency (five transplantations in a series of 22 cases) (Holmdahl and Blohmé, 1995). According to the authors, the lack of efficacy may have been due to the delay in starting the procedures. Plasma exchanges have been also performed with no better efficacy (Delpech et al., 1990; Delpech et al., 1991). In one case, the combination of hemodialysis and plasma exchange, though started in the early phase of the intoxication (44th hour), did not prevent chronic renal insufficiency (Montoli et al., 1999).

Actually, the toxicokinetics of orellanine remains mostly unknown both in man and in animals. It was shown that orellanine was undetectable in plasma on the 2nd–3rd day after mushroom ingestion in eight cases of human poisonings (Rohrmoser et al., 1997) and in rat urine after 24 h (Prast and Pfaller, 1988a); orellanine might be fixed very early in renal tissue (Nieminen and Pyy, 1976c). From these results, and especially as the patient's admission is generally delayed, hemoperfusion cannot be recommended.

To prevent the effects of the toxin or to speed up recovery, some therapeutic associations, such as furosemide/diltiazem/amino acids, have been proposed in one case; though no recovery was obtained, a subjective impression of efficacy was claimed by the authors (Delpech et al., 1990; Delpech et al., 1991). It should be emphasized that pretreatment with furosemide in animals worsened renal lesions (Nieminen et al., 1976a). Corticosteroids were ineffective in 12 cases (Bouget et al., 1990). N-acetylcysteine was given in one case on the 11th day without any better efficacy (Kilner et al., 1999).

3.4. Outcome

Out of the 90 cases that could be analyzed in detail, 62 patients (69%) progressed towards renal insufficiency, which justified dialysis in 46 cases (Table 4). About half of the 62 cases progressed towards chronic renal insufficiency. Intermittent dialysis was necessary in 10 cases and renal transplantations were performed in 12 cases.

Five deaths were recorded among the 90 cases we analyzed: four in Poland in 1953 (*C. orellanus*) (Grzymala, 1965) and one in Lyon (France) in 1979 (*C. splendens*); the latter death was related to a cerebrovascular complication of anticoagulant therapy (Gérault, 1981). The death rate was 15% in the historical series of Grzymala (1965). Nowadays, hemodialysis should prevent death in most cases.

In the other cases, renal function came back to normal in weeks or months. Anorexia, asthenia, dry mouth, digestive disorders and sweats may persist for a longer time.

The series of the 26 poisoned soldiers gives more information (Bouget et al., 1990). Though they had all ingested a roughly similar quantity of mushrooms, 12 had acute renal failure and eight had to be dialyzed; four of the dialyzed patients progressed towards chronic renal insufficiency. Fourteen of them had no renal failure (creatinine blood level <150 μmol/l). This significant inter-individual variability is also confirmed by the Gérault's series (1981):

- It is not caused by any metabolic specificity; acetylation and hydroxylation tests that were performed showed no differences between patients with or without renal failure (Bouget et al., 1990).
- Toxic effects seem to be dose-dependant in some 'sensitive' patients (Gérault, 1981; Grzymala, 1965). This has been confirmed in animal experiments (Nieminen and Pyy, 1976b). Moreover, a difference in sensitivity was observed between male and female animals (Nieminen and Pyy, 1976c).

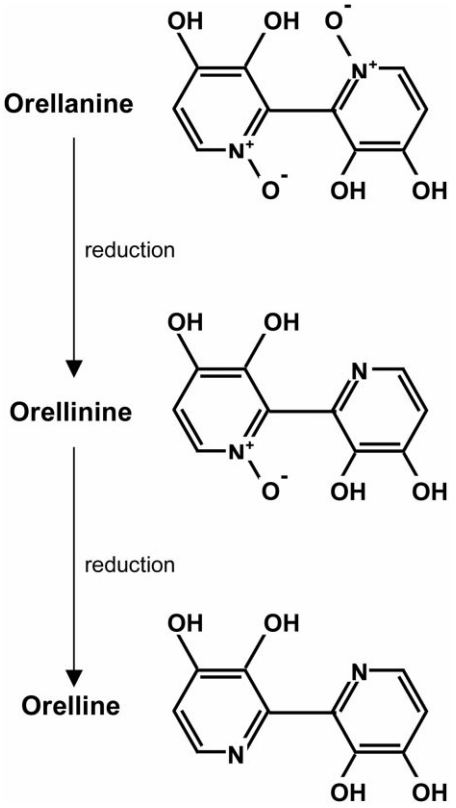

Fig. 1. Chemical structures of orellanine, orellinine and orelline (from Oubrahim et al., 1998).

3.5. *Prognosis*

As early as 1965, Grzymala had established a relationship between the duration of the latent period and poisoning severity (Grzymala, 1965). In his series, the latent period was:

- 10–17 days in patients presenting with thirst, burning sensation in the mouth, and polyuria (mild intoxication);
- from 6 to 10 days in patients presenting with digestive disorders, polyuria or oliguria, hematuria, leucocyturia, but no significant renal impairment;
- from 2 to 3 days in patients with acute renal failure. Death rate in this particular group was 50%.

The French series of 26 soldiers confirms this data (Bouget et al., 1990). The amount of mushrooms ingested, early gastrointestinal disorders, early renal insufficiency, and a past history of renal troubles, have all been proposed as prognostic criteria.

3.6. *Toxicological analysis*

Among the 90 detailed cases, orellanine was looked for in blood, urine and renal tissue in four cases (Andary et al., 1989; Franz et al., 1996; Hölzl et al., 1997; Montoli et al., 1999; Rapior et al., 1989). The toxin was identified in two cases (Andary et al., 1989; Franz et al., 1996; Rapior et al., 1989). Three other publications reported 12 cases with toxicological data (Bedry et al., 1998; Moore et al., 1991; Rohrmoser et al., 1997); the results were positive in six cases, but highly questionable in two cases (Bedry et al., 1998; Moore et al., 1991).

Several analytical methods have been developed in recent years (thin layer chromatography, electrophoresis, paramagnetic electronic resonance) (Cantin-Esnault et al., 1989; Oubrahim et al., 1997; Rapior et al., 1988; Rapior et al., 1989; Rohrmoser et al., 1997). They allowed identification of orellanine in mushroom at concentrations as low as 1.2–1.4% of their dry weight (Cantin-Esnault et al., 1989; Prast et al., 1988b), in plasma on day 10 (Andary et al., 1989; Rapior et al., 1989), or in renal tissue on day 10 (Andary et al., 1989; Rapior et al., 1989; Rohrmoser et al., 1997), day 35 (Franz et al., 1996), and at six months (Andary et al., 1989; Rapior et al., 1989). In the last case, lack of control as well as the reported concentrations brought the results into question (Rohrmoser et al., 1997). Similarly, in another case (Moore et al., 1991), the way orellanine or orelline identifications in plasma and in urine were reported, without any details on the time the samples were taken and the analytical methods used, puts the results in question (Benjamin, 1995; Jaeger, 1994).

Most of these methods are difficult to perform. False positives and lack of sensitivity are their main limits. More sophisticated and specific methods do exist but are not available on a routine basis (Oubrahimet al., 1997).

However, it appears that orellanine identification in biological fluids and tissues should be the corner stone of diagnosis whenever poisoning is suspected. Significant treatment advances will depend on future toxicokinetics studies. From a practical point of view, it must be remembered that biological samples must be taken at the earliest possible stage, stored frozen, away from light, and analyzed as soon as possible.

3.7. *Toxins and toxic mechanisms*

The main toxin was identified rather early (Grzymala, 1965). The structure of orellanine was described (Antkowiak and Gessner, 1979) and synthesis was performed (Dehmlow and Schulz, 1985). Orellanine undergoes an early photochemical degradation into the toxin orellinine, itself transformed into orelline which is non-toxic (Antkowiak and Gessner, 1985) (Fig. 1). The role of cortinarines (cyclic decapeptides) has also been studied (Tebbett and Caddy, 1984); their own existence has been put into question (Laatsch and Matthies, 1991; Matthies and Laatsch, 1991; Prast et al., 1988b).

In mice, intraperitoneal and oral LD50 are respectively 12.5 and 90 mg/kg. In animal, purified orellanine

administration induces all the symptoms of poisoning (Richard et al., 1988).

Tubular epithelium is probably the target of orellanine (Nieminen and Pyy, 1976c). Many different toxic mechanisms have been put forward (Prast and Pfaller, 1988a), one of them being the production of superoxide anions (Cantin-Esnault et al., 1998; Oubrahim et al., 1998; Richard et al., 1995). Depletion of glutathione (Cantin-Esnault et al., 1998; Oubrahim et al., 1998) and ascorbic acid (Oubrahim et al., 1998) has been shown in vitro.

3.8. *Nephrotoxic Cortinarius species*

The main suspected species in this literature review were *C. orellanus* (53 cases) and *Cortinarius speciosissimus* (19 cases) (Table 5). *C. splendens* was implicated in two publications (14 cases) (Gérault, 1981; Schliessbach et al., 1983). An association with several species was reported in 17 cases.

Because of the long latent period, the mushrooms actually picked and eaten are generally no longer available for identification. Therefore, mushrooms are often recognized by the patients or their relatives, either from drawings or photographs, or identified by a mycologist from species collected at the same location, sometimes long afterwards. This is how species such as *C. splendens* were implicated in the onset of *Cortinarius* spp. poisoning.

Orellanine toxin was identified in *C. orellanus*, *C. orellanoïdes*, *C. speciosissimus*, *C. henrici*, *C. rainierensis*, *C. fluorescens* and *C. bruneofulvus* (Oubrahim et al., 1997; Rapior et al., 1988). On the contrary, no orellanine traces could be found in *Cortinarius cinnamomeus*, *C. sanguineus* and *C. splendens* (Oubrahim et al., 1997; Rapior et al., 1988), though some of these species were incriminated in human poisonings or in some old (Viallier et al., 1968) or limited (Gérault, 1981) animal experiments. However, the lack of toxicity of these species has not been proven; anthraquinone derivatives were identified in *C. cinnamomeus* and *C. sanguineus* (Bresinski and Besl, 1990), and unknown toxic principles may well be present. Therefore, it is obviously impossible to establish an extensive list of toxic *Cortinarius* species; a wise recommendation is to avoid all *Cortinarius* species.

4. Conclusion

Our literature review allows a better description of the main characteristics of *Cortinarius* spp. poisoning. The severity of *Cortinarius* spp. poisoning is clearly confirmed, as half the cases of acute renal failure progressed towards chronic renal insufficiency. Further knowledge of orellanine toxicokinetics and toxicity mechanisms is still necessary to be able to propose a proper treatment.

The consumption of mushrooms such as *Cortinarius* species must be systematically suspected whenever tubulo-interstitial nephritis is diagnosed, especially as mushrooms may have been ingested one to two weeks before.

References

Andary, C., Rapior, S., Delpech, N., Huchart, G., 1989. Laboratory confirmation of Cortinarius poisoning. Lancet 1, 213.

Antkowiak, W.Z., Gessner, W.P., 1979. The structures of orellanine and orelline. Tetrahedron Lett. 21, 1931–1934.

Antkowiak, W.Z., Gessner, W.P., 1985. Photodecomposition of orellanine and orellinine, the fungal toxins of *Cortinarius orellanus* Fries and *Cortinarius speciosissimus*. Experentia 41, 769–771.

Bedry, R., Neau, D., Dupon, M., Dutronc, H., Ragnaud, C.E., Favarel-Garrigues, J.C., 1998. Intoxications par les champignons: une nouvelle étiologie de rhabdomyolyse? XXXVIIIe Congrès de la société nationale de médecine interne, Bordeaux, 18–20 juin 1998 (abstract). Rev. Med. Interne. 19(suppl 1), 84s.

Benjamin, D.R., 1995. Delayed-onset renal failure syndrome. Orellanine or cortinarin poisoning. In: Benjamin, D.R. (Ed.). Mushrooms Poisons and Panaceas. Freeman, W.H. and Company, New York, pp. 242–263.

Bouget, J., Bousser, J., Pats, B., Ramee, M.P., Chevet, D., Rifle, G., Giudicelli, C.P., Thomas, R., 1990. Acute renal failure following collective intoxication by *Cortinarius orellanus*. Intensive Care Med. 16, 506–510.

Bresinski, A., Besl, H., 1990. A Colour Atlas of Poisonous Fungi. Wolfe Publishing, London.

Brousse, A., Hervé, J.P., Leguy, P., Cledes, J., Leroy, J.P., 1981. L'intoxication par champignons de type *Cortinarius orellanus*. Une cause rare d'insuffisance rénale. Nouv. Presse Med. 10, 1940.

Busnach, G., Dal Col, A., Perrino, M.L., Surian, M., Rovati, C., Barbiano DiBelgioiosi, G., Minetti, L., 1983. Plasma exchange in acute renal failure by *Cortinarius speciosissimus*. Int. J. Artif. Organs 6(suppl 1), 73–74.

Calvino, J., Romero, R., Pintos, E., Novoa, D., Güimil, D., Cordal, T., Mardaras, J., Arcocha, V., Lens, X.M., Sanchez-Guisande, D., 1998. Voluntary ingestion of *Cortinarius* mushrooms leading to chronic interstitial nephritis. Am. J. Nephrol. 18, 565–569.

Cantin, D., Richard, J.M., Allary, J., 1989. Chromatographic behaviour and determination of orellanine, a toxin from the mushroom *Cortinarius orellanus*. J. Chromatogr. A 478, 231–237.

Cantin-Esnault, D., Richard, J.M., Jeunet, A., 1998. Generation of oxygen radicals from iron complex of orellanine, a mushroom nephrotoxin; preliminary ESR and spin-trapping studies. Free Radic. Res. 28 (1), 45–58.

Dehmlow, E.V., Schulz, H.J., 1985. Synthesis of orellanine, the lethal poison of a toadstool. Tetrahedron Lett. 26 (40), 4903–4906.

Delpech, N., Rapior, S., Cozette, A.P., Ortiz, J.P., Donnadieu, P., Andary, C., Huchard, G., 1990. Evolution d'une insuffisance rénale aiguë par ingestion volontaire de *Cortinarius orellanus*. Presse Med. 19 (3), 122–124.

Delpech, N., Rapior, S., Donnadieu, P., Cozette, A.P., Ortiz, J.P., Huchard, G., 1991. Intoxication volontaire par *Cortinarius orellanus*: interêt d'un traitement précoce original après dosage de

l'orellanine dans les milieux biologiques et tissulaires. Nephrologie 12, 63–66.

Eigler, A., Neman, I., Schiffl, H., 1997. Orellanus syndrome: a rare cause of uremia. Nephron. 76, 485–486.

Favre, H., Leski, M., Christeler, P., Vollenweider, E., Chatelanat, F., 1976. Le *Cortinarius orellanus*: un champignon toxique provoquant une insuffisance rénale aiguë retardée. Schweiz. Med. Wochenschr. 1976 (33), 1097–1102.

Franz, M., Regele, H., Kirchmair, M., Kletzmayr, J., Sunder-Plassmann, G., Hörl, W.H., Pohanka, E., 1996. Magic mushrooms: hope for a 'cheap-high' resulting in end-stage renal failure. Nephrol. Dial. Transplant. 11, 2324–2327.

Gérault, A., 1981. Intoxication collective de type orellanien provoquée par *Cortinarius splendens* R. Hy. Bull Soc Mycol France 97, 67–72.

Grzymala, S., 1965. Étude clinique des intoxications par les champignons du genre *Cortinarius orellanus* Fr. Bull. Med. Leg. Toxicol. Med. 8, 60–70.

Holmdahl, J., Blohmé, I., 1995. Renal transplantation after *Cortinarius speciosissimus* poisoning. Nephrol. Dial. Transplant. 10, 1920–1922.

Holmdahl, J., Mulec, H., Ahlmén, J., 1984. Acute renal failure after intoxication with *Cortinarius* mushrooms. Hum. Toxicol. 3, 309–313.

Hölzl, B., Regele, H., Kirchmair, M., Sandhofer, F., 1997. Acute renal failure after ingestion of *Cortinarius speciocissimus*. Clin. Nephrol. 48 (4), 260–262.

Horn, S., Horina, J.H., Krejs, G.J., Holzer, H., Ratschek, M., 1997. End-stage renal failure from mushroom poisoning with *Cortinarius orellanus*: report of four cases and review of the literature. Am. J. Kidney Dis. 30 (2), 282–286.

Hulmi, S., Sipponen, P., Forsstrom, J., Vilska, J., 1974. Seitikkisienen aiheuttama vakava munuaisvaurio [Mushroom poisoning caused by *Cortinarius speciosissimus*. A report of four cases]. Duodecim. 90 (14), 1044–1050.

Jaeger, A., 1994. Orellanine mushrooms. In: Spoerke, D.G., Rumack, B.H. (Eds.). Handbook of Mushroom Poisoning. Diagnosis and Treatment. 2nd ed. CRC Press, Boca Rota, pp. 249–264.

Kilner, R.G., D'Souza, R.J., Oliviera, D.B.G., MacPhee, I.A.M., Turner, D.R., Eastwood, J.B., 1999. Acute renal failure from intoxication by *Cortinarius orellanus*: recovery using antioxidant therapy and steroids. Nephrol. Dial. Transplant. 14, 2779–2780.

Laatsch, H., Matthies, L., 1991. Fluorescent compounds in *Cortinarius speciosissimus*: investigation for the presence of cortinarins. Mycologia 83 (4), 492–500.

Leski, M., Favre, H., Chatelanat, F., Vollenweider, E., Baczko, A.M., 1976. Insuffisance rénale aiguë provoquée par l'ingestion d'un champignon: *Cortinarius orellanus*. J. Urol. 82, 976–981.

Marichal, J.F., Triby, F., Wiederkehr, J.L., Carbiener, R., 1977. Insuffisance rénale chronique après intoxication par champignons de type *Cortinaire orellanus* Fries. Nouv. Presse. Med. 6, 2973–2975.

Matthies, L., Laatsch, H., 1991. Cortinarins in *Cortinarius speciosissimus*? A critical revision. Experientia 47, 634–640.

Montoli, A., Confalonieri, R., Colombo, V., 1999. Lack of efficacy of early plasma exchange in renal toxicity from *Cortinarius orellanus*. Nephron. 81, 248.

Moore, B., Burton, B.T., Lindren, J., Rieders, F., Kuehnel, E., Fisher, P., 1991. Cortinarius mushroom poisoning resulting in anuric renal failure. Vet. Hum. Toxicol. 33 (4), 369 (abstract).

Nieminen, L., Pyy, K., Hirsimäki, Y., 1976. The effect of furosemide on the renal damage induced by toxic mushroom *Cortinarius speciosissimus* in the rat. Br. J. Exp. Path. 57, 400–403.

Nieminen, L., Pyy, K., 1976. Individual variation in mushroom poisoning induced in the male rat by *Cortinarius speciosissimus*. Medical Biology 54, 156–158.

Nieminen, L., Pyy, K., 1976. Sex differences in renal damage induced in the rat by the Finnish mushroom. *Cortinarius speciosissimus*. Acta Path. Microbiol. Scand. 84, 222–224 sect A.

Nolte, S., Hufschmidt, C., Steinhaur, H., Rohrbach, R., Künzer, W., 1987. Terminale Niereninsuffizienz durch interstitielle nephritis nach pilzvergiftung durch *Cortinarius speciosissimus*. Monatsschr Kinderheilkd 135, 280–281.

O'Donnell, M., Fleming, S., 1997. The renal pathology of mushroom poisoning. Histopathology 30, 280–282.

Oubrahim, H., Richard, J.M., Cantin-Esnault, D., Seigle-Murandi, F., Trécourt, F., 1997. Novel methods for identification and quantification of the mushroom nephrotoxin orellanine. Thin layer chromatography and electrophoresis screening of mushrooms with electron spin resonance determination of the toxin. J. Chromatogr. A 758, 145–157.

Oubrahim, H., Richard, J.M., Cantin-Esnault, D., 1998. Peroxidase-mediated oxidation, a possible pathway for activation of the fungal nephrotoxin orellanine and related compounds. ESR and spin-trapping studies. Free Radic. Res. 28 (5), 497–505.

Prast, H., Pfaller, W., 1988. Toxic properties of the mushroom *Cortinarius orellanus* (Fries). II. Impairment of renal function in rats. Arch. Toxicol. 62, 89–96.

Prast, H., Werner, E.R., Pfaller, W., Moser, M., 1988. Toxic properties of the mushroom *Cortinarius orellanus*. I. Chemical characterization of the main toxin of *Cortinarius orellanus* (Fries) and *Cortinarius speciosissimus* (Kühn & Romagn) and acute toxicity in mice. Arch. Toxicol. 62, 81–88.

Rapior, S., Andary, C., Privat, G., 1988. Chemotaxonomic study of orellanine in species of *Cortinarius* and *Dermocybe*. Mycologia 80 (5), 741–747.

Rapior, S., Delpech, N., Andary, C., Huchard, G., 1989. Intoxication by *Cortinarius orellanus*: detection and assay of orellanine in biological fluids and renal biopsies. Mycopathologia 108, 155–161.

Richard, J.M., Cantin-Esnault, D., Jeunet, A., 1995. First electron spin resonance evidence for the production of semiquinone and oxygen free radicals from orellanine, a mushroom nephrotoxin. Free Radic. Biol. Med. 19 (4), 417–429.

Richard, J.M., Creppy, E.E., Benoit-Guyod, J.L., Dirheimer, G., 1991. Orellanine inhibits protein synthesis in Madin-Darby canine kidney cells, in rat liver mitochondria, and in vitro: indication for its activation prior to in vitro inhibition. Toxicology 67, 53–62.

Richard, J.M., Louis, J., Cantin, D., 1988. Nephrotoxicity of orellanine, a toxin from the mushroom *Cortinarius orellanus*. Arch. Toxicol. 62, 242–245.

Rohrmoser, M., Kirchmair, M., Feifel, E., Valli, A., Corradini, R., Pohanka, E., Rosenkrane, A., Pöder, R., 1997. Orellanine poisoning: rapid detection of the fungal toxin in renal biopsy material. J. Toxicol. Clin. Toxicol. 35 (1), 63–66.

Schliessbach, B., Hasler, S., Friedli, H.P., Müller, U., 1983. Akute Niereninsuffizienz nach pilzvergiftung mit *Cortinarius splendens* (Fries) oder 'schöngelbem klumpfuss' (sog. Orellanus Syndrom). Schweiz Med. Wochenschr. 113, 151–153.

Schumacher, T., Hoiland, K., 1983. Mushroom poisoning caused by

species of the genus Cortinarius (Fries). Arch. Toxicol. 53, 87–106.

Short, A.I.K., Watling, R., MacDonald, M.K., Robson, J.S., 1980. Poisoning by *Cortinarius speciosissimus*. Lancet 2, 942–944.

Tebbett, I.R., Caddy, B., 1984. Mushroom toxins of the genus Cortinarius. Experientia 40, 441–446.

Tidman, M., Sjöström, P., 1992. Akut njursvikt orsakad av svampförgiftning med toppig giftspindelskivling [Acute renal failure caused by mushroom poisoning with *Cortinarius speciosissimus*]. Lakartidningen 89 (35), 2763–2764.

Viallier, J., Oddoux, L., Paliard, P., Lahneche, J., 1968. Lésions rénales et hépatiques provoquées chez l'animal par l'ingestion de *Cortinarius orellanus* Fr. et de quelques espèces voisines. In Les hépatonéphrites toxiques, Comptes rendus de la 8e réunion nationale des centres de lutte contre les poisons, Grenoble, 28–29 avril 1967. Masson, Paris, pp. 79–84.