Vigilances No 20 – November 2023

VIGILANCE FOR NATURAL TOXINS

- Many mushroom poisoning cases reported in 2022 ... 7

VIGILANCE FOR BIOCIDES PRODUCTS AND PLANT INPUTS

 Improperly used disinfectants responsible for skin burns in young children12

PHYTOPHARMACO-VIGILANCE

 Re-authorisation of the herbicide terbuthylazine: conditions of authorisation adjusted following monitoring of surface water?....... 16



Confusion between autumn crocus and wild garlic: beware of severe poisoning!

Autumn crocus is a poisonous or even deadly plant that grows in the same places as wild garlic, an edible wild plant popular in salads or home-made pesto. Wild garlic is harvested in spring before its flowers – and those of autumn crocus – appear, which can lead to confusion. This article describes cases of confusion between autumn crocus and wild garlic or, more rarely, another edible wild plant, many-flowered garlic, recorded by French poison control centres (PCCs) between 2020 and 2022. The poisoning cases were sometimes responsible for serious health effects, including death. ANSES and the PCCs are reiterating their recommendations for avoiding such confusion.

In 2020, following a death, ANSES and the PCCs issued a warning about the risks of mistaking autumn crocus (*Colchicum autumnale*), a plant that is toxic and even fatal to both humans and animals, for wild garlic (*Allium ursinum*), which is edible [1].

Despite this warning, cases of poisoning caused by confusion between autumn crocus and wild garlic, or more rarely between autumn crocus and another edible plant, many-flowered garlic (*Allium polyanthum*), are still regularly reported to poison control centres.

Autumn crocus, wild garlic and many-flowered garlic grow in the same undergrowth or meadows, in damp or shady areas (see box). Autumn crocus flowers are very different from those of wild garlic or many-flowered garlic but, they only appear at the end of summer. In spring, the season when people forage for wild garlic and many-flowered garlic, the lack of flowers to tell these plants apart can contribute to confusion.

The toxicity of autumn crocus is due to colchicine, a very potent alkaloid found in all parts of the plant (leaves, flowers, seeds and roots). It blocks cell division in the body, which explains its particular digestive and haematological toxicity, as gastric, intestinal and bone-marrow cells must be rapidly renewed.

The first signs of poisoning are digestive and occur a few hours after ingestion: intense abdominal pain, vomiting and profuse diarrhoea may occur, leading to severe dehydration, which in turn causes a drop in blood pressure and a risk of cardiorespiratory arrest. Other serious problems appear later: bone marrow failure¹, which causes a drop in the number of circulating blood cells, may appear around the third day and entails a risk of infection and haemorrhage. Hair loss may occur around the tenth day.



What are the different cases of confusion?

To improve understanding and prevention, ANSES and the PCCs studied cases of confusion between autumn crocus and wild or many-flowered garlic recorded by the PCCs between 1 January 2020 and 31 December 2022.

All dossiers coded on the agents "autumn crocus", "wild garlic" or "many-flowered garlic", recorded during this period in the PCCs' information system (SICAP), were extracted and reviewed. In each case, the patient thought they had eaten wild or many-flowered garlic, but then developed symptoms after the meal.

The case definitions in the study were as follows:

A confirmed case of autumn crocus poisoning corresponded to one in which autumn crocus had been identified among the leftovers by a member of the Phytoliste, and in which the patient had presented with clinical signs suggestive of colchicine poisoning.

Cases of poisoning in which no autumn crocus was identified by the Phytoliste and no meal was shared with a confirmed case of autumn crocus poisoning were described as *suspected cases of consumption of a plant mistaken for wild or many-flowered garlic.* Confusion with a toxic plant was suspected, but could not be proved.

From 2020 to 2022, the PCCs recorded 28 confirmed cases of poisoning due to autumn crocus being confused with wild garlic (22 cases), many-flowered garlic (two cases), or both at the same time (four cases). In addition, there were 127 cases of poisoning following the suspected consumption of a toxic plant mistaken for wild garlic (121 cases) or many-flowered garlic (six cases).

^{1.} Inability of the bone marrow to produce blood cells normally.

^{2.} Phytoliste: a secure email distribution list connecting PCC toxicologists with experienced botanists, who can rapidly identify the plant species responsible for the poisoning (based on photographs, a description of the plant, etc.).

The 155 poisoning victims were aged between 3.8 and 74 years (average: 38.7 years). Of these, 38% were men and 60% women (the remaining 2% were not specified).

The same meal may have been shared by several diners and poisoned from one to four people. There were 17 meals associated with the consumption of autumn crocus and 102 meals containing a plant mistaken for wild or many-flowered garlic.

Cases of confusion during springtime mainly observed in the eastern half of the country

There were more confirmed cases of autumn crocus being mistaken for wild or many-flowered garlic in 2021 than in 2022 or 2020 (Figure 1).

These poisonings occurred mainly in spring, at the start of the leaf-growing season for these three plants. April saw a peak in suspected cases of consumption of a plant mistaken for wild or many-flowered garlic (40% of meals in this category) (Figure 2). One case of poisoning resulted from consumption of a plant mistaken for wild garlic that had been used to prepare pesto, which was then stored in the refrigerator. This occurred in August, long after the season. Another occurred in December, and was due to consumption of a plant mistaken for wild garlic that had been frozen. The confirmed cases of autumn crocus ingestion were all observed between March and May.

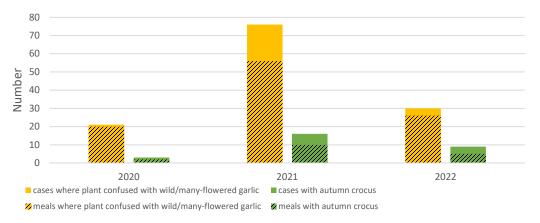


Figure 1 : Annual breakdown of the number of poisoning cases and meals where several diners may have eaten autumn crocus, or a plant mistaken for wild or many-flowered garlic. 2020-2022. Source: SICAP.

Half of the meals containing autumn crocus were in Auvergne-Rhône-Alpes (53%, nine meals) and one third in Grand-Est (35%, six meals). Such confusion between autumn crocus and wild garlic is regularly described in continental Europe [2, 3]. Suspected consumption of a plant mistaken for wild or manyflowered garlic was also dominant in Auvergne-Rhône-Alpes (46%, 47 meals) and Grand-Est (22%, 22 meals), and occurred to a lesser extent in the other regions of France.

Wild plants gathered from the countryside

In more than three-quarters of the meals, the diners themselves had picked the plant responsible for poisoning (respectively 76% (13/17 meals) and 78% (80/102 meals) of confirmed cases of confusion with autumn crocus, and suspected cases of confusion with wild or many-flowered garlic) (Figure 3). Plants given by a third party accounted for 7% (8/119 meals) of the meals causing poisoning, which also calls for vigilance.

Wild garlic was purchased commercially for six meals: in an organic shop or from a market gardener (one meal each), and in a supermarket or from a market (two meals each). Poisoning cases involving a commercially purchased plant were never confirmed as being due to autumn crocus.

Prepared in pesto or marinade in almost half of all meals

Wild garlic is used in many culinary recipes: in almost half of all meals (44%), the leaves were prepared raw in pesto or marinade (Figure 4). This method of preparation requires a large quantity of leaves to be picked and used, increasing the risk of confusion and poisoning.

The leaves were also eaten raw, in a salad or on bread for 22% of meals, or cooked in a quiche or pan-fried dish for 21% of meals (Figure 4).

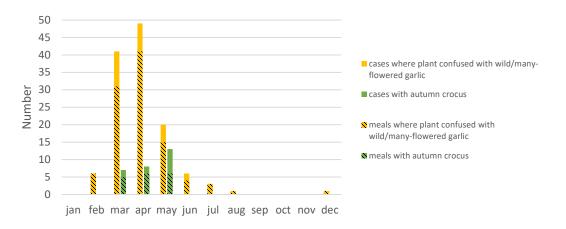


Figure 2: Cumulative monthly breakdown of the number of poisoning cases, and meals where several diners may have eaten autumn crocus or a plant confused with wild or many-flowered garlic. 2020-2022. Source: SICAP.

Although it was not possible to estimate precisely the quantity of leaves collected from the information in the dossiers, the ingestion of a single autumn crocus leaf or teaspoon of pesto was enough to cause poisoning.

Cases of confusion responsible for deaths

Among the 28 people poisoned by autumn crocus, 93% (26 cases) presented with digestive symptoms: diarrhoea (79%), vomiting (68%), abdominal pain (46%) and nausea (18%).

Half of the patients (14 cases) had pronounced or prolonged signs (persistent diarrhoea or vomiting), and four of them had severe life-threatening symptoms, such as serious liver disorders (two cases) or haematological disorders (three cases). A fatal outcome was reported for two patients:

the first death involved a person familiar with collecting wild garlic, who had picked a large quantity of leaves. They died of multiple organ failure five days after a meal containing "home-made" pesto. Colchicine was found in all the patient's biological samples (blood, urine, gastric fluid).

the other person had eaten a quiche supposedly made with wild garlic, picked that day. They died at home the following day. Analysis of the quiche leftovers showed the presence of colchicine. A second person who had shared the meal presented with signs of severe colchicine poisoning. The outcome was favourable after treatment in intensive care.

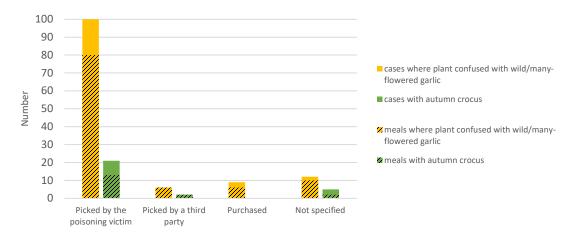


Figure 3 : Method of obtaining the plant in poisoning cases and meals where several diners may have eaten autumn crocus or a plant mistaken for wild or many-flowered garlic. 2020-2022. Source: SICAP.

Vigilance des toxines naturelles

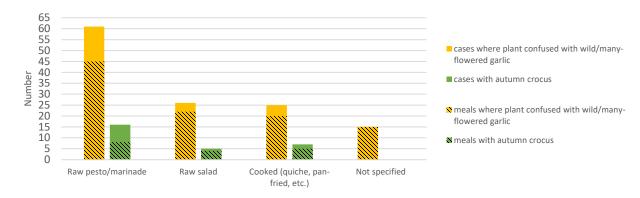


Figure 4 : Method of preparing the plant in poisoning cases and meals where several diners may have eaten autumn crocus or a plant mistaken for wild or many-flowered garlic. 2020-2022. Source: SICAP.

Symptoms were mild in the remaining ten poisoning cases (36%).

In addition, all the people involved in suspected consumption of a plant mistaken for wild or many-flowered garlic had mild symptoms (127 cases). While digestive signs predominated (84% of cases), oropharyngeal pain or irritation was reported in 15% of cases. Confusion with another toxic plant (autumn crocus, arum, lily of the valley, crocus, etc.) could therefore not be ruled out.

Recommendations for avoiding confusion between plants

Following this review, ANSES and the poison control centres renewed their recommendations on picking wild or many-flowered garlic [4]:

- Make sure you know the plant you are picking;
- Do not eat a plant if you have any doubts about its identity;
- Do not pick leaves by the armful to avoid mixing toxic species with edible ones;
- When picking wild garlic, check that each leaf has a garlic odour when rubbed;
- Take photographs of the plants you pick before eating them, for easier identification in the event of poisoning;
- Stop eating the plant immediately if it has a bitter or unpleasant taste;
- Contact a poison control centre immediately if you have any doubts after ingestion, or if you experience any digestive or other symptoms within hours of eating a dish supposedly containing wild garlic or many-flowered garlic.

Sandra SINNO-TELLIER (ANSES), Nathalie PARET (Lyon PCC, Hospices Civils de Lyon) and Christine TOURNOUD (Eastern France PCC – Nancy Regional University Hospital).

TO FIND OUT MORE:

Confusions alimentaires de colchique et d'ail des ours ou de poireau sauvage. Bilan des cas enregistrés par les centres antipoison (de 2020 à 2022). Rapport d'étude de toxicovigilance

	Autumn crocus	Wild garlic	Many-flowered garlic
Toxic	Colchicine	Edible plant	Edible plant
substance	Resistant to cooking and freezing		
	(thermostable)		
	All parts of the plant		
Growing	Meadows, wet grasslands, shady	Undergrowth, damp, shady	Limestone vineyards, meadows
location	edges of woodland, mountains	areas	and gardens in wine-growing
		Deciduous and alluvial forests	regions
		Up to 1600 m altitude	
Leaves	Long and spear-shaped	Oval and spear-shaped	Very elongated, parallel edges
	No stem or petiole	Long petiole	Sheath the stem at the base
	Seem to emerge directly from the	Strong garlic smell	Smell of leek
	ground	Grow in spring	Grow in spring
	Grow in spring		
Flowers	Mauve, pale lilac	White, in umbels	Purple, spherical
	From September to November	From April to June	From June to July
Fruit	Large capsules between the leaves	Small capsules	Small capsules
Bulbs	Large, scaly bulb (corm)	Thin, elongated bulb	Numerous round bulblets

References

[1] Press release by ANSES and the poison control centres of 4 May 2020 "Confusion between autumn crocus and wild garlic: a fatal case of poisoning reported by the poison control centres". https://www.anses.fr/en/system/files/PRES2020CPA08EN.pdf

[2] BfR – German Federal Institute for Risk Assessment. Wild garlic: confusion often leads to poisoning, 04.04.2023.

https://www.bfr.bund.de/en/press information/2023/07/wild garlic confusion often leads to poisoning-310525.html

[3] Razinger, Gasper, Gordana Kozelj, Vojka Gorjup, Damjan Grenc, and Miran Brvar. 2021. "Accidental poisoning with autumn crocus (*Colchicum autumnale*): a case series". *Clinical Toxicology* 59 (6): 493-99. https://doi.org/10.1080/15563650.2020.1832234.

[4] ANSES news item of 19 April 2023 "Confusion between autumn crocus and wild garlic can lead to fatal poisoning". <u>https://www.anses.fr/en/content/actu-en-confusion-between-autumn-crocus-and-wild-garlic</u>

Many mushroom poisoning cases reported in 2022

Every year, foraging for wild mushrooms leads to more than a thousand cases of poisoning, some of which can be fatal. In 2022, many more poisoning cases were reported than in previous years. A specific data collection questionnaire was developed to gain a better understanding of the reasons behind these cases. The results show that the fungi in question were mainly picked in woodlands, with Satan's boletes and yellow stainers topping the list of identification errors. Nearly 40 serious cases occurred in 2022, including two deaths. ANSES has reiterated its recommendations on good foraging practices to be followed to prevent poisoning.

In France, more than 3000 species of "higher" fungi or macromycetes have been documented. Although many people enjoy eating wild mushrooms, some species are nevertheless toxic or even fatal to humans. Every year, more than a thousand cases of mushroom poisoning are recorded by the poison control centre (PCC) network in France. Of these, an average of 30 are very serious and three result in death.

Since 2016, ANSES has been monitoring these poisoning cases from July to December, as most mushrooms grow in summer and autumn. Prevention messages are relayed by the national and local media to coincide with the period when the number of poisoning cases tends to rise.

Many poisoning cases in 2022, as in 2019

For the 2022 season, 1923 symptomatic poisoning cases were reported to PCCs during the monitoring period between 1 July and 31 December 2022. This number was higher than in previous years (typically around 1300 cases per year) and roughly the same as in 2019 (2025 cases), when the number of poisonings was the highest since 2016.

Mushroom growth varies from one year to the next depending on various factors such as precipitation and sunshine. The monthly peak for poisoning in 2022 occurred in October, as in five of the last six years of monitoring.

A specific questionnaire to find out more about the poisoning circumstances

The numerous risk factors for mushroom poisoning include poor storage (for example, plastic bags encourage bacterial growth), consumption of old specimens in poor condition, mushrooms that are undercooked or eaten in excessive quantities, and a consumer's individual sensitivity. However, the main risk still comes from confusion of an edible species with a toxic one.



A specific data collection questionnaire was introduced by the PCCs for the 2022 monitoring period. It was proposed to each person calling a PCC about mushroom poisoning in a food context, in order to systematically collect additional data on how the mushrooms were obtained, the type of mushrooms sought by the picker, the method of identification, and their awareness of ANSES's prevention messages.

Of the 1923 cases reported to the PCC in 2022, 1862 concerned people who had been poisoned during a meal containing mushrooms. The other cases involved accidental ingestion by young children (41 cases in children under 10 years of age) or adults with mental disorders (20 cases), who had eaten mushrooms found in a garden, playground or forest without the knowledge of their parents or carers. These cases are not detailed below.

The poisoning cases were linked to 1371 meals, whether shared or not. In 58.5% of cases (771 meals) only one person was poisoned, while in 41.6% of cases (545 meals) several people (at least two symptomatic individuals) were affected.

Mushrooms mostly found in woodland

Information on the origin of the mushrooms was available for 1146 meals (87%). They had mostly been foraged (92.8% of meals) rather than purchased in a supermarket, market or greengrocer (5.3%), or eaten in a restaurant (1.8%). In 76.9% of cases, they were picked by the poisoning victims themselves, and to a lesser extent by third parties (22.6%) such as friends or neighbours. Foraging took place mainly in woodland (52.5% of cases) and less frequently in a garden (15.5%). Although not recommended, 2.8% of mushrooms had been picked by the roadside.

(Source: SICAP	SICAP).						
	2016	2017	2018	2019	2020	2021	2022
July	18	87	38	24	51	174	93
August	29	182	125	193	48	147	33
September	38	493	221	124	195	132	380
October	271	529	293	1157	764	603	1018
November	232	64	368	404	267	223	307
December	19	31	80	123	40	61	92
Total	607	1386	1125	2025	1365	1340	1923

Table 1: Monthly breakdown of accidental mushroom poisoning cases observed by poison control centres between 2016 and 2022, from 1 July to 31 December. The worst-affected month of the year is shown in blue (Source: SICAP).

Table 2 : Origin of the mushrooms (Source : SICAP).

	Number of meals	%
Picked by an individual	1064	92.8
Picker		
Poisoning victim	818	76.9
A third party	231	21.7
Not specified	15	1.4
Picking location		
Woodland	555	52.2
Garden	165	15.5
Roadside	30	2.8
Don't know	314	29.5
Purchased	61	5.1
Place of purchase		
Greengrocer or supermarket	34	55.7
Market	17	27.9
Mushroom farm	2	3.3
Don't know	8	13.1
Type of mushroom purchased		
Cultivated	19	31.2
Wild	2	3.8
Don't know	40	65.6
Form of mushroom purchased		
Fresh	23	39.3
Dried	24	18.0
Frozen	3	4.9
Don't know	23	37.7
Consumed in a restaurant/obtained from a caterer	21	1.8
Total	1146	100

The purchased mushrooms mainly came from a greengrocer/supermarket (55.7% of meals), or from a market (27.9%).

These purchased mushrooms were mainly cultivated varieties (31.2% of meals), mostly sold fresh (39.3% of meals) or dried (18.0% of meals).

The most sought-after species (not necessarily the ones actually picked) were ceps (27.2%), *Lepiota* (19.9%), boletes (18.4%), *Agaricus* (17.3%), fairy ring mushrooms (5.3%), girolles (5.0%) and chanterelles (3.9%).

When picking the mushrooms, some people tried to identify them prior to consumption using various means such as books, smartphone apps or the internet, or with the help of a third party, pharmacist or mycologist belonging to an association. This information on the attempt to identify the picked mushrooms was available for 660 meals (62.0%). A quarter of the mushrooms had been identified: by a third party in almost half of these cases, by a professional (pharmacist, mycologist) in 24% of cases, or using a smartphone app in 10.5% of cases.

Satan's boletes and yellow stainers responsible for most cases of mistaken identity

Since 2014, thanks to the national "Mycoliste" network linking PCCs and mycology experts, any fungi suspected of causing poisonings for which a PCC was contacted can now be identified, when the necessary information is provided (photographs, description, etc.). This rapid identification enables the PCCs' toxicologists to adapt patient treatment.

In almost half the cases, the collected mushrooms subsequently identified by a Mycoliste mycologist (n = 377) included one or more toxic species. The most frequently identified were Satan's boletes (24.7%), yellow stainers (21.5%), *Entoloma sinuatum* (10.5%), *Macrolepiota venenata* (7.7%), Jack o'lanterns (7.3%) and fly agarics (5.7%).

Table IV shows the most common confusions, when information was available from the Mycoliste network on the species initially sought and on identification of the fungi actually picked.

Most of the mushrooms were eaten fresh (669 meals) and pan-fried (750 meals). Although not recommended, wild mushrooms had been eaten raw in 94 meals.

Poisonings may be benign, but can sometimes be fatal

Poisoning victims mainly suffered from digestive symptoms (1736 people, or 93.2%), and presented with at least one sign of vomiting, nausea, diarrhoea or abdominal pain. Neurological signs were also observed in 17.1% of patients (dizziness, headaches, tremors) and general signs in 10.5% (asthaenia, discomfort, hyperthermia).

Lastly, some people had dermal symptoms (7.5%), mainly excessive perspiration, skin rash or pruritus, as well as cardiovascular symptoms (4.4%) such as hypotension or tachycardia

Although there were more poisoning cases in 2022 than in previous years, the number of very serious cases was no higher (37, or 1.8%).

Most patients involved in the serious cases had amanita poisoning¹ (48.6%), followed to a lesser extent by pantherina syndrome² (21.6%) and sudorian syndrome³ (10.8%).

Two people had both pantherina syndrome and sudorian syndrome, and one person had amanita poisoning and orellanine syndrome. In 10.8% of these very serious cases, no mycotoxic syndrome was identified.

Three patients suffered sequelae from their poisoning: a liver transplant in one case, kidney failure in another and post-anoxic encephalopathy in the third.

In addition, two people died from amanita poisoning after mistaking a toxic species for an edible species. One of the patients reported having picked and eaten what they thought were horse mushrooms, and the other field mushrooms, both of which are edible. In the absence of any photographs, it was not possible to identify the species actually consumed.

Lastly, among the very serious cases, an 11-month-old child was hospitalised in intensive care for severe hepatitis following consumption of mushrooms picked by the family. It is important to reiterate that very young children should not eat wild mushrooms.

Although recommendations are issued by ANSES every year, avoidable poisoning cases are regularly reported to the PCCs, involving the consumption of raw mushrooms, consumption by young children during meals, or use of a mushroom recognition app on a smartphone.

1. Gastroenteritis and hepatic syndrome mainly due to Amanita phalloides, Amanita virosa, Amanita verna, certain macrolepiota and Galerina.

2. Myco-atropine syndrome, especially neuropsychic, after ingestion of Amanita pantherina, Amanita muscaria, Amanita regalis and Amanita jonquillea in particular.

3. Gastroenteritis and cardiovascular syndrome due to ingestion of white clitocybes and inocybes.

Mushrooms identified?	Number of meals	%
Νο	494	74.8
Yes	166	25.2
By a third party	79	49.4
By a pharmacist	31	16.0
Using a book	26	14.3
Using a smartphone app	19	10.5
By a mycologist from an association	14	8.0
Internet	10	7.5

Table 3 : Means of identify the picked mushrooms

<u>**Tableau 4**</u> : Species sought versus species picked and eaten, identified by a mycologist and responsible for poisoning (source: SICAP)

Species sought	Species actually picked
Girolle	Jack o'lantern
Сер	Satan's bolete / Fly agaric / Rubroboletus legaliae
Parasol mushroom	Death cap / Chlorophyllum brunneum / Panther cap / Entoloma sinuatum
Unspecified bolete	Satan's bolete / European white egg
Field mushroom	Yellow stainer
Saint George mushroom	Inocybe / Clitocybe / Brown roll-rim
Grey knight	Entoloma sinuatum
Caesar's mushroom	Fly agaric
Fairy ring mushroom	Inocybe / Entoloma sinuatum
Scarletina bolete	Rubroboletus legaliae / Bitter beech bolete / Satan's bolete
Puffball	European white egg
Charcoal burner	Russula badia
Amethyst deceiver	Rosy bonnet
Trooping funnel	Entoloma sinuatum
Miller	Entoloma sinuatum
Laccaria	Мусепа

	2016	2017	2018	2019	2020	2021	2022
Serious cases	11	41	24	27	34	41	37
% of total cases	1.30%	2.40%	2.30%	1.30%	2.50%	3.20%	1.80%
Deaths	0	2	1	3	5	4	2
% of total cases	0%	0.10%	0.10%	0.10%	0.30%	0.30%	0.10%

Tableau 5 : Number of serious cases and deaths per year

To limit the risk of poisoning, ANSES recommends:

- Only picking mushrooms that you know very well: some highly poisonous fungi closely resemble edible species. In addition, poisonous fungi can grow in the same place that you picked edible mushrooms the previous year.
- If you have the slightest doubt about the condition or identification of any of the mushrooms you have picked, do not consume them until you have had them checked by a specialist. You can seek help from a pharmacist, or local mycology associations and societies.
- Only pick specimens in good condition and take the entire mushroom (stalk and cap), to facilitate identification.
- Avoid picking mushrooms near potentially polluted sites such as roadsides, industrial zones and landfills.
- While picking, carefully separate the mushrooms according to species, to avoid mixing pieces of poisonous fungi with edible mushrooms.
- Place the mushrooms in a box, crate or basket and never in a plastic bag, which accelerates their decomposition.

- Store the mushrooms in the refrigerator (maximum 4°C) while avoiding contact with other foods, and eat within two days of picking.
- Consume in reasonable quantities after cooking them thoroughly (pan-fry for 20 to 30 minutes or boil in water for 15 minutes), and never eat wild mushrooms raw.
- Never feed the mushrooms you have picked to young children.
- Ensure that children never put mushrooms found in the garden or school playground in their mouths.
- Do not consume mushrooms identified solely by a fungi recognition app on a smartphone, due to the high risk of error.
- Do not eat mushrooms sold by street vendors.

Chloé GREILLET (Anses)

TO FIND OUT MORE:

"Mushroom foraging" information sheet

Poisonings due to wild mushroom consumption: stay alert!

Advice from ANSES on video

Improperly used disinfectants responsible for skin burns in young children

Following several reports of severe skin disorders, ANSES analysed accidents between 2017 and 2022 involving young children in community settings and linked to the use of biocidal disinfectants. Most of these accidents, which were more common during the COVID-19 pandemic, occurred in nursery schools when toilets were being disinfected. Varying conditions of use for the same product may have contributed to errors, and labelling was sometimes deficient. In addition, the conditions of use were not always complied with. ANSES issued recommendations for reducing the risk of accidents due to the use of disinfectant biocidal products in community settings.

During the months of May and June 2021, ANSES received several reports of severe skin disorders affecting young children in community settings, associated with the use of disinfectant biocidal products. In view of the increase in the number of cases and the fact that some of them were serious, ANSES conducted a study of data from poison control centres (PCCs) to identify the circumstances of these accidents and the products involved, and to recommend preventive measures.

An increase in accidents during the COVID-19 pandemic

An "event" was defined as the occurrence of an accident affecting one or more children, on the same date, in the same place and with a given product.

The cases of interest were children (under 18 years of age) who had been indirectly exposed to a PT2 or PT4¹ disinfectant biocidal agent in a community facility, i.e. following the cleaning of a surface or object, and who developed symptoms after contact with the disinfected area.

Over the period from 01/01/2017 to 31/12/2022, the PCCs recorded 37 events representing a total of 118 cases of skin disorders among children in community settings, associated with the use of disinfectant biocidal products. These were either isolated cases, i.e. a single child affected by the event (n=20), or clustered cases (n=98) corresponding to several children affected by the same event.



Over the period from 01/01/2017 to 31/12/2022, the PCCs recorded 37 events representing a total of 118 cases of skin disorders among children in community settings, associated with the use of disinfectant biocidal products. These were either isolated cases, i.e. a single child affected by the event (n=20), or clustered cases (n=98) corresponding to several children affected by the same event.

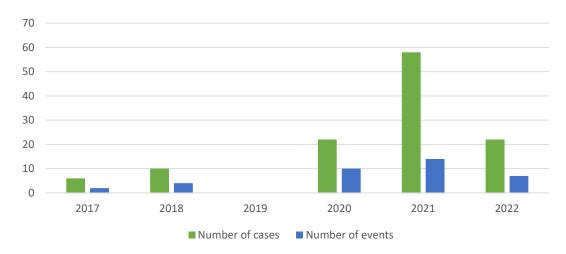
The clustered cases were divided into 17 different events, each involving between two and 26 children.

The sharp rise in the number of cases from 2020 onwards raised suspicions of a link with the COVID-19 epidemic. This pandemic led to new practices in terms of the frequency of disinfection, the surfaces disinfected and the products used, especially in places hosting children.

Disinfection of toilets in nursery schools responsible for many accidents

Most of the accidents occurred in schools (n=28), and more specifically in nursery schools (n=16). Disinfection of toilets/sanitary facilities was responsible for 56.7% (n=21) of events, with this figure rising to 94% for events occurring in nursery schools (15/16). Whereas prior to 2020, accidents of this type were almost exclusively due to disinfection of toilets, a wider variety of situations leading to skin disorders were observed in 2020 and 2021: disinfection of tables, chairs, balls and boats.

^{1.} Biocidal products are classified into 22 biocidal product types (PTs), organised into four main groups corresponding to their specific uses. PT2 refers to disinfectants and algaecides not intended for direct application to humans or animals, and PT4 to products used on surfaces in contact with food and feed.



<u>Figure 1</u>: Annual breakdown of the number of events and number of cases of skin disorders in children following indirect exposure to a disinfectant biocidal product in a community facility, registered by poison control centres. (Source SICAP: 2017-2022).

In contrast, almost all the accidents in 2022 were again due to disinfection of toilets. This finding is consistent with the recommendations issued during the pandemic to scale up cleaning and disinfection efforts, especially for surfaces and objects, and for the servicing of sanitary facilities.

This problem mainly concerned young children (under 6 years of age), especially young girls, which can be explained by the fact that they sit down on the toilet seat far more than boys. In addition, the skin of young children is more fragile and therefore more sensitive to disinfectants. The vast majority of skin disorders were minor (n=113). Four children nevertheless had moderately severe symptoms (second-degree burns) and one case was very serious (third-degree burn).

Dermal symptoms were mainly mild, namely pruritus (20% of cases, n=24) associated with erythema/first-degree burns (64.4% of cases, n=76) or pruritic skin rashes (22% of cases, n=26).

Eleven children suffered second-degree burns and one had a third-degree burn requiring a skin graft; this was the case that led to the alert and establishment of the study.

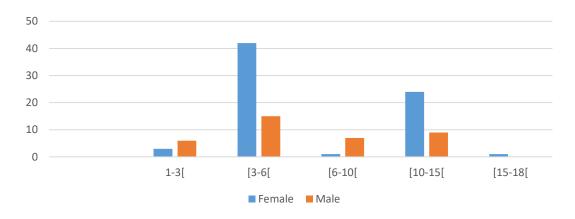


Figure 2 : Breakdown by age group of the number of children with skin disorders following indirect exposure to a disinfectant biocidal product in a community facility, registered by poison control centres (Source SICAP: 2017-2022).

Conditions of use that varied from one product to another, and labelling sometimes deficient

The conditions of use on product labels and other documents (such as technical data sheets) were examined. This showed that for the same product, these conditions of use sometimes differed according to the surface to be disinfected, potentially leading to errors in use.

For example, while 14 products were ready-to-use and 13 required dilution before application, with another six products the need for dilution depended on the type of surface to be disinfected (for example a product to be used undiluted on floors but diluted for other surfaces). Rinsing instructions also varied. With 14 products, rinsing was mandatory after application, another five did not require rinsing, and for seven products, rinsing depended on the surface being disinfected. Lastly, three products could be rinsed, dried or wiped, with the choice left up to the operator, and for the last product rinsing was optional.

Analysis of the products showed that the recommendations for use did not always appear on the labels. They were sometimes found on documents such as technical data sheets.

However, these documents are not always made available to the people handling the products, which can lead to errors in their use.

Lastly, some labels contained confusing information, such as "no rinse" (whereas the technical data sheet stated that the product could be rinsed, dried or wiped), or "use the ready-to-use solution immediately" (for a product that needed diluting).

Product conditions of use not always complied with

For most of the events reported (n=32/37), only one biocidal product had been used.

For 25 events, the product used was actually intended to disinfect the surface involved in the event. On the other hand, for 11 events, the product did not seem to be the most appropriate, or was even unsuitable, for the purpose for which it was used (for example, a moss remover for roofs and façades was used to clean a playground slide). For the last event, only one of the two products used was suitable for the purpose.

In order to determine the cause of each accident, the conditions of use stated in the technical specifications were compared with the way in which the products had actually been used during the event.

Compliance with product handling and application conditions	Number of events	Number of cases	
No	14	34	
If no, failure to follow instructions regarding:			
Rinsing	3	7	
Dilution	5	16	
Drying	3	7	
Rinsing + waiting before contact	2	3	
Product left within reach of children	1	1	
Yes	12	60	
but product unsuitable for the purpose	4	23	
Not specified	11	24	
but product unsuitable for the purpose	3	3	
General total	37	118	

Table 1 : Breakdown of conditions of use (source: SICAP)

For 14 events, the conditions of use had not been complied with. Five of these involved a problem with dilution, such as a dilution error, a failure to dilute the product, or dilution carried out in an unsuitable place. Three events concerned a problem with rinsing the product. Others concerned a failure to wait for the specified time before contact (n=2), or a problem with drying (n=3). For one event, the product had been left within the child's reach.

For 12 events, the product had been used in accordance with the recommended conditions of use, but in four of these it was unsuitable for the purpose, which may explain why the accidents occurred.

For 11 events, it was not possible to identify the reason for the accident. However, for three of these, the product used was in any case unsuitable for the purpose.

Reducing the risk of accidents due to the use of disinfectant biocidal products in childcare facilities

Although the number of accidents associated with the use of disinfectant biocidal products in community settings fell in 2022, after two years in which the number of incidents was particularly high, they have not gone away and a new series of cases was reported to the PCCs in early 2023, reflecting the persistence of the problem.

Based on this study's findings, the following recommendations were made for reducing the risk of accidents due to the use of disinfectant biocidal products in community facilities, particularly those hosting children:

- use products that are suitable for the surfaces to be disinfected;
- opt for the least hazardous products, especially in community facilities where there are young children;
- choose ready-to-use products to avoid dilution errors, and products with clear, simple instructions for use;

- keep products away from the public and, if dilution is necessary, do this in an equipment room dedicated to this purpose;
- rinse products after application or accidental spillage, or at least wipe the surfaces dry;
- wait for the specified period after disinfection before giving children access to the disinfected area/surface, in accordance with the instructions of the products used;
- do not carry out cleaning and disinfection tasks in the presence of children;
- train staff in the correct use of disinfectants;
- in the event of skin contact, remove any clothing soaked in the product and wash skin thoroughly with water. Take care not to allow the product to remain between the skin and clothing, watches, shoes, etc. If the affected area is extensive and/or skin lesions appear, see a doctor or call a poison control centre.

Chloé GREILLET (Anses), Gaëlle CREUSAT (Poison control centre of Nancy) and Patrick NISSE (Poison control centre of Lille)

TO FIND OUT MORE:

Rapport d'étude de toxicovigilance. Atteintes cutanées chez les enfants en lien avec l'utilisation de désinfectants en collectivité - Observations enregistrées par les Centres antipoison et de toxicovigilance français (2017-2022)

Re-authorisation of the herbicide terbuthylazine: conditions of authorisation adjusted following monitoring of surface water

While all herbicides in the triazine class were withdrawn from the French market in the early 2000s because of their propensity for long-term contamination of groundwater, terbuthylazine was made available on the market again in 2017, at a reduced dose and solely for controlling weeds in maize. In the year that followed, residues of this substance were regularly detected in watercourses, but without exceeding the risk thresholds for aquatic organisms or the threshold that means the water can no longer be used for drinking. Based on this observation and with the aim of preserving the quality of water resources, ANSES decided to restrict the conditions of use for products containing terbuthylazine, in order to limit the risk of water pollution.

In early 2020, Brittany's Regional Directorate for Food, Agriculture and Forestry notified ANSES that terbuthylazine residues were once again being found Brittany's regularly watercourses. These in observations coincided with the re-authorisation of this substance for controlling weeds in maize fields. At the same time, monitoring of the Champigny limestone aquifer in Seine-et-Marne by Aqui'Brie¹ revealed the presence of terbuthylazine for the first time since monitoring began in 2012. These two alerts led ANSES, as part of its phytopharmacovigilance mission, to analyse the situation at national level and the circumstances behind this contamination.

A triazine herbicide back on the market

In France, the majority of terbuthylazine-based products were prohibited between 2001 and 2003 as part of a policy to restore water quality, following the widespread presence of this substance, and of triazines in general, in environmental water. However, in 2017, in application of the European regulations and taking account of a reduced dose, ANSES granted marketing authorisation to Syngenta, the applicant, for the product CALARIS, which contains a combination of terbuthylazine and mesotrione, for use solely controlling weeds² in maize. In particular, the product limits the growth of jimsonweed, a weed that is difficult to manage. Although it is a nuisance to farmers in the field, jimsonweed does not pose any risk of contaminating maize grain harvests, as its seeds are much smaller than those of maize, making them easy to sort at harvest time.



In 2018, 115.3 tonnes of terbuthylazine were sold, making it the 80th most traded substance, out of the 464 available on the French market. Between 2019 and 2021, sales rose slightly again: 125 tonnes in 2019 (putting it in 55th place out of 450), 178.4 tonnes in 2020 (52nd place out of 452) and 146.5 tonnes in 2021 (56th place out of 448). Brittany had the highest concentration of sales, with a quarter of the national total, followed by the Pays-de-la-Loire, Grand-Est and Nouvelle-Aquitaine regions, which each accounted for around 11-12% of national sales.

Immediate contamination of watercourses, but at concentrations below the thresholds for concern

Despite the cessation of its use in 2003, terbuthylazine and its metabolites terbuthylazine-desethyl, terbuthylazine-desethyl-2-hydroxy and hydroxyterbuthylazine were found in watercourses (at residual background levels) at 1 to 6% of sampling points. This is due to their persistence in soil and runoff into watercourses; this long-term degradation is a property common to all substances in the triazine class.

In the year following its reuse, terbuthylazine and its metabolites were quantified more frequently, at up to 14% of sampling sites. At a regional level, this increase in the quantification frequency could be seen in the maize-growing parts of France (Brittany, Ile-de-France, Grand-Est).

^{1.} Aqui'Brie is an association bringing together all the stakeholders of the water in the Champigny limestone aquifer

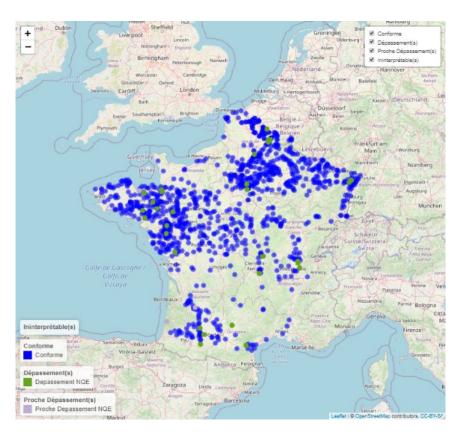
^{2.} A weed is a plant that grows unintentionally in a field and competes with the crop.

Everything you need to know about water monitoring³

Environmental water refers to both surface water (rivers, streams, lakes, etc.) and groundwater (water tables). It is monitored by water agencies under the European Water Framework Directive. Some environmental water is used to produce tap water, also known as drinking water or "water intended for human consumption". Environmental water intended for the production of drinking water, and drinking water itself, are also monitored by the regional health agencies.

The results of this monitoring are generally expressed in terms of annual frequencies (of quantification, of thresholds exceeded, etc.). For example, the quantification frequency of a given substance for a given year corresponds to the number of sampling sites where the substance was quantified at least once during the year, in relation to the total number of sampling sites where the substance was screened for during the year.

The threshold values for these three types of water differ: in surface water, there is an ecotoxicity threshold value for organisms living there, which varies depending on the substance. In groundwater and drinking water, this value is $0.1 \mu g/L$. The quality limit for raw water of any origin used for the production of drinking water, excluding bottled spring water, is a single value of $2 \mu g/L$ per individual pesticide substance, including relevant metabolites.



<u>Figure 1</u>: Distribution of surface water monitoring points where terbuthylazine was quantified at least once, and monitoring points where the environmental quality standard for terbuthylazine was exceeded, in metropolitan France, for 2018

3. Anses - Pesticides dans l'eau du robinet

In these three regions, the quantification frequency sometimes exceeded 20%. Terbuthylazine and its metabolites were also found most frequently in watercourses during the months when it was used, i.e. mainly in May-July and to a lesser extent in October-November.

However, these quantifications did not reach concentration levels that are cause for concern, whether for aquatic organisms or for the potential potability of the water. The environmental quality standard, which is the threshold value used in the European Water Framework Directive⁴, was thus exceeded at no more than 0.86% of sampling sites, while the threshold value with no effect on aquatic organisms and the threshold value that allows the water to be used for drinking (2 μ g/L) were never exceeded (Figure 1).

In groundwater, similarly as for surface water, terbuthylazine and its metabolites have been found continuously at high background levels since its ban, with quantification percentages ranging from 1.17 to 2.84% for terbuthylazine, from 3.46 to 7.87% for terbuthylazine-desethyl and from 0.18 to 5.92% for hydroxyterbuthylazine, depending on the year. However, unlike surface water, no increase in the quantification frequency has been observed since 2018. This is due to the greater inertia of groundwater compared with surface water. It is therefore important to remain vigilant to groundwater contamination by terbuthylazine, and especially its metabolites, given what is known about the physico-chemical properties of triazines.

In water intended for human consumption, terbuthylazine and its metabolites were also found at a frequency that did not increase in 2018, ranging from 0.53% to 1.49% for terbuthylazine, from 2.1% to 4.85% for terbuthylazine-desethyl and from 1.16% to 7.93% for hydroxyterbuthylazine, depending on the year. However, the threshold of 0.1 μ g/L, which indicates that the water is not compliant, was rarely exceeded: the maximum number of non-compliant samples in any one year was 0.13% of sampling sites for terbuthylazine, 0.33% for terbuthylazine-desethyl and 0% hydroxyterbuthylazine.

Marketing authorisation amended in order to reduce contamination

These results were presented to ANSES's MA Monitoring Committee for plant protection products. The committee concluded that although the thresholds for concern in the various types of water had not been exceeded, this compound should be retained in the arsenal of products available to combat certain plants presenting health issues (jimsonweed, ragweed) but its conditions of use should be amended in order to preserve the quality of water resources. ANSES incorporated the committee's recommendations into the marketing authorisation⁵:

- application is only possible once every three years (instead of two years previously), with no reduction in dose because the currently authorised dose is necessary in certain situations.
- application is not possible within 20 metres of water points, and a five-metre strip of vegetation must be left along their edges.

Ohri YAMADA (Anses)

References

ANSES (2021). Occurrence of terbuthylazine in surface water: https://www.anses.fr/fr/system/files/PPV2020VIG0189Ra.pdf

ANSES (2023). Pesticides in tap water: https://www.anses.fr/en/content/pesticides-tap-water

ANSES (2021). Decision on an application for renewal of marketing authorisation for the plant protection product CALARIS: https://www.anses.fr/fr/system/files/phyto/decisions/CALARIS_PREX_2017-2392_D.pdf

Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy: <u>https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32000L0060</u>

^{4.} https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32000L0060 .

^{5.} https://www.anses.fr/en/content/pesticides-tap-water

Publication director: Benoit Vallet Editor in chief: Juliette Bloch Editorial secretariat: Chloé Greillet Edition follow up: Flore Mathurin

Editorial board

For the network of French Poison Control Centres: Magali Labadie Nutrivigilance: Fanny Huret Veterinary pharmacovigilance: Sylviane Laurentie Phytopharmacovigilance : Ohri Yamada Toxicovigilance: Sandra Sinno-Tellier Vigilance for chemical products: Cécilia Solal Vigilance for biocides products and plant inputs: Chloé Greillet National network for the monitoring and prevention of occupational diseases: Eva Ougier ANSES is in charge of several health vigilance systems: pharmacovigilance for veterinary medicinal products, nutrivigilance, phytopharmacovigilance, toxicovigilance and vigilance for occupational diseases. Our vigilance activities make little noise and are therefore poorly known to public health actors, health professionals, marketers and users in general. And so, in order to make our work more visible we have decided to create adedicated newsletter entitled Vigil'Anses.

As news on each of our vigilance topics crops up, this quarterly newsletter presents the main results of the work carried out by ANSES within the framework of its vigilance missions, in conjunction with its partners, professional networks and expert groups, as well as the actions we have undertaken.

The articles are deliberately short, and are intended for all those involved in the occupational and environmental health and safety field: public authorities, health agencies, institutes and expert bodies that are partners of ANSES, prevention policy managers, the

scientific community, professionals, associations and users. Vigil'Anses also invites the interested reader to delve deeper and discover publications, opinions and reports available online that will further their knowledge.



FRENCH AGENCY FOR FOOD, ENVIRONMENTAL AND OCCUPATIONAL, HEALTH & SAFETY 14 rue Pierre et Marie Curie 94 701 Maisons-Alfort Cedex

www.anse.fr / @Anses_fr