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French agency for food, environmental and occupational health & safety

Investigate, evaluate, protect

THE BULLETIN OF VIGILANCE No.12

November 2020

VigilAnses

Once again, the coronavirus epidemic and its sometimes unexpected consequences are the subject of an article in this issue 12 of Vigil'Anses. **The hand sanitisers** provided for disinfection purposes in public places have led to **young children being sprayed in the eyes**. ANSES was alerted to this by ophthalmologists and French poison control centres; our article reviews the situation.

The second article presents the results of a 27-month study carried out by poison control centres and ANSES on **accidental injection of humans with vaccines intended for animals**. It details the circumstances, risk factors for complications and health consequences.

Lead poisoning is generally synonymous with unsanitary housing, due to the persistence of old lead-based paint or water pipes. However, there is another cause of lead exposure. Much less widely known to the public and healthcare professionals, the **practice of sport or professional shooting** nevertheless causes cases of lead poisoning in children and adults every year. An article in this issue discusses this topical subject, following several clustered cases identified by poison control centres.

The last article reports on a recent example of serious adverse effects following consumption of food supplements, which are often wrongly considered harmless. ANSES's nutrivigilance scheme was notified of two cases of **severe acute hepatitis associated with consumption of a food supplement** used to maintain healthy hair and containing vitamins A and E. Analysis of the cases and the literature suggested toxicity of the food supplement due to the concomitant use of a progestin contraceptive.

Juliette Bloch, Editor-in-Chief of Vigil'Anses

Take care to prevent hand sanitiser from getting into young children's eyes !

The easing of lockdown has enabled many public places such as shops to reopen. These premises now provide hand sanitiser at their entrance so that people can disinfect their hands. Because young children's faces are often at the same height as the dispensers, several serious cases of them being sprayed in the eyes with hand sanitiser have been treated by ophthalmologists or recorded by French poison control centres. Besides the information to be provided to the public and to establishments open to the public, the first step to be taken in the event of an accident involving a child is to rinse the eye immediately and thoroughly with clean water, *without delay*. Any delay in rinsing increases the risk of damage to the eye that may require surgery.

Due to the COVID-19 epidemic, the French government decreed a total lockdown, which ended on 11 May 2020. The easing of this national lockdown enabled many public places such as shops and restaurants to reopen. In order to comply with the barrier measures introduced to combat the epidemic, these premises began providing hand sanitiser to enable people to disinfect their hands.

This was made available by means of dispensers placed in a visible position at the entrance to the premises. Some dispensers are one metre tall, operated with a foot pedal or triggered automatically by an infrared sensor. They are designed to be at the height of an adult's hands... which is also unfortunately the same height as a young child's face. Because they see it as a game or wish to copy the adults accompanying them, children are tempted to operate the dispenser pump to disinfect their hands, at the risk of spraying the product directly into their eyes.

Eye damage that can be serious in young children

In July 2020, ophthalmologists from the Rothschild Foundation Hospital in Paris and the French Ophthalmological Society issued an alert, in view of the increased number of children consulting for eye injuries due to hand sanitiser splashes in this context.

The ophthalmologists stressed the seriousness of certain injuries that required emergency surgical treatment. Indeed, the higher the alcohol concentration in the hand sanitiser (at least 60% for authorised products), the greater the eye damage. The serious cases were characterised by damage to the cornea and required admission to hospital. An amniotic membrane transplant for the eye, under general anaesthetic, was sometimes necessary to accelerate healing of the damaged cornea and avoid superinfection.

In August 2020, French Poison Control Centres (PCCs) also reported an increase in calls about this type of accident: a total of 63 cases involving children with eye symptoms and occurring in the circumstances described were recorded between 11 May and 24 August 2020 (Figure 1). Only four other cases were reported between 1 January 2018 and 10 May 2020 (three cases in 2018 and one in 2020), showing how these accidents were linked with the coronavirus epidemic and easing of lockdown.

The children were aged from 9 months to 10 years, with 50% of them being under 4 years of age. There were slightly more girls than boys, which is unusual in everyday accidents.

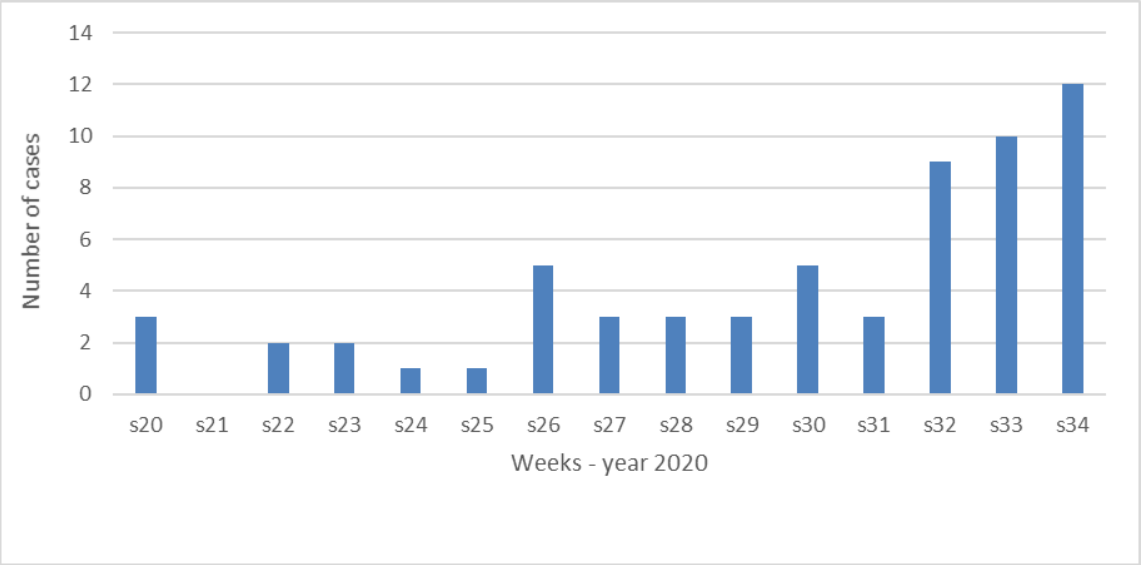

Figure 1 : Weekly breakdown of cases of eyes sprayed with hand sanitiser in young children under ten years of age, following use of a dispenser in a public place, recorded by the PCCs between 11/05/2020 and 24/08/2020 (N=63). Source: SICAP.

Sixty-one children (97%) had low-severity eye damage: the most common symptoms observed were eye redness or pain, redness or swelling of the eyelid, or increased sensitivity to light. In two cases, the splashes caused corneal damage, confirmed by ophthalmological examination. This damage was reversible after symptomatic treatment. Thirteen of the 63 children (20.6%) were taken to an emergency department, and one child was seen by their doctor.

The other children were supervised by their relatives at home after prolonged rinsing of the eye.

Three-quarters (76.2%) of accidental sprays of hand sanitiser had occurred in a shop or shopping centre (Table I). The remainder were in restaurants, swimming pools, public gardens or the street from a dispenser provided by the municipality.

Tableau I : Locations where young children were sprayed in the eyes with hand sanitiser, following use of a dispenser in a public place, recorded by the PCCs between 11/05/2020 and 24/08/2020 (N=63). Source: SICAP.

Location	Number of cases
Shop, shopping centre	48
Restaurant, cafeteria, bar	6
Public road, pavement, street	2
Extracurricular facility, day-care centre, summer camp	2
Public garden, park	2
Nature, outdoors	1
Swimming pool, thermal baths, spa, hammam	1
Outdoor sports field	1
Total	63

In the majority of cases, it was the child that had activated the hand sanitiser dispenser causing the accident. In two cases, an adult had brought the child's hands to the dispenser and sprayed the product into the hands himself, but this had not prevented the child's eye from being splashed. In another case, the child had been sprayed when the parent pumped the dispenser to disinfect their own hands.

With three of the children, a pedal-operated dispenser was mentioned at the time of the call to the PCC, but in the vast majority of cases no information on the type of dispenser was given.

What action should be taken if hand sanitiser gets into the eyes?

If hand sanitiser comes into contact with the eyes, they should be rinsed immediately and thoroughly under a trickle of lukewarm water at low pressure, eyelids open, for at least 15 minutes. Contact between the product and the eye should be as short as possible to avoid corneal damage. It is therefore essential to quickly find a supply of water (sink tap, etc.), or use a water bottle. **Any delay in rinsing is detrimental and increases the risk of severe damage.**

If the child has severe and persistent pain after rinsing and/or the eye remains very red (although the pain may subside after a few hours), it is necessary to call a PCC, which will offer medical guidance, or consult an ophthalmologist.

Raise awareness among the public and professionals in places open to the public, to prevent such accidents

Although it is an essential barrier measure for preventing the risk of contamination by the new coronavirus, hand sanitiser should only be used, particularly by young children, when hand washing with soap and water is impossible.

In places open to the public, it is preferable for the accompanying person to take a small amount of the product in their own hands before applying it to the child's hands. It is of course inadvisable to let the child use the dispenser himself, or to help the child bring their hands up to the dispenser.

Following this alert, ANSES and the Directorate General for Health issued a joint press release on 31 August 2020, with the support of the Poison Control Centres and the French Ophthalmological Society, in order to prevent the risks incurred when very young children use these dispensers, and to indicate some preventive measures and the initial steps to be taken in case of exposure [1, 2].

Published just prior to the start of the school year, the information was also disseminated to the State services responsible for children and families, so that preventive measures could be implemented. Shops and other places open to the public are also invited to disseminate recommendations reiterating the need to keep children away from hand sanitiser dispensers, as well as the immediate action to be taken if eyes are sprayed. A leaflet containing recommendations is available on the ANSES website [1].

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TO FIND OUT MORE :

[1] https://www.anses.fr/en/content/hand-sanitiser-take-care-protect-young-children-accidentally-splashing-their-eyes-0
[2] https://solidarites-sante.gouv.fr/actualites/presse/communiques-de-presse/article/sha-projections-accidentelles-dans-les-yeux

Lead poisoning in shooting ranges: a risk that persists, despite being known

Visiting a shooting range, whether for leisure or work, can lead to exposure to lead dust through inhalation or ingestion. This is a health risk, especially for children and pregnant or breastfeeding women. Although this risk is known and is governed by regulations and good practice guidelines, lead levels above the vigilance thresholds are regularly reported by poison control centres and occupational disease consultation centres in France.

The Nancy and Lyon poison control centres (PCCs) recently notified ANSES of several clustered cases of lead poisoning among people practising sport shooting in clubs. Although the phenomenon is far from new, these alerts are an opportunity to highlight the risk presented by this exposure for the shooters themselves, particularly children and pregnant women, but also for their families and professionals.

Lead poisoning: "non-threshold" toxicity

Lead poisoning results from the excessive penetration of lead into the body. While there is no threshold for non-toxicity, exposure is most hazardous in children, even at low concentrations, and can lead to a decrease in cognitive (attention, learning, reasoning, etc.) and sensorimotor performance, in particular affecting hearing acuity, inhibiting height and weight growth, and causing sexual maturation disorders [1]. Lead exposure during pregnancy harms foetal development. In adults, even at low doses, it can lead to high blood pressure, increase the risk of chronic kidney disease and promote male fertility problems. Population exposure has decreased sharply in recent years due to the ban on lead paints (prohibited as early as 1909 but still found in housing built before 1949 and in some paints until the 1970s), the replacement of lead pipes supplying water, the ban on leaded petrol (from 2000), the control of industrial emissions, and the lowering of the threshold for lead in drinking water (European Directive 98/83/EC of 1998).

Childhood lead poisoning is a disease often associated with poverty because lead is still found in old or unsanitary homes, due to old lead-based paints and the dust they generate indoors, which young children can put in their mouth or inhale. Because of its seriousness, childhood lead poisoning is a notifiable disease, monitored by *Santé Publique France*[1]. It must be notified when the blood lead level is 50 µg/L or more in a minor child. This is a threshold for intervention and not a toxicity threshold since, as already mentioned, there is no "zero toxicity" threshold. Blood lead levels between 25 and 50 µg/L should therefore also be monitored (this is known as the vigilance zone) [2]. For adults, the French Labour Code defines different blood lead levels for workers exposed to lead: monitoring to be established from 100 µg/L for women or 200 µg/L for men[2], threshold not to be exceeded of 300 µg/L for women or 400 µg/L for men[3].

1.Public Health France

2. Article R4412-160 of the French Labour Code states that reinforced medical surveillance of these workers is necessary if the concentration in the air is greater than 50 $\mu g.m^{-3}$ as a weighted average for an eight-hour period, or if the blood lead level is greater than 200 $\mu g.L^{-1}$ in men or 100 $\mu g.L^{-1}$ in women. Blood lead levels must not exceed 400 $\mu g.L^{-1}$ in men or 300 $\mu g.L^{-1}$ in women.

3. Article R4412-160 of the French Labour Code.

Regional health agencies (ARSs) and poison control centres are central to the scheme for monitoring and treating lead poisoning in children and adults. Occupational medicine takes care of monitoring workers exposed to lead.

The alert

Every year, cases of lead poisoning in children associated with the practice of shooting are recorded by the mandatory reporting scheme of *Santé Publique France*. The clustered cases reported here are noteworthy for their number. They concern both adults (for whom there is no surveillance) and children accompanying their parents during the shooting activity.

In 2019, the PCC of Nancy and the ARS Grand-Est became aware of 13 cases of adults attending the same shooting club in the Bourgogne-Franche-Comté region and presenting high blood lead levels, ranging from 172 to 565 µg/L. Five people experienced unspecific symptoms, which they attributed to lead poisoning (headaches, asthenia, abdominal pain), without this link being formally established. This club offers various disciplines at three different ranges. Measures were immediately taken by the club itself: closure of one of the ranges, recommendation that shooters get their blood lead levels measured, dissemination of information on the risk of lead exposure and the good practices to be implemented to limit it. The ARS drafted and distributed a document on risk and good prevention practices to all the presidents of the leagues in the region so that they, in turn, could circulate it to all shooting range managers.

In the same region, a child shooting at another club was identified by the national surveillance system for childhood lead poisoning, while at the same time, several adult members of this club were found to have high blood lead levels. The range was closed and dust sampling identified significant environmental contamination before cleaning (100,000 µg/m^2 in the shooting area and 10,000 µg/m^2 in the communal areas). As an indication, according to a study published in 2015 and cited in the recent ANSES report on lead contamination of outdoor public areas [3], the concentrations measured in samples of playground or indoor dust were less than 500 µg/m^2. In the United States, a maximum threshold of 108 µg/m^2 is proposed for dust in homes [4].

In 2020, clustered cases of lead poisoning in children were reported to the Lyon poison control centre and the ARS Auvergne-Rhône-Alpes, in children or adolescents practising competitive shooting in the same shooting gallery. This range hosted nearly 70 children, half of them under 10 years old (children can practice shooting from 7-8 years old depending on their morphology). Of the 18 children tested, eight had blood lead levels above the threshold of 50 µg/L, with a maximum of 129 µg/L. The others had blood lead levels between 18 and 50 µg/L. In addition, two children, aged 7 and 11 years, who were not shooting but were brothers of other children in the club, had blood lead levels in the vigilance zone (38 and 26 µg/L, respectively). The inspector sent to the site identified numerous failings with respect to the premises; the shooting gallery was therefore closed temporarily and work was initiated. An information campaign was conducted among parents and children, physicians in the *département* and the departmental shooting federation. It should be noted that the COVID-19 lockdown period (which began shortly after the site was closed) led to a strict cessation of exposure with a decrease in lead concentrations in the children tested.

What is the source of the lead that accumulates in a shooter's body?

Bullets in firearms are made mostly from lead, but a large quantity of lead is also found in the primer, which ignites in the barrel of the gun to provide propulsion for the projectile. Only jacketed bullets do not contain lead, whether in the powder or the primer. As it passes through the barrel, part of the lead bullet disintegrates into fine fragments. Lead particles, as well as dust and smoke from the primer and bullet fragments, are then ejected from the gun barrel at high pressure when fired. Inhalation of these fine lead particles by the shooter is one route of exposure. Fine or coarser particles emitted when a gun is fired can also settle on hands, clothing or other surfaces in the vicinity of the shooter: ingestion through hand-to-mouth contact (cigarettes, food, handling of mobile phones) is therefore a second route of contamination. Lead dust is also generated when the bullet hits its target or the bulletproof device, and accumulates in the dust on the ground. Shooters may take these particles home with them, on their equipment, clothing or footwear, thereby exposing their families. Lastly, another source of exposure is the home-made manufacture of ammunition, with a risk of pollution spreading from the garage or workshop to living areas, especially if the household vacuum cleaner is used to clean the room where the ammunition is produced. The use of recycled material – the collection of old warheads (which involves high exposure to dust) or purchase of lead from scrap metal dealers – increases the risk of poisoning.

Workers also exposed

Professional or amateur shooters are not the only ones exposed to lead. Anyone involved in picking up casings, handling bullets, cleaning shooting ranges, including the removal of lead particles from floors and surfaces, targets and ventilation systems (for indoor ranges) is at risk, especially if they have been performing this work for a long time at the club.

A retrospective study of data from the National Network for Monitoring and Prevention of Occupational Diseases (RNV3P), which is coordinated by ANSES, identified the cases of lead poisoning associated with shooting ranges recorded by the 30 occupational disease consultation centres (CCPPs) in France between January 2010 and December 2018. These concerned both occupational exposure (21 cases) and non-occupational exposure of recreational shooters (37 cases). Only six centres had recorded cases and one centre accounted for 80% of cases.

The professionals exposed were predominantly men (19 men and two women), with a median age of 50, working in a variety of occupations such as police officers, trainers, instructors, sport shooting coaches, bullet collectors, cleaning and maintenance workers, and receptionists. In half of the cases they had been referred to the CCPPs by their occupational physician, and in one third of cases by their general practitioner. The blood lead levels were reported and entered in the RNV3P database in 13 cases. They ranged from 100 µg/L to nearly 1000 µg/L with a median of 445 µg/L (above the threshold not to be exceeded[1]).

The non-professionals also tended to be men (33 men out of 37), with a median age of 45 years. For the 31 cases where it was reported, their blood lead levels ranged from 100 µg/L to 750 µg/L, with a median of 300 µg/L, lower than those of the occupationally exposed workers. They were mainly referred by their general practitioner (40%) and 19% of them came on their own initiative. It should be noted that two men were consulting for fertility problems.

How can poisoning be prevented?

This contamination is not inevitable. The recommendations of the French National Research and Safety Institute (INRS) primarily concern professionals [5] but can also help reduce the risks for amateurs. The French Labour Code defines the occupational exposure limit (OEL) for lead in air of 0.1 mg/m^3 as an average value for an eight-hour period. It requires ventilation systems to be checked annually and compliance with the OEL. If the limit is exceeded, activities must cease until the shooting range has been decontaminated. Professionals assigned to positions exposing them to lead must be informed of this risk, the hygiene rules to be observed and the means of prevention. In particular, they must not eat, drink or smoke while dressed for work. In addition, the Labour Code prohibits pregnant or nursing women from being assigned to or kept in a job that exposes them to lead.

The INRS recommends that all shooting ranges should have adjoining premises, including two changing rooms (one for street clothes and one for work clothes), shower facilities, an office for instructors, a waiting room for shooters, and an equipment room for targets and bullet traps. This list is not exhaustive. Indoor ranges must be equipped with a ventilation and filtration system, which must be maintained in good condition and checked regularly.

For professionals and amateurs alike, it is imperative that they wash hands and face with soap and water after shooting, handling spent shell casings or cleaning weapons, especially before eating, drinking or smoking. Wipes for cleaning the skin without water should be used if access to soap and water is limited. Clothes and shoes should be changed before leaving the range and washed separately from other family clothes back home.

Anyone melting their own ammunition should heat the lead under optimal ventilation conditions, if possible in the open air, and in any case wear a mask with a suitable filter cartridge. Again, hand washing afterwards is imperative.

4. For a description of the RNV3P: https://www.anses.fr/en/content/rnv3p-national-network-monitoring-and-prevention-occupational-diseases

5. Article R 4412-149 du Code du travail

While special medical supervision is provided for professionals, with regular monitoring of blood lead levels, nothing is provided for amateur users, including children. Each shooting licence is awarded subject to an annual medical check-up (as opposed to every 3 years for most other sports). The High Council for Public Health (HCSP) recommends screening for young people aged 6 to 17 when they are exposed to one or more sources of lead or have signs that suggest lead poisoning [2]. General practitioners and paediatricians should therefore be made aware of this problem and prescribe tests to measure blood lead levels when in doubt. The French National Authority for Health (HAS) could be asked to consider whether or not to make the measurement of blood lead levels mandatory, according to procedures that have yet to be defined. Suitable information for shooters or the parents of adolescents who practice shooting could help raise awareness and bring about the necessary changes in behaviour.

Conclusion

These recent cases of lead poisoning in shooting enthusiasts, especially children or the adults accompanying them, highlight the problem of exposure to a substance whose high toxicity has long been known. Although the Labour Code organises the management of this risk for professionals working at shooting ranges, these cases show that the regulations and preventive measures are still insufficiently applied, and that both adult shooters and parents of children practising shooting underestimate or are unaware of the risk. The seriousness of this exposure, particularly in children, warrants measures to be taken in communication, prevention and screening, together with enforcement of the regulations by shooting galleries.

Juliette BLOCH, Hervé LABORDE-CASTEROT (Paris-Fernand Vidal PCC & CCPP), Nathalie PARET (Lyon PCC) and Emmanuel PUSKARCZYK (Nancy PCC)

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[3] AVIS de l'Anses relatif à la contamination d'espaces publics extérieurs par le plomb. Janvier 2020 https://www.anses.fr/fr/system/files/AIR2019SA0147.pdf

|4] Hazard Standards and Clearance Levels for Lead in Paint, Dust and Soil (TSCA Sections 402 and 403) https://www.epa.gov/lead/hazard-standards-and-clearance-levels-lead-paint-dust-and-soil-tsca-sections-402-and-403#:~:text=The%20agency's%20proposal%20would%20lower,2%20for%20window%20sill%20dust.

[5] Jean-Claude Sérieys, François Diébold, Jean-Raymond Fontaine, Mesures de prévention de l'exposition au plomb des salariés des stands de tir. INRS - Hygiène et sécurité au travail, 4ème trimestre 2012 – 229/25-29 http://www.inrs.fr/media.html?refINRS=ND%202369

Veterinary vaccines: oil-based adjuvants increase the risk of complications in the event of accidental injection in humans

In humans, accidental injection with veterinary vaccines carries a greater risk of inflammatory and/or infectious complications if the vaccine contains oil-based adjuvants, which are added to increase vaccine efficacy. A prospective study of calls recorded by French poison control centres between May 2016 and September 2018, based on a specific follow-up questionnaire, was used to quantify the risks of complications, surgery or sequelae in the presence of an oil-based adjuvant, considering associated factors (injection of the hand or another site, use of a manual syringe or a jet injector). Farmers, breeders or veterinarians are advised to wear protective gloves when vaccinating animals, to prevent these accidents.

Farmers, breeders or veterinarians may accidentally prick themselves when vaccinating an animal from their herd or farm, or during a consultation. As part of their medical teleconsultations, French Poisons Control Centres (PCCs) receive about 80 calls a year from people presenting with symptoms after being injected with a veterinary vaccine, and wishing to know the risks associated with the injection and the appropriate medical care.

The puncture and the injection of a large or small quantity of vaccine can cause complications in the injured area (finger, hand, other site), as well as possible persistent impairment. Studies have shown that certain vaccine components may increase this risk: this is the case with the oil-based adjuvants or excipients[1] contained in veterinary vaccines [1, 2].

To improve knowledge of this phenomenon in France, ANSES and the PCCs' network set up a prospective national study to describe the circumstances of the injection, the clinical signs observed at the time of the call and subsequently, as well as the care provided to patients.

Accidents mainly occurring in the workplace

Data collection took place from 1 May 2016 to 30 September 2018 and included 199 people; an average of seven per month with no particular seasonality, as veterinary vaccinations are prescribed throughout the year.

The individuals involved were between 9 and 87 years of age, with half of them being under 36 years of age. As expected, this was a problem of the adult working population, since 85% of patients were between 20 and 60 years of age. Seventy-one per cent of these accidental injections concerned men (142 versus 57 women).

Three-quarters of the cases (76%) were agricultural employees or farmers, 18% were retired farm workers or family members of a person working in this area. There was a relatively small number of veterinarians, with just 4% of cases, while in the remaining 2% the status of the individual was unknown.

1. Vaccine adjuvants are substances added, together with antigens, to increase the intensity of the immune response, reduce thevaccine dose and number of injections, and increase the stability of the vaccine.

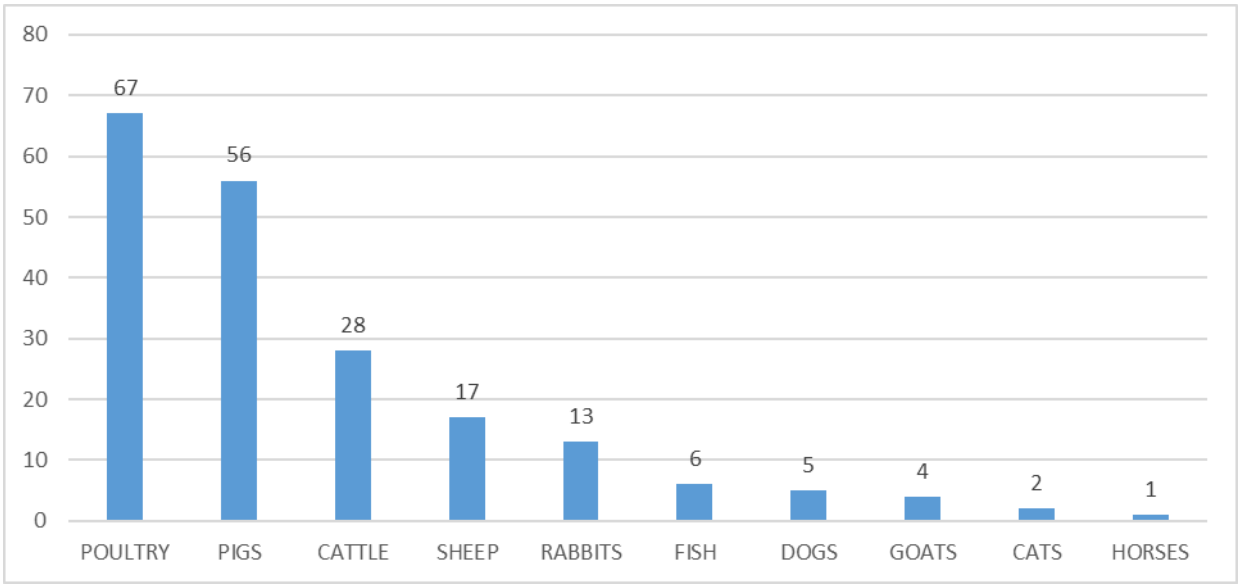

Figure 1 : Number of cases of accidental injections with veterinary vaccines in humans according to the type of animal or farm. May 2016 – September 2018. N=199. Source: SICAP.

Lastly, almost one in two cases (48%) occurred in Pays-de-la-Loire or Brittany; these two regions have large numbers of pig and poultry farms (sources: AGRESTE and IFIP, the French Pork and Pig Institute).

Nearly 90% of the individuals had injected themselves during their occupational activity. Two situations involved confusion between medicinal products: a 9-year-old child was administered the vaccine intended for his rabbit, which had mistakenly been brought to the general practitioner by his father; and a home nurse gave a patient a veterinary vaccine that had been stored in the refrigerator next to the patient's injection treatment.

Most accidents occurred while vaccinating livestock: poultry (34%), pigs (28%), cattle (14%) (Figure 1).

Syringe injections and oil-based vaccines in the majority

Veterinary vaccines can be injected either by automatic syringes injecting the unit dose under pressure ("jet injectors") or by conventional syringes activated manually by the operator. High-pressure injections have been reported as causing complications and, in particular, injuries to the tendons of the hand [3].

In this study, the accident resulted from a syringe injection in 69% of cases and a high-pressure injection in 17% of cases. In the remaining 14% of cases, the individual had been pricked without any vaccine being injected, although diffusion of the product at the injection site was possible.

In the overwhelming majority of cases (86%), the needle that had pricked the person had just been used to vaccinate other animals and was no longer sterile. This may increase the risk of infection.

Lastly, in 59% of cases the vaccine in the injection contained an oil-based adjuvant.

The hand injected in two thirds of cases

The accidental injection was most often into the hand (68%), with the thumb (20%) or index finger (18%) being the most common sites (Figure 2).

In nearly a third of cases another site was involved: the arm, the leg, or the abdomen (Figure 2). This is because for livestock (poultry, pigs, cattle, etc.), depending on the size of the animal, there may be two operators: one who holds the animal and the other who administers the injection. If the animal moves, one of the operators may then be pricked in the thigh or arm.

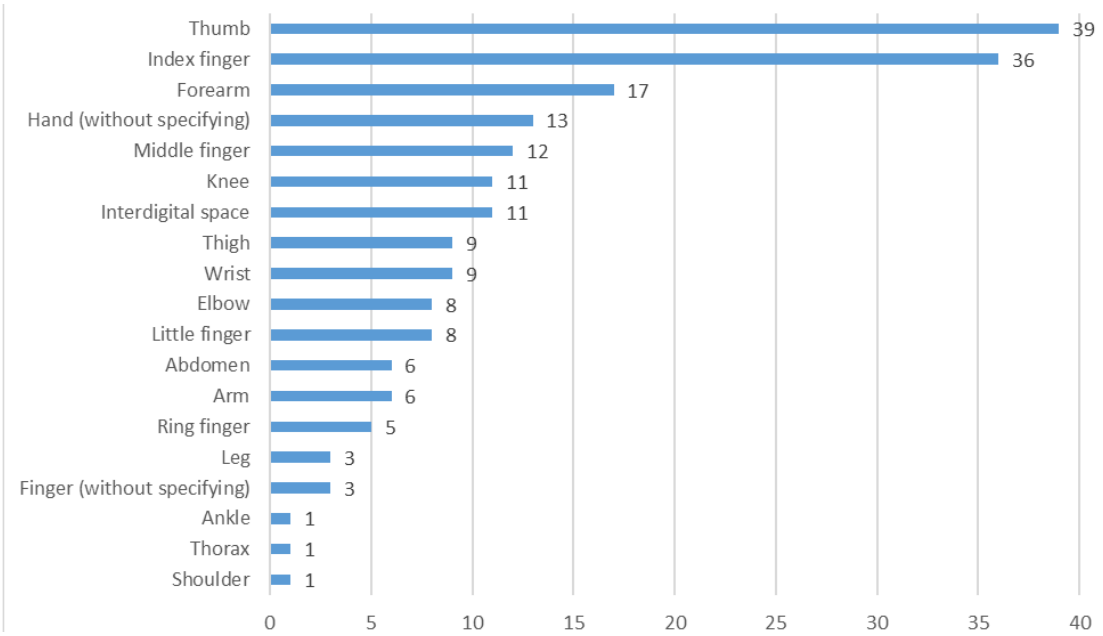

Figure 2 : Site of the accidental injection of a veterinary vaccine in humans. May 2016 – September 2018. N=199. Source: SICAP. .

What were their effects on health?

Inflammatory signs at the puncture site, either at the time of the call or occurring within 72 hours, were reported in almost all cases (93%). Individuals experienced pain and/or swelling and/or local redness.

While these inflammatory signs were all initially mild, more serious inflammatory and/or infectious complications were observed in 9.5% of cases (n=19). These concerned phlegmons (diffuse infection of a tissue, tendon or muscle, which can develop into an abscess), arthritis (joint inflammation) or tenosynovitis (tendon inflammation). In 17 cases these complications were observed in the hand, in one case they were in the forearm, and in the last case the knee. As with the site of the accidental injection, the grip involving the thumb and index finger used to hold the animal was the most frequently affected (10 cases).

Nearly one-third (29%) of accidental injections in the workplace resulted in an absence from work, which ranged from 24 hours to 4.3 months and was less than one week in 40% of cases.

More than three-quarters (78%) of those injected were given antibiotic therapy and 8% had taken non-steroidal anti-inflammatory drugs, on prescription or as self-medication.

Oil-based adjuvants increase the need for surgery

Fifteen per cent of injuries required surgery, mainly of the hand (86%), with 75% being operated within 72 hours of the injection.

The risk of surgery was **more than five times higher** with injections involving oil-based vaccines compared with non-oil-based vaccines, and **almost three times higher** with injections into the hand than with other sites (statistically significant increases, Figure 3), taking into account the circumstances of the injection.

Six months later, 10% of individuals had suffered sequelae

Specifically for this survey, the PCCs contacted individuals again up to six months after the accident to find out how their symptoms had progressed. Twenty patients, half of whom had undergone surgery, had sequelae at the end of follow-up.

These mainly concerned stiffness or difficulty bending the finger, tingling in one finger, persistent pain or residual nodules in the injection site, whether in the hand, forearm or knee. No other complications were observed.

There were higher, but not statistically significant, risks of complications (2.5-fold increase in risk) and sequelae (2.7-fold increase in risk) with oil-based versus non-oil-based vaccines (Figure 3).

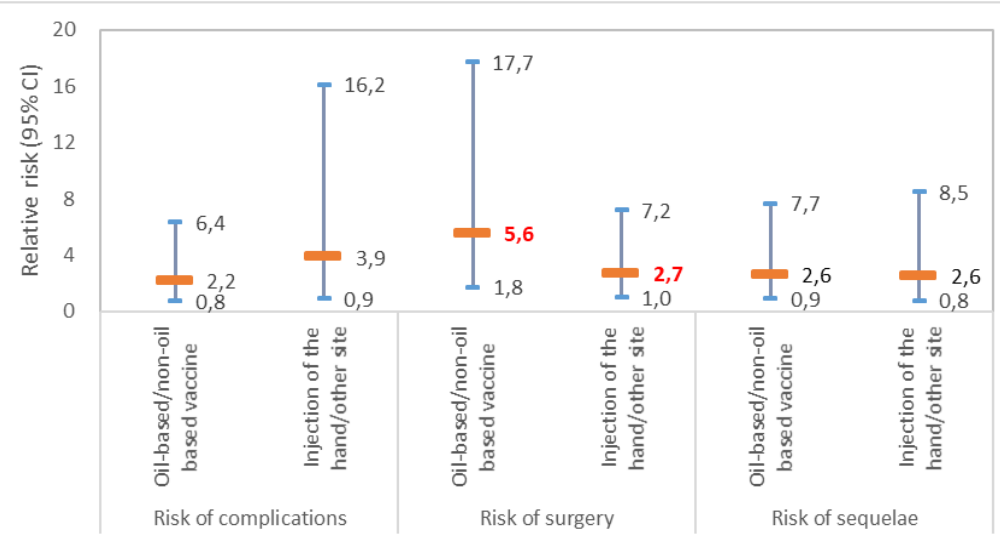

Figure 3 : Relative risk (RR) and 95% confidence interval of the RR (95% CI, delimited by a lower and an upper bound), estimating the risk of complications, sequelae or surgery depending on the vaccine type and the injection site, and adjusted for the circumstances of the injection. *An RR >1 expresses an excess risk*, which is statistically confirmed if the lower bound of the confidence interval of the RR is also >1. Multivariate statistical model. May 2016 – September 2018. N=199. Source: SICAP.

Call a Poison Control Centre in the event of accidental injection with a veterinary vaccine

This study, based on data collected prospectively at the national level, reinforces the hypothesis that in the event of accidental injections in humans, veterinary vaccines containing oil-based adjuvants are more likely to cause inflammatory and/or septic complications – some of which may require surgery and/or cause sequelae – than vaccines that do not contain them. These adjuvants cause tissue necrosis if the wound is not treated promptly.

The precautions to be taken by the person administering the vaccine and the action to be taken in the event of accidental injection are stated in the package leaflet. This is why, in the event of accidental injection with a veterinary vaccine, it is advisable to keep all the references concerning the vaccine (name, box, leaflet, etc.) and to immediately call a PCC or consult a doctor, mentioning the precautions stated in the leaflet. The PCC will be able to identify the risks associated with the vaccine type. It may also advise a medical consultation to ensure appropriate care in the first few hours after the injection. This should limit the occurrence of any complications. Prescription of antibiotic therapy will be at the discretion of the doctor treating the patient [4].

The wearing of protective gloves that are flexible and resistant to needle puncture should be encouraged too, in order to avoid these accidents and their complications.

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TO FIND OUT MORE :

ANSES's study report will be published shortly

References

[[1] Oil based veterinary vaccines. WHO Drug Information 1988, 2:30.
[2] Géraldine Meyer, Florence Jegou, Jean-François Hamel & David Boels (2018) Risks linked to accidental inoculation of humans with veterinary vaccines: a 7-year prospective study, Clinical Toxicology, 56:9, 852-855.
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[4] Plaies aiguës en structure d'urgence. Référentiel de bonnes pratiques. Société française de médecine d'urgence. 2017. 32 p.

Severe acute hepatitis associated with consumption of a food supplement

ANSES received two reports of severe acute hepatitis likely to be associated with consumption of the food supplement Chewable Hair Vitamins® marketed by the company HairBurst. Causality was deemed to be very likely. Given the severity of the reported adverse effects, ANSES felt it necessary to bring this case to the attention of the general public and health professionals, and strongly advises women using oral contraception not to take this food supplement.

As part of its nutrivigilance scheme, which was set up in 2009, ANSES received two reports in 2019 of severe acute hepatitis likely to be associated with consumption of the food supplement Chewable Hair Vitamins® marketed by the company HairBurst [1]. This product sold in chewable form contains vitamins A, B5, B6, B8, B12, C, D and E, as well as zinc, sodium selenite, glucose syrup, sugar, gelatine of bovine origin, dextrose, sorbitol, malic acid, coconut, palm and sunflower vegetable oils, carnauba wax, blackcurrant and strawberry flavourings, carmine.

The alert

The first case concerned a 29-year-old woman with no prior medical history other than a latex allergy. There was no evidence of alcohol abuse or tobacco use, recent travel or medical treatment, other than the recent initiation of a micro-dosed progestin oral contraceptive containing desogestrel. In August 2019, she began taking the food supplement Chewable Hair Vitamins® (one chewable pastille per day). In late September, she complained of debilitating fatigue and digestive disorders associated with icterus[1], with dark urine and discoloured stools. She began receiving symptomatic treatment and stopped taking the food supplement. Three days later, the patient was admitted to hospital with persistent nausea, vomiting and sweating. The tests carried out indicated severe acute hepatitis. About 10 days after hospitalisation, a fever associated with a diffuse rash occurred. A skin biopsy suggested drug-induced toxidermia[2]. Corticosteroid therapy was then initiated on the assumption of autoimmune hepatitis[3]. The patient was discharged after more than a month and a half of hospitalisation; her condition continued to improve after cessation of corticosteroid therapy.

The product consumed by the patient was analysed by the Joint Laboratories Service (SCL)[4] following a request from the French Customs' Observatory of Medicinal Products, on the assumption that other substances had been fraudulently added to it. However, no medicinal substances were found that could explain the onset of the disease in this patient. Quantification of the vitamins A and E contained in the product revealed levels higher than those stated on the product label: 2.6 times higher for vitamin E and 1.3 times higher for vitamin A.

1. Jaundice.

2. Toxic damage to the skin caused by medication.
3. Chronic inflammatory disease of the liver of unknown cause, almost always associated with the presence of autoantibodies.
4. The Joint Laboratories Service (SCL) is a service of the Ministry of the Economy and Finance with national competence. As the State laboratory of this ministry, it carries out analyses for the Directorate General for Customs and Indirect Taxation and the Directorate General for Competition, Consumer Affairs and Fraud Control.

Moreover, the label of the analysed product did not correspond to the labelling declared to the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF).

The second case concerned a 36-year-old woman with no prior medical history. In April 2019, after the birth of her second child, she began taking the food supplement Chewable Hair Vitamins® while also taking a progestin oral contraceptive containing desogestrel. After a month, jaundice began to appear, accompanied by fatigue. The patient had no abdominal pain, diarrhoea or joint pain. She had not travelled in the recent past or had any contact with contagious individuals. In late May, her biological test results showed hepatic cytolysis[5] and cholestasis[6] with signs of liver failure. The patient was admitted to hospital and stopped taking the food supplement. The thoracic-abdominal CT scan and liver biopsy indicated severe acute hepatitis. An autoimmune origin was suggested and corticosteroid therapy was initiated. Faced with the onset of hepatic encephalopathy, the patient was given an emergency liver transplant, which was successful.

Since the product consumed by this patient had not been kept, it could not be analysed.

To date, no further reports concerning the food supplement Chewable Hair Vitamins® have been registered by the French nutrivigilance scheme. At European level, out of the 37 countries approached, 25 replied and stated that they had not received any reports related to this product.

Were the observed signs related to the use of this food supplement?

The food supplement's causality in the occurrence of these two cases of severe acute hepatitis was estimated using the method developed for the nutrivigilance scheme [1]. As a reminder, it is calculated on the basis of three components: the onset time, the progression after discontinuation and – as the case may be – in the event of reintroduction, and the absence of any other possible explanation for the observed adverse effect.

In the first case, the onset time for the effect was found to be "compatible". Since the effect abated after the patient discontinued the food supplement, progression was described as "suggestive". The Chewable Hair Vitamins® product was not reintroduced. The aetiologic investigation ruled out an infectious cause as well as idiopathic autoimmune hepatitis, based on the biological data and the lack of aggravation of symptoms on rapid and complete cessation of corticosteroid therapy. The underlying assumption was therefore toxic hepatitis.

In the second case, the onset time for the effect was found to be "compatible". As the symptoms continued to worsen for a month and transplantation became necessary due to a life-threatening emergency, progression was described as "suggestive". The Chewable Hair Vitamins® product was not reintroduced. The full aetiological investigation carried out, including a complete pathological examination of the explanted liver, did not find any risk factor for hepatitis. A disorder related to the recent pregnancy, such as HELLP syndrome, was also ruled out.

The food supplement was therefore deemed very likely responsible for the occurrence of these two cases of severe acute hepatitis, i.e. I4, on a scale ranging from I0 = excluded to I4 = very likely [2].

5. Biological sign of liver cell destruction.
6. A decrease or cessation of biliary secretion.

Where should reports be sent?

Adverse effects can be reported on the Adverse Health Event Reporting Portal of the Ministry of Social Affairs and Health or directly by completing the online reporting form.

TO FIND OUT MORE :

ANSES opinion on updating the method for determining causality in reports of adverse effects in nutrivigilance

ANSES opinion on two cases of severe acute life-threatening hepatitis associated with consumption of the food supplement Chewable Hair Vitamins

Have identical cases been described in the scientific literature?

The literature search focused on the potential hepatotoxicity in humans of each ingredient in the food supplement Chewable Hair Vitamins®.

Four clinical cases related to vitamin A consumption were reported. These corresponded to chronic hepatitis associated with prolonged oral consumption of vitamin A at doses far higher than those ingested by the two consumers of the food supplement Chewable Hair Vitamins® described here. However, since the food supplement Chewable Hair Vitamins® is presented as a chewable pastille, and not as a tablet or capsule as described for the four cases identified in the literature, the amount of vitamins absorbed may have been higher than if they had been in tablet or capsule form, due to greater absorption through the oral mucosa than through gastrointestinal absorption.

The literature search did not identify any cases of liver damage related to the other ingredients of the food supplement Chewable Hair Vitamins®.

Besides the search for data on the product's intrinsic components, it should be emphasised that in both cases described here, the patients were taking a desogestrel-based contraceptive. While the literature data show that desogestrel alone is not known to cause hepatotoxic effects, an interaction with the food supplement Chewable Hair Vitamins® cannot be ruled out.

Conclusion and recommendations

For both of these cases, it was considered very likely that the occurrence of severe acute hepatitis, in which one of the patients required a liver transplant, was attributable to consumption of this product. This food supplement contains numerous ingredients, mainly vitamins and minerals, and many excipients. No reports of liver damage associated with any of these ingredients under similar conditions of consumption have been identified in the literature to date.

ANSES retained the possibility of a complex effect of the combination of the product's many ingredients, an interaction with other substances (particularly oral contraceptives), or possible contamination or adulteration by a substance that was not screened for.

ANSES also pointed out that the measured levels of vitamins A and E in one of the products were higher than the labelled levels and those declared to the DGCCRF [3].

In view of all these points, ANSES recommends that women using oral contraception should not take the food supplement Chewable Hair Vitamins®.

Lastly, ANSES reiterates its usual advice concerning food supplements. It recommends that consumers:

- notify a healthcare professional of any adverse effect occurring after consumption of a food supplement;
- comply with the conditions of use specified by the manufacturer;
- avoid taking food supplements on a multiple, prolonged or repeated basis throughout the year without having sought the advice of a healthcare professional (doctor, nutritionist, pharmacist, etc.);
- exercise great vigilance with regard to any therapeutic claims;
- exercise great vigilance regarding the purchase of products via alternative channels (internet, gyms, etc.) and without personalised advice from a healthcare professional.

ANSES also reminds healthcare professionals of the need to report to its nutrivigilance scheme any cases of adverse effects they suspect are associated with the consumption of food supplements.

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References

[[1] ANSES opinion on two cases of severe acute life-threatening hepatitis associated with consumption of the food supplement Chewable Hair Vitamins. Request No 2019-SA-0212. 14 p.

[2] ANSES opinion on updating the method for determining causality in reports of adverse effects in nutrivigilance. Request No 2018-SA-0026.16 p.

[3] DGCCRF. 2019. "NUTRIMENTS Recommandations sanitaires."

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 a dedicated 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.

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