

The National Institute of Health and the Italian Poison Centers Network: results of a collaborative study for the surveillance of exposures to chemicals

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Abstract

Background. The Public Health Surveillance Systems are essential to improve and protect public health, as highlighted by the World Health Organization. According with this consideration, a systematic collaboration between the National Institute of Health and the Poison Centers of Northern, Central and Southern Italy was established. Its aim was to improve the national network for the surveillance of dangerous exposures to chemicals. The developed network provided harmonized data essential for evidence-based interventions and significantly ameliorated the data flow between the Poison Centers and the Central Health Institutions.

Methods. The improvement of the system was obtained through several actions, such as the development of the “Online Surveillance Card” for the detection of sentinel events in real time and the harmonization of the data collection flow, including the product categorization according to the European Product Categorization System. Data analysis was carried out by Microsoft’s IBM SPSS Statistics version 26, Access and Excel.

Results. Important information was obtained, regarding also exposures to chemicals and their management in pediatric populations. The surveillance network was proved effective not only under “normal” conditions but also to promptly monitor changes during exceptional health emergencies, such as the COVID-19 pandemic. During the 2020 lockdown the surveillance system registered a significant increase in the frequency of exposures to disinfectants ($p\text{-value}=0.002$), an evidence that highlighted the need of tailored intervention.

Conclusions. This Italian Project model proves to be reliable and suitable to be transferred to other European

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Legend: ADP: Archive of Dangerous Preparations; CCCP-ISS: Center for Chemicals, Cosmetics and Consumer Protection- Istituto Superiore di Sanità; CLP: Classification, Labeling and Packaging; ECHA: European Chemicals Agency; EU: European Union; EuPCS: European Product Categorization System; ISS: Istituto Superiore di Sanità; PC: Poison Center; PC-CLN: Cleaning, care and maintenance products; PP-BIO: Biocidal products; REACH: Registration, Evaluation, Authorization and restriction of Chemicals; SDS: Safety Data Sheet; SENTINEL EVENT: an unexpected occurrence involving death or serious physical or psychological injury. It is called “sentinel” because they signal the need for immediate investigation and response; SIN-SEPI: National Informative System for Surveillance of Toxic Exposures and Poisonings; WHO: World Health Organization

countries, in order to realize an European Poison Centers' Network, able to overcome unsolved health problems and to globally improve the "evidence-based" prevention of exposures to chemicals.

Introduction

The World Health Organization (WHO) (1) defines the health surveillance systems as *"An ongoing, systematic collection, analysis and interpretation of health-related data essential to the planning, implementation, and evaluation of public health practice"*. Therefore, the surveillance system is essential for Public Health management to improve and protect people's health. National Poison Centers (PCs) are one of the most important surveillance systems that collect data to monitor hazardous exposures, including exposures to chemicals.

Information provided by such facilities is essential to identify chemical products on the market which are more involved in intoxication cases. These products require the adoption of prevention measures (e.g. modification of the packaging or revision of methods of use) in order to reduce their related risk of exposure. Data collected by the National PCs also make it possible to monitor exposures within groups of population by studying the association between different age classes, gender and environments (occupational and domestic), in order to differentiate the risk assessment and to identify Evidence Based Prevention strategies (2).

Furthermore, it is possible to propose risk management measures and to verify the compliance to the requirements established by European provisions. In particular, the requirements concerning the hazard of the mixtures, their classification and the information needed to ensure their correct use, must be verified (REACH and CLP regulations) (3, 4).

A good example of chemical surveillance is the ability to monitor the increase of intoxications due to laundry detergents in pods. After very colorful pods were put on the market, an increasing trend of cases among children up to 5 was observed by several PCs, and in particular by the Milan PC (5). As a consequence of this finding, the EU Commission forced the companies to make safer packaging, modifying EC regulation no. 1272/2008 (CLP) on the classification, labeling and packaging of substances and mixtures (4). In particular, for soluble packaging for single use it was stated that *"The outer packaging shall be opaque or obscure so that it impedes the visibility of the product or individual doses..."*. After a major company introduced opaque outer packaging, Settimi et al. (5) detected a statistically significant decrease of the exposures among the children.

The Italian PCs provide both health personnel and citizen with information and toxicological advice. Their activities concern toxicological analysis, surveillance, alerting, scientific research, education and training about prevention, diagnosis and treatment of intoxications according to the Agreement of the Permanent Conference "Italian State-Regions", 28th February 2008 (6), that defined rules and activities of PCs. At present, there are ten PCs accredited at the Competent Authority, having full access to the Archive of Dangerous Preparation (ADP) located at the National Institute of Health (Istituto Superiore di Sanità or ISS) (7). The consultation of this archive is essential to know the composition of dangerous products marketed in Italy and so to be able to put in place the best therapeutic strategy.

These activities are a matter for the National Center for Chemicals, Cosmetics and Consumer Protection at the ISS (CCCP-ISS), which was entrusted with the surveillance of chemicals by the Decree of the Italian Ministry of Health on March 2nd 2016 (8). The next Decree on Registries and Surveys of March 2017 (9) entrusted the ISS as the site of the National Informative System for Surveillance of Toxic Exposures and Poisonings (in Italian SIN-SEPI) and as the national contact for prevention and surveillance activities on chemical exposures and intoxications.

Close collaboration and open communication among CCCP-ISS, Ministry of Health and PCs are required to optimize the surveillance of exposures to chemicals. For this reason, in 2017 CCCP-ISS researchers and medical toxicologists from some PCs of Northern, Central and Southern Italy established a multicentric project. The main targets of the project were to bolster collaboration, to share best practices and to facilitate networking between members.

Starting from data analysis of the consultations managed during 2016, the present paper reports step by step the significant improvement of the PCs network, of the data quality and of their usability. The exceptional health emergency of COVID-19 pandemic permits to show the effectiveness of this improvement in highlighting some critical situations, such as the trend variation in the frequency of dangerous exposures to household cleaners and disinfectants.

The results of the scientific activities carried out in the project frame prove that the study is of great importance, because it allowed data harmonization in order to put in place evidence based interventions.

Materials and methods

The descriptive analysis shows information starting from 2016. Data of 2020 were timely processed to highlight critical situations due to COVID-19 pandemic.

Institutions enrolled

At the beginning of the project, the following Italian PCs gave voluntary adhesion:

PAVIA: (Northern Italy)

1) Policlinico San Matteo Pavia
Fondazione IRCCS (PC-PV)

ROME: (Central Italy)

1) Ospedale Pediatrico Bambino Gesù
(PC-HBG);

2) Azienda Ospedaliero-Universitaria
Policlinico Umberto I (PC-UMB_I);

3) Fondazione Policlinico Universitario
Agostino Gemelli (PC-GEM)

FOGGIA (Southern Italy)

1) Policlinico Riuniti di Foggia (PC-FG)

Data collection

To collect data two ways were followed:

Collecting data yearly: Excel file sent by email. It includes the consultancies managed year by year by each PC for the elaboration of the annual report. The data set was standardized and the following variables were selected: date of the call, Italian region, patient age and gender, caller (hospital, non-hospital), trade name and number of chemicals involved, reason for exposure (inadvertent or not), route of exposure, symptoms (yes, no), intoxication severity evaluated by Poison Severity Score (10), site of treatment (domestic/hospital) and number of calls per event. The categorization of products was harmonized according to the European Product Categorization System (EuPCS) (11).

Collecting data in real time: The Online Surveillance Card. It was developed a surveillance form where toxicologists could

report cases for prompt surveillance actions. The following data are reported: place of event, patient demographics, presence and type of symptoms, therapy and information about the chemical product involved. Operators can perform notifications at any time, accessing the on-line form by their own password through the ADP webpage. An automatic email system sends the notification to the authorized ISS researchers in real time.

Study design

Data analysis included only cases involving human subjects with exposures (proved or presumed) to chemicals, both symptomatic and asymptomatic. Before analysis, quality control was carried out to verify the consistency of the information and to recover missing data.

Yearly data coming from “*Excel file sent by email*” are used to perform a case series study. Descriptive statistical methods are used to monitor the consultancy activities and to highlight some criticisms, such as a possible increase in cases over time (date of the call) and space (Italian region). Categorical variables were used to aggregate data.

Real time data coming from the *Online Surveillance Card* are studied to ascertain whether:

- 1) the event is a “probable” or “less probable” sentinel event that must be notified to the Prevention Department of the Ministry of Health for surveillance actions. The peculiarities to define a sentinel event are: the colors and/or shape of the involved product packaging recall those of other products; the route of exposure is unusual; symptoms are unusually severe; there is an unusual increase of the frequency of cases due to a specific product, over time or in a defined territory;

- 2) the event is a case of REACH-CLP non-compliance (e.g.: the lack of notification to ADP according to art. 45 of

CLP Regulation) and must be notified to promote an enforcement action according to REACH and CLP regulation (3, 4).

To study exposures to chemicals during COVID-19 pandemic, the biological and poisoning characteristics in pre lockdown (January-February 2020) and during lockdown (March-May 2020) were compared. Statistical differences among groups were tested within dichotomous categories using a 2x2 contingency table by the Chi-Square Test. When at least one cell in the contingency table had an expected value less than 5, the Fisher Exact Test was applied.

Data analysis was performed by Microsoft’s IBM SPSS Statistics version 26, Access and Excel.

Results

Annual Report

The first study carried out by the PCs consultancies for the year 2016 (12) allowed to obtain important information, even if, at that time, the PCs databases were not yet harmonized.

Data analysis showed significant territorial differences both for number of annual consultancies and for population peculiarities. The PC-UMB_I received less than 500 consultancies; the PC-FG 1,000, from almost exclusively regional users (93% of consultancies); the PC-HBG, that mostly includes pediatric population, almost 1,000; the PC-GEM about 3,500; and the PC-PV more than 25,000. The great number of PC-PV consultancies is mainly due to people coming from regions other than Lombardy (where the PC is sited).

There was an overall agreement about the percentage of intoxications due to domestic products (percentage range 34% - 48%). For the pediatric PC, data analysis month by month showed a significant peak in June and December, when children are not in kindergartens or schools. Analysis

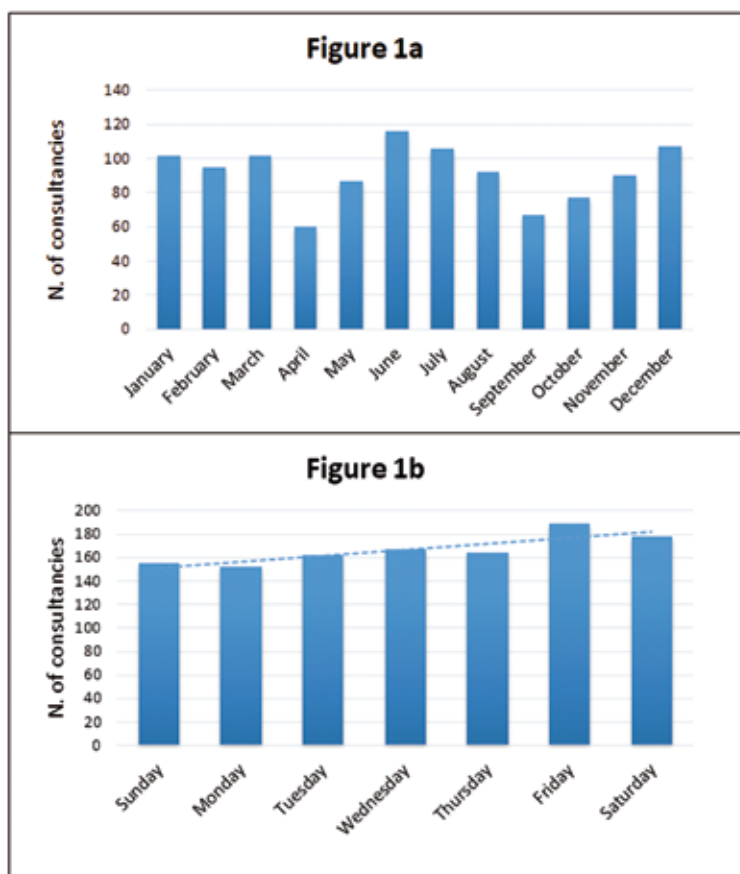


Figure 1 - Number of consultations managed in the year 2016 by PC-HBG per month (1a) and day of the week (1b).

of disaggregated data showed an excess of consultations on weekends (Friday-Saturday). Figure 1 a and b.

Online Surveillance Card

In the period May 2018-September 2019, through the “*Online Surveillance Card*”, the PCs notified 64 cases of sentinel events including the exposure to 63 different chemicals. In particular, in January-March 2019 the products involved (n.13) are more than the subjects (n.12), because a woman (44 years old) inhaled the gas released by mixing two bath cleaners for misuse. On the contrary,

there can be more subjects simultaneously intoxicated by the same product.

The 22% of these cases were considered “probable sentinel events” (or confirmation of previously reported sentinel events), the 30% “less probable” sentinel events and the 48% “unlikely” sentinel events (Table 1). The “unlikely” sentinel events include: non-compliance by the manufacturer in respect of the labeling and the Safety Data Sheet (SDS); failure in notification to the ADP; evidence of an intentional action (self-injurious) or misuse so that the product is absolved from being the cause of the event. Table 1 shows an increasing trend of

Table 1 - Sentinel events reported by the PCs between May 2018 and September 2019.

| Reports sent to Ministry of Health | Subjects exposed N | Products involved N | Sentinel events (magnitude of evidence) | | |
|------------------------------------|-----------------------|------------------------|---|------------------------|-------------------|
| | | | Unlikely N (%) | Less probable N (%) | Probable N (%) |
| May-September 2018 | 22 | 22 | 13 (59) | 5 (23) | 4 (18) |
| October-December 2018 | 7 | 7 | 4 (57) | 2 (29) | 1 (14) |
| January-March 2019 | 12 | 13 | 8 (62) | 2 (15) | 3 (23) |
| April-June 2019 | 9 | 9 | 4 (44) | 3 (33) | 2 (22) |
| July-September 2019 | 14 | 12 | 1 (8) | 7 (58) | 4 (33) |
| Total (% where applicable) | 64 | 63 | 30 (48) | 19 (30) | 14 (22) |

Table 2 - Biological and poisoning characteristics of subjects exposed to *Cleaning, care and maintenance products* and *Disinfectant products*: comparison before lockdown (January-February 2020) and during lockdown (March-May 2020).

| Variables | January-February N (%) | March-May N (%) | p-value (Chi-square Test) |
|------------------------------------|---------------------------|--------------------|------------------------------|
| <i>Biological characteristics</i> | | | |
| <i>Gender</i> | | | |
| Female | 37 (60.7) | 96 (53.0) | 0.301 |
| Male | 24 (39.3) | 85 (47.0) | |
| <i>Class of age (years)</i> | | | |
| 1-5 | 12 (19.7) | 35 (19.3) | 0.954 |
| 6-19 | 2 (3.3) | 9 (5.0) | ^a 0.735 |
| 20-39 | 8 (13.1) | 39 (21.5) | 0.150 |
| 40-59 | 29 (47.5) | 62 (34.3) | 0.064 |
| 60+ | 10 (16.4) | 33 (18.2) | 0.745 |
| Unknown | - | 3 (1.7) | ^a 0.574 |
| <i>Poisoning characteristics</i> | | | |
| <i>Caller</i> | | | |
| Hospital | 24 (39.3) | 24 (13.3) | <0.001 |
| Non-Hospital-Private citizen | 30 (49.2) | 137 (75.7) | <0.001 |
| Non-Hospital-Other | 7 (11.5) | 20 (11.1) | 0.927 |
| <i>Reason for exposure</i> | | | |
| Inadvertent | 56 (91.8) | 166 (91.7) | 0.982 |
| Occupational | 1 (1.6) | 7 (3.9) | ^a 0.683 |
| Intentional | 4 (6.6) | 8 (4.4) | ^a 0.504 |
| <i>Route of exposure</i> | | | |
| Ingestion | 34 (55.7) | 109 (60.2) | 0.538 |
| Inhalation | 20 (32.8) | 49 (27.1) | 0.393 |
| Other | 7 (11.5) | 23 (12.8) | 0.801 |
| <i>Symptoms</i> | | | |
| Yes | 42 (68.9) | 114 (63.0) | 0.408 |
| No | 19 (31.1) | 67 (37.0) | |
| <i>Number of products involved</i> | | | |
| 1 | 51 (83.6) | 158 (87.3) | 0.468 |
| ≥2 | 10 (16.4) | 23 (12.8) | |
| Total (%) | 61 (25.2) | 181 (74.8) | |

^aFisher Exact Test

“probable sentinel events” percentages even if it is not statistically significant.

The surveillance form was further ameliorated both by the new product categorization system according to EuPCS and by the possibility of attaching product images and other documents to complete the report.

Up to now, five quarterly technical reports were sent to the Ministry of Health and some of them were taken into account for supervisory actions.

Modifications in exposure trends during COVID-19 pandemic lockdown

The effectiveness of the surveillance system was tested in the year 2020 by comparing data before (January-February) and during (March-May) the lockdown.

During the first five months of the year the PC-FG collected 180 exposures to *Cleaning products* and 61 exposures to *Disinfectant products*, while a patient was exposed to both categories of agents. Significant modifications in exposure trends for *Cleaning, care and maintenance products* (EuPCS categories: PC-CLN-1

to PC-CLN-17) and *Disinfectant products* (EuPCS categories: PP-BIO-1 to PP-BIO-5) were highlighted when lockdown started. In fact, for *Cleaning products* the mean number of exposures/day during lockdown was 1-fold and a half greater than in January-February months (January-February: 0.92 exposures/day; March-May: 1.37 exposures/day). *Disinfectant products* ratio was 5-fold greater (January-February: 0.12 exposures/day; March-May: 0.60 exposures/day) (Figure 2).

Table 2 summarizes the biological and poisoning characteristics of cases. Gender differences are not statistically significant but the percentage of males increased (January-February: 39.3% vs March-May: 47.0%) during lockdown (March-May). Hospital calls significantly decreased (January-February: 39.3% vs March-May: 13.3%; $p < 0.001$), whilst calls from private citizens increased (January-February: 49.2% vs March-May: 75.7%; $p < 0.001$). There are no significant differences in the reason for exposure, the route of exposure, the presence of symptoms and the number of products involved in the exposure (Table 2).

Table 3 takes into account the distribution

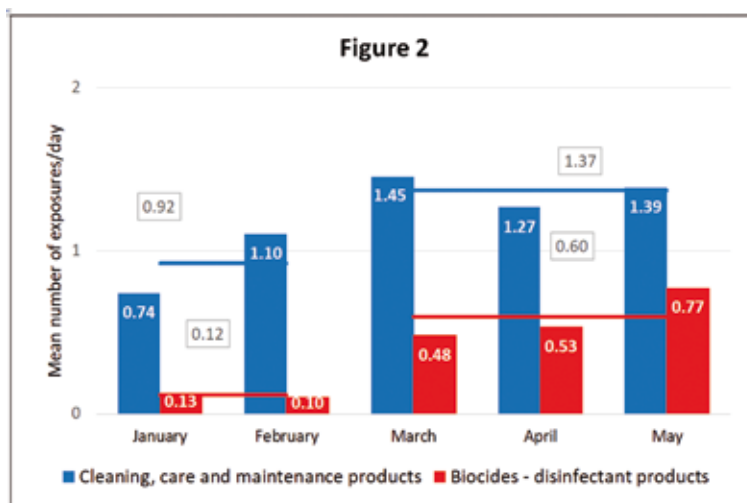


Figure 2 - Mean number of exposures/day from January to May 2020.

Table 3 - Distribution of *Cleaning, care and maintenance products* and *Disinfectants* involved in dangerous exposures. Comparison before lockdown (January-February 2020) and during lockdown (March-May 2020).

| EuPCS category | January - February | March - May | p-value (Chi-square Test) |
|--|--------------------|-------------|------------------------------|
| | N (%) | N (%) | |
| Cleaning, care and maintenance products (PC-CLN) | 63 (90.0) | 146 (72.3) | 0.002 |
| Bleaching products for cleaning or laundry use (PC-CLN-3) | 22 (31.4) | 66 (32.7) | 0.848 |
| All-purpose (or multi-purpose) non-abrasive cleaners (PC-CLN-2) | 15 (21.4) | 34 (16.8) | 0.388 |
| Bathroom and toilet cleaning/care products (PC-CLN-11) | 12 (17.1) | 13 (6.4) | 0.008 |
| Descaling products (PC-CLN-4) | 5 (7.1) | 6 (3.0) | *0.157 |
| Other | 9 (12.9) | 27 (13.4) | 0.914 |
| Disinfectants (PP-BIO-1 to PP-BIO-5) | 7 (10.0) | 56 (27.7) | 0.002 |
| Biocidal products for human hygiene (PP-BIO-1) | 1 (1.4) | 4 (2.0) | *1.000 |
| Disinfectants and algaecides not intended for direct application to humans or animals (PP-BIO-2) | 5 (7.1) | 52 (25.7) | 0.001 |
| Biocidal products for food and feed area (PP-BIO-4) | 1 (1.4) | - | *0.257 |
| Total (%) | 70 (25.7) | 202 (74.3) | |

*Fisher Exact Test

of *Cleaning, care and maintenance products*, *Disinfectant products* and their sub-categories involved in the exposures. Furthermore, Table 3 shows that the percentage of *Disinfectants* significantly increased during lockdown (January-February: 10.0% vs March-May: 27.7%; $p=0.002$), in particular among the *Disinfectants and algaecides not intended for direct application to humans or animals* (January-February: 7.1% vs March-May: 25.7%; $p=0.001$). The percentage of *Cleaning products* (PC-CLN) decreased (January-February: 90.0% vs March-May: 72.3%; $p=0.002$) as a result of the increase in *Disinfectants*, and for some categories the decrease was significant (PC-CLN-11: January-February: 17.1% vs March-May: 6.4%; $p=0.008$). *Bleaches* (PC-CLN-3) only showed a slight, not significant increase (January-February: 31.4% vs March-May: 32.7%).

Discussion

The project aimed at creating a network between CCCP-ISS and Italian PCs in order to obtain harmonized data about the annual advice of chemical exposures and to provide evidence-based tools for intervention. During the years, ISS, Ministry of Health and PCs improved their collaboration and communication so that each partner was able to ameliorate its activity. PCs obtained more information suitable to handle cases and the health institutions acquired more information useful to plan and realize public health policies.

The most interesting evidences regard children, mainly highlighted by data from the pediatric Hospital Bambin Gesù of Rome. Consultancies about children show a typical seasonal trend and are mostly due to household chemical products. In particular, a peak of consultancies during school holidays

was observed, as registered by PC-HBG in June 2016 (12). Similar remarks were reported also by Alzahrani et al. (13) in Saudi Arabia and more recently by Kazanasmaz et al. (14) in Turkey. It is likely that pediatric intoxications increase in summer because schools are closed and children have more access to cleaning products and other chemicals at home. Using data coming from an ophthalmology center in Canada, during COVID-19 pandemic, Gulamhusein and Sabri (15) showed an increased children's exposure to single dose laundry detergents named PODs. The authors hypothesized that children, spending more time indoors, have increased opportunities to handle detergent PODs. The packaging of these products may be a significant risk factor especially for intoxications in children. In 2018, Settini et al. (5) showed that the introduction of PODs on the market led to increased children's poisonings in Italy and concluded that the vivid colors of PODs were very attractive to children. The prevention strategy was to use dark colors and four months after this intervention poisoning cases significantly decreased.

The results of the collaborative study also provided important suggestions to plan a workforce re-organization in terms of expertise and number of operators enrolled to handle patients' requests. For example, consultancies come mainly from private citizens, thus confirming the data of previous studies (16), and occur especially on weekends (12). A recent study by British anesthesiologists (17) reports more frequent emergency interventions during the weekend, including gastroenterology and ophthalmology intervention deriving from PCs consultancies. Nevertheless, the operators in service on the weekend are usually fewer and less experienced than those on working week. This evidence highlights that PCs should better organize work and provide adequate staff in number and expertise even during weekends and

holidays. Another criticism was highlighted by Anderson et al. (18), who performed a study about the trend of PCs data from 2000 to 2015: their findings showed that intentional exposures are on the rise, so that more attention and more specific psychological or psychiatric skills are required to PCs staff.

As regards the data collection, a critical factor for the effectiveness of the surveillance system is the data set standardization. In the preliminary phase, it was not possible to distinguish the actual cases of exposure from simple information requests. Subsequently, ISS researchers established the definition of "clinical case" as "the episodes with actual exposure" and shared it with PCs. After several meetings, ISS and PCs representatives set up the "Minimum Data Set" to harmonize the information flow and to improve the description of the exposure (date of exposure, caller and reason for exposure subcategories) including the intoxication severity (10).

The categorization according to EuPCS was applied as an innovative strategy to make a reliable comparison of data among different PCs databases. The categorization was sometimes difficult to apply because chemicals were indicated without their purpose of use or too generically, and a great effort was made to realize this target.

The PCs appreciated the introduction of the online Surveillance Card, probably because notifications are directly sent to ISS researchers who catalogue, evaluate and present them to the Competent Authority by the quarterly report. In addition, an increasing trend of "probable sentinel events" percentages was observed, but due to the small population it is impossible to achieve a statistical significance. However, this evidence may show that toxicologists have notified more suitable sentinel events over time.

Interventions to avoid dangerous exposures, for example by changing the

packaging of a product, can also be provided. For instance, in the period May 2018–September 2019, PCs toxicologists reported seven episodes in which adults drank a stain remover product, mistaking it with a bottle of water. Inadvertent errors due to ingestion of colorless liquid in place of water are well described (19, 20). ISS researchers reported this finding to the General Directorate for health prevention of the Ministry of Health with the suggestion of an enforcement action toward the company producing the stain remover (art. 35 of CLP violation about Packaging characteristics (4)). Researchers also suggested that a packaging with a different shape than water bottles could decrease the frequency of exposures among citizens.

One of the positive results obtained is that, for the first time, a PCs representative was elected by the PCs network in the frame of the European activities. The elected representative took part in the ECHA “Workshop on Appointed Bodies and Poison Centers’ working practices and use of the PCN database” held in Helsinki, on 10th December 2019.

Finally, the surveillance system was proved able to detect the unusual increased frequency of exposures to *Disinfectants* during COVID-19 pandemic lockdown, sustained by a statistical significance. The limitation of the study was mainly due to the fact that exposure data did not cover the entire Italian territory and concerned only five months of observation. On the other hand, notwithstanding these limits, the obtained results allow us to provide reliable and timely information and to make them available for alert actions. Furthermore, the use of the EuPCS categorization makes it possible to compare data at a European level for the first time.

Using data from the National Poison Data System in the United States, also Chang et al. (21) registered an increase of poisonings due to cleaners and disinfectants during COVID-

19 pandemic. Furthermore, the authors described a case report regarding a pre-school girl exposed to ethanol-based hand sanitizer. These findings are also consistent with the results recently obtained in other European countries (22). Chronic exposures due to daily cleaning activities need to be considered. In fact, Li et al. (23) found that children undergo a greater number of exposures than other age groups, especially due to their more frequent hand contact with disinfected surfaces and mouthing activities.

Due to these evidences, the CCCP-ISS launched an alert to avoid the rise of exposures to chemicals, especially with regard to children (24).

The effectiveness of this innovative surveillance system was further established by the request (note n. 0072529-11 / 11/2020-DGDMF-MDS-P) submitted to ISS by the General Directorate for Medical Devices and Pharmaceutical Service (DGDMF) of the Ministry of Health, i.e. the competent Authority for Biocides and REACH - CLP, in order to obtain data about exposures to biocidal products. The report for the European Commission is pursuant to art. 65 paragraph 3 of Regulation (EU) 528/2012. Descriptive analysis of human exposure cases to biocidal products in the years 2017–2018–2019 was carried out using data of the Italian PCs network.

Based on the positive results obtained, the PCs network was expanded by further collaboration agreements with the PCs of Firenze, Napoli and Bergamo.

Conclusion

A call to a poison center may be the first alert of public health relevance and therefore PCs are an excellent source of information about exposures to chemicals and their management. All that considered, the establishment of a network to easily share

information between PCs and central health institutions is an effective help to improve public health response and to minimize morbidity and mortality associated with exposures to chemicals.

The collaboration between ISS and PCs, by improving the surveillance network, contributes to the detection of sentinel events and to the intervention in case of chemical exposures. The collaborative study could be further ameliorated but the results obtained so far show that this kind of information is useful for health surveillance, as well as for tailored interventions, such as towards pediatric population. Furthermore, these evidences provide suggestions for communication strategies that, for example, can help parents to avoid at-risk behaviors. The optimization of the database and the inclusion of further Italian PCs will be the next steps to implement the network, to optimize intervention and to sustain the development of “evidence based” regulations. An effort to further develop this system came from the Italian Competent Authority in a recent (ISS, 15th December 2020) Conference entitled “Detergents: state of the art and future prospects”. This event, organized by CCCP-ISS and the Italian Ministry of Health, was very appreciated by the General Directorate for health prevention of the Ministry of Health and the results achieved by the PCs network were considered a milestone for planning health strategies against dangerous exposures to chemicals.

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Riassunto

L'Istituto Superiore di Sanità e la rete italiana dei Centri Antiveleni: risultati di uno studio collaborativo per la sorveglianza delle esposizioni a prodotti chimici

Background. I sistemi di sorveglianza di sanità pubblica sono essenziali per migliorare e proteggere la salute dei cittadini, come evidenziato dall'Organizzazione Mondiale della Sanità. Ciò considerato, nell'anno 2017 è stata istituita una collaborazione tra l'Istituto Superiore di Sanità e i Centri Antiveleni del Nord, Centro e Sud Italia. Il suo scopo era quello di migliorare la rete sanitaria nazionale per la sorveglianza delle esposizioni pericolose a sostanze chimiche. La rete di sorveglianza messa in atto ha fornito dati armonizzati essenziali per promuovere interventi basati sull'evidenza e ha migliorato significativamente il flusso di dati tra i Centri Antiveleni e le istituzioni sanitarie centrali (Istituto Superiore di Sanità, Ministero della Salute).

Metodi. Il miglioramento del sistema è stato realizzato tramite diverse azioni, come la messa a punto della “Scheda di sorveglianza online” per la segnalazione degli eventi sentinella in tempo reale e l'armonizzazione del flusso per la raccolta dei dati, inclusa la categorizzazione dei prodotti in accordo all'European Product Categorization System. L'analisi dei dati è stata realizzata utilizzando Microsoft's IBM SPSS Statistics version 26, Access ed Excel.

Risultati. Sono state ottenute importanti informazioni, anche riguardo le esposizioni a prodotti chimici in età pediatrica e la loro gestione. La rete di sorveglianza si è dimostrata efficiente non solo in condizioni “normali”, ma anche in situazioni eccezionali di emergenza sanitaria, come la pandemia COVID-19. In particolare, durante il periodo di confinamento del 2020, è stato osservato un significativo aumento di esposizioni pericolose a prodotti

disinfettanti (valore $p = 0,002$), un'evidenza che ha sottolineato la necessità di interventi mirati.

Conclusioni. Questo modello di rete italiano dimostra di essere affidabile ed adatto ad essere trasferito al contesto europeo, con lo scopo di realizzare un network europeo di Centri Antiveneni capace di superare i problemi di salute pubblica ancora aperti e di migliorare al livello globale le azioni "basate sull'evidenza" nell'ambito della prevenzione delle esposizioni a sostanze chimiche.

References

1. World Health Organization (WHO). Geneva: World Health Organization; 2021. Immunization, Vaccines and Biologicals. Public health surveillance; 2021. Available on: https://www.who.int/immunization/monitoring_surveillance/burden/vpd/en/ [Last accessed: 2021 Mar 24].
2. Brownson RC, Fielding JE, Maylahn CM. Evidence-based public health: a fundamental concept for public health practice. *Annu Rev Public Health*. 2009; **30**: 175-201. doi: 10.1146/annurev.publhealth.031308.100134.
3. Europe. Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. Available on: <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32006R1907&rid=1>. [Last accessed: 2021 Mar 24].
4. Europe. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. Available on: <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008R1272&rid=2> [Last accessed: 2021 Mar 24].
5. Settini L, Giordano F, Lauria L, Celentano A, Sesana F, Davanzo F. Surveillance of paediatric exposures to liquid laundry detergent pods in Italy. *Inj Prev*. 2018; **24**(1): 5-11. doi: 10.1136/injuryprev-2016-042263.
6. Italy. Conferenza Permanente per i Rapporti tra lo Stato, le Regioni e le Province autonome di Trento e Bolzano. Accordo, ai sensi dell'articolo 4 del decreto legislativo 28 agosto 1997, n. 281, tra il Governo, le Regioni e le Province autonome di Trento e Bolzano concernente la definizione di attività ed i requisiti basilari di funzionamento dei Centri Antiveneni. Rep. Atti n.56/CSR del 28 febbraio 2008. Roma: Presidenza del Consiglio dei Ministri; 2008. Available on: http://archivio.statoregioni.it/Documenti/DOC_017682_56%20csr.pdf [Last accessed: 2021 Mar 24].
7. Istituto Superiore di Sanità (ISS). Preparati Pericolosi. Roma: Istituto Superiore di Sanità; 2020. CAV list; 2020. Available on: <https://preparatipericolosi.iss.it/cav.aspx>. [Last accessed: 2021 Mar 24].
8. Italy. Decreto del Ministero Della Salute, 2 marzo 2016. Approvazione del regolamento di organizzazione e funzionamento dell'Istituto Superiore di Sanità, ai sensi dell'articolo 3 del decreto legislativo 28 giugno 2012, n. 106. (16A02937). *Gazzetta Ufficiale [Official Gazette of Italian Republic]* n. 88, 15 aprile 2016. Available on: <https://www.gazzettaufficiale.it/eli/gu/2016/04/15/88/sg/pdf>. [Last accessed: 2021 Mar 24].
9. Italy. Decreto del Presidente del Consiglio dei Ministri, 3 marzo 2017. Identificazione dei sistemi di sorveglianza e dei registri di mortalità, di tumori e di altre patologie. (17A03142). *Gazzetta Ufficiale [Official Gazette of Italian Republic]* n.109, 12 maggio 2017. Available on: <https://www.gazzettaufficiale.it/eli/id/2017/05/12/17A03142/sg>. [Last accessed: 2021 Mar 24].
10. Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino J. Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol*. 1998; **36**(3): 205-13. doi: 10.3109/15563659809028940.
11. European Chemical Agency (ECHA). The European product categorisation system: A practical guide. Helsinki: European Chemicals Agency, 2019. doi: 10.2823/552626.
12. Draisci R, Giordano F, Malaguti Aliberti L, et al. Esposizione a sostanze e miscele pericolose: risultati preliminari del progetto pilota multicentrico basato su dati provenienti da centri antiveneni. *Not Ist Super Sanita*. 2018; **31**(11): 13-8.

13. Alzahrani SH, Ibrahim NK, Elnour MA, Alqahtani AH. Five-year epidemiological trends for chemical poisoning in Jeddah, Saudi Arabia. *Ann Saudi Med.* 2017; **37**(4): 282-9. doi: 10.5144/0256-4947.2017.282.
14. Kazanasmaz H, Kazanasmaz Ö, Çalık M. Epidemiological and sociocultural assessment of childhood poisonings. *Turk J Emerg Med.* 2019; **19**(4): 127-31. doi: 10.1016/j.tjem.2019.06.001.
15. Gulamhusein, H., Sabri, K. Detergent pods and children: a health hazard on the rise. *Can J Emerg Med.* 2021; **23**: 137-8. doi: 10.1007/s43678-020-00032-4.
16. Settimi L, Davanzo F, Cossa L, Giordano F, Giarletta AM, Urbani E. Sistema informativo nazionale per la sorveglianza delle esposizioni pericolose e delle intossicazioni: casi rilevati nel 2013. Ottavo rapporto annuale. Roma: Istituto Superiore di Sanità; 2017. (Rapporti ISTISAN 17/22).
17. Kemp H, Marinho S, Cook TM, et al. An observational national study of anaesthetic workload and seniority across the working week and weekend in the UK in 2016: the 6th National Audit Project (NAP6) Activity Survey. *Br J Anaesth.* 2018; **121**(1): 134-45. doi: 10.1016/j.bja.2018.04.010.
18. Anderson BD, Seung H, Klein-Schwartz W. Trends in types of calls managed by U.S. poison centers 2000-2015. *Clin Toxicol (Phila).* 2018; **56**(7): 640-5. doi: 10.1080/15563650.2017.1410170.
19. Bairros AV, Saldanha GA, Berlato DG, et al. Accidental ingestion of methyl ethyl ketone peroxide: N-acetylcysteine treatment and toxicological analysis. *Clin Chim Acta.* 2020; **511**: 47-9. doi: 10.1016/j.cca.2020.09.034.
20. Behera C, Chopra S, Garg A, Kumar R. Sulphuric acid marketed in water bottle in India: A cause for fatal accidental poisoning in an adult. *Med Leg J.* 2016; **84**(2): 97-100. doi: 10.1177/0025817216629857.
21. Chang A, Schnall AH, Law R. et al. Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 - National Poison Data System, United States, January 1, 2020-March 31, 2020. *MMWR Morb Mortal Wkly Rep.* 2020; **69**(16): 496-8. doi: 10.15585/mmwr.mm6916e1.
22. Le Roux G, Sinno-Tellier S, Puskarczyk E, et al. Poisoning during the COVID-19 outbreak and lockdown: retrospective analysis of exposures reported to French poison control centres. *Clin Toxicol (Phila).* 2021; **12**: 1-21. doi: 10.1080/15563650.2021.1874402.
23. Li D, Sangion A, Li L. Evaluating consumer exposure to disinfecting chemicals against coronavirus disease 2019 (COVID-19) and associated health risks. *Environ Int.* 2020; **145**: 106108. doi: 10.1016/j.envint.2020.106108.
24. Draisci R, Deodati S, Ferrari M, Guderzo S, Mancinelli R, Giordano F. Disinfettanti, Igienizzanti, Detergenti...USALI IN SICUREZZA [Brochure]. Rome: Istituto Superiore di Sanità, 2020. Available on: <https://www.iss.it/documents/20126/0/Opuscolo+disinfettanti.pdf/eb136a1d-8f89-4b74-cd5a-6bbbae823aa3?t=1585734030713> [Last accessed: 2021 Mar 24].

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