

## Accidental or intentional exposure to potentially toxic medications, natural toxins and chemicals during pregnancy: analysis of data from Tox Info Suisse

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### Summary

**OBJECTIVE:** Affected women and health professionals are still often unsure about how to react to exposures to potentially harmful agents during pregnancy. We wanted to find out which agents worry both pregnant women and professionals, under what circumstances the exposures take place, how they are currently dealt with and how serious they are.

**METHODS:** Making use of the archives of Tox Info Suisse, the foundation that provides poisons information in Switzerland both for members of the general public and for healthcare professionals, we set up an analysis of exposures to possibly harmful agents during pregnancy. Queries during pregnancy between 1995 and 2015 were analysed. Demographic information, exposure and agent characteristics as well as – in a subgroup of cases – the corresponding treatments were considered in the present descriptive, retrospective analysis.

**RESULTS:** Over the 21-year period, 2871 exposures during pregnancy were identified. The majority of the calls were made by members of the general public (2035, 70.9%; most often by the affected women themselves), followed by physicians (733, 25.5%). General public queries were mostly due to exposures connected with household chemicals (675/2035, 33.2%); those of physicians were most often due to medications (415/733, 56.6%). The majority of agent exposures occurred accidentally at home, at work, outdoors or at various other places (2297/2871, 80.0%). Less frequently, the exposures were intentional and had a suicidal, abusive, criminal or other character (471/2871, 16.4%). Of the 2871 calls, 905 cases with symptoms were recorded. Of the 1268 symptoms, 820 were mild (64.7%), 144 moderate (11.3%), 24 severe (1.9%, including 12 abortions) and 280 were not further specified (22.1%). In 1867 cases (65%), a total of 2331 measures were recommended by Tox Info Suisse, 1961 thereof to be carried out immediately. The

two most common immediate measures were exposure interruption (412/1961, 21.0%) and forwarding to another institution (345/1961, 17.6%). In 70 cases, physicians' follow-up reports could be analysed; paracetamol was the agent most frequently involved (15 cases), followed by mefenamic acid (9) and the household product sodium hypochlorite (9).

**CONCLUSIONS:** Tox Info Suisse recorded an average of 137 cases of agent exposure during pregnancy per year, mostly due to accidents with household products. Suicidal intentions played a role in a considerable number of exposures. Measures are needed to prevent accidental exposure of pregnant women to toxic substances and to support them in this exceptional life period.

**Key words:** pregnancy, poisoning, intoxications, household products, medication, suicide, Switzerland, Tox Info Suisse

### Introduction

Pregnancy is an exceptional period in a woman's life and brings numerous physiological, psychological and social changes for the future mother. The sudden responsibility for the unborn child's health can cause uncertainty, especially concerning potentially detrimental and possibly preventable factors such as exposure to harmful agents [1]. The still sparse knowledge about exogenous influences on the health of a pregnant woman and on the development of her unborn child can cause insecurity among health professionals [2], employers of pregnant women and even manufacturers of products that might be used by pregnant women.

As early as 1909, Féré had the idea that external influences could have an impact on the child's intrauterine maturation and was one of the first investigators to start experimenting with various chemicals applied to chicken embryos to produce abnormalities [3]. Since the thalidomide scandal of 1961/62, both the research community and the general public have become keenly aware that medications can be

**Author contributions**  
 APSW suggested the project. TV, SL, CRL and AP-SW designed the present analysis. TV extracted the data on the first calls from the free-text fields of the database (n = 2871) and analysed them. RB extracted the data on the physicians' follow-up reports from the free-text fields of the database (n = 70) and analysed them. TV wrote the first version of the manuscript. All authors reviewed the manuscript, then read and approved the submitted version. TV's contribution constitutes her MD thesis; RB's contribution constitutes her Master's thesis in medicine; APSW supervised both theses.  
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dangerous for a child's intrauterine development. However, it remains a challenge to ensure the safety of unborn children, mainly because prospective clinical trials can be performed on pregnant women only in exceptional cases. In this context, retrospective studies on cases of accidental and suicidal poisonings with medications, and on outcomes after immediate treatment of acute intoxications can provide important information concerning teratogenicity and abortion induction [4–9]. Finally, how physicians and pregnant women perceive the teratogenic risk of several medications has been investigated [10, 11]. These studies focused on the use of medications during pregnancy, whereas pregnant women are exposed to many other potentially harmful agents daily, such as food products and household chemicals.

The present work provides an overview of exposures to all potentially harmful agents of pregnant women in Switzerland, as documented by Tox Info Suisse. This organisation provides poisons information in Switzerland both for members of the general public and for healthcare professionals. In addition to this service, Tox Info Suisse contributes to clinical and evidence-based knowledge about intoxications through systematic documentation of cases, treatment instructions and outcomes.

## Methods

### Ethical statement

The data were generated from the database of Tox Info Suisse and handed over to the authors with patient identities encrypted (approval by the ethics committee of the canton of Zurich, BASEC-Nr PB 2016-00472).

### Tox Info Suisse

Tox Info Suisse is a financially independent foundation, established in 1966 and associated with the University of Zurich since 2011. Its principal responsibility is operating a free 24-hour helpline (telephone number 145), which covers all Switzerland, for all questions concerning poisoning. The information is provided by physicians, veterinarians, pharmacists and nurses trained in clinical toxicology. The service is provided in three of the four official languages in Switzerland (German, French, Italian), as well as in English, and covers a population of about 8.5 million people. In the electronic in-house database, demographic information, agents involved in exposures, circumstances of exposure, route of application, and any specific measures advised are recorded in a systematic and standardised manner. Further information such as questions posed by the calling party, symptoms described and specific measures recommended by Tox Info Suisse are noted in free-text fields. In cases of calls from health professionals, Tox Info Suisse asks for follow-up reports on the clinical course of the exposure. This supplementary information includes the systematic assessment of the overall severity of the exposure and the causal correlation between symptoms and exposure as evaluated by the trained staff of Tox Info Suisse. Furthermore, as in the primary calls, information on symptoms, clinical course, decontamination measures, and both specific and symptomatic therapies is noted, both in a standardised way and in free-text fields.

### Identification of cases

Appropriate cases were identified from among those archived between 1995 and 2015 in the Tox Info Suisse in-house database. The inclusion criterion was “exposure during pregnancy”, and all calls addressing effects on the mother and/or on the child were considered. It should be noted that “agent exposure” is not synonymous with “intoxication”. The latter is defined as an agent exposure that causes symptoms, whereas agent exposure *per se* does not necessarily cause symptoms.

Since the criterion “exposure during pregnancy” was not systematically recorded, the free-text field for the patient's medical history was screened for expressions synonymous with or related to pregnancy in the English, German, French and Italian languages. These included conception, gestation, gravidity, pregnant, pregnancy, Gravidia (Ger.: pregnant woman), schwanger (Ger.: pregnant), SSW (Ger. abbr.: week of pregnancy), SSM (Ger. abbr.: month of pregnancy), enceinte (Fr.: pregnant), gravidité (Fr.: pregnancy), grossesse (Fr.: pregnancy), gravidanza (It.: pregnancy) and incinta (It.: pregnant). The cases identified were extracted from the database and reviewed one by one to eliminate those mentioning the search terms in contexts other than pregnancy at the time of agent exposure (e.g., “since her pregnancy, two years ago, the patient...”).

For the evaluation of follow-up reports by health professionals, only exposures where the association between women's symptoms and the agent was considered proven or likely or no symptoms occurred at all were included in the analysis. For sake of clarity, exposures with agents involved in four or fewer cases are not shown.

### Primary calls

The queries made by the caller were assigned to one of eleven predefined question categories. The symptoms were allocated to either the mother or the child, assessed for severity based on the Poisoning Severity Score first presented by Persson et al. [12], and assigned to the organ or functional system afflicted. Since the description of complaints was not always precise enough to assign them to one symptom or its associated system, certain symptoms were combined into larger symptom-groups (for example: irritation of pharynx/larynx/trachea). Finally, headache was assigned to the organ system “neurological”, stomach ache to “gastrointestinal” and “irritation of pharynx/larynx/trachea” to otorhinolaryngeal, although strictly speaking they do not afflict only one single system.

The correlation between the patient's account, the agent involved and symptoms was evaluated by the specialised staff of Tox Info Suisse with the support of their internal database, books, publications, specialist literature, swissmedinfo.ch and material safety data sheets. A correlation was defined as adequate if at least one symptom fitted the possible clinical manifestation of the agent involved.

### Follow-up reports by health professionals

In addition to the systematically recorded parameters, information in the free text fields was translated into new phrased parameters. These included additional symptoms – assigned to the corresponding organ system or functional system – the decontamination measures, and specific and symptomatic therapy.

**Data analysis**

All parameters were analysed with descriptive statistics using the statistics program “SPSS” Version 22.0. Unless otherwise mentioned, data are shown as number (n) and as percentage (%).

**Results**

**Sociodemographic characterisation**

A total of 2871 cases of exposure during pregnancy were identified. The majority of the calls were made by members of the general public (2035/2871, 70.9%), followed by physicians (733/2871, 25.5%) and in 103 cases (out of 2871, 3.6%), Tox Info Suisse was contacted by other parties (pharmacists, veterinarians, toxicological centres, other organisations, unknown callers; fig.1). Among the calls made by members of the general public, most were made by the affected women themselves (1562/2035, 76.8%), but in some cases their partners, parents, relatives, friends and others phoned.

The latency between exposure and time of phone call was documented in 1806 cases and was usually 24 hours or less (1576/1806, 87.3%). In a few cases, it was less than 1 hour (298/1806, 16.5%). In 230 cases (out of 1806, 12.7%), more than a day had passed by the time Tox Info Suisse was contacted. In cases where the stage of pregnancy at the time of the call was noted (1962), only 46 calls (2.3%) were made postpartum (fig. 1); all others (1916/1962, 97.7%) were made during pregnancy. The number of calls decreased slightly from the first to the third trimester (731, 637 and 548, respectively). This decrease was due to declining queries from physicians (265, 173 and 124, respectively).

**Circumstances of exposure**

The majority of agent exposures (2297/2871, 80.0%) occurred accidentally: 1854 at home, 232 at work, 33 outdoors and 178 in another place. Less frequently, exposures were intentional (471/2871, 16.4%). In 103 cases, the circumstances were adverse drug reactions, iatrogenic applications or not further specified (fig. 2). Accidental exposures mostly happened at home (1854/2297, 80.7%) or

at work (232/2297, 10.1%). Intentional exposures were in more than half of all cases with suicidal intentions (254/471, 53.9%); otherwise they had an abusive (41), criminal (3) or other (173) character. Physicians called more often because of intentional intoxications (331/733, 45.2%) than did members of the general public (115/2035, 5.7%). The frequency of accidental exposures where the trimester at the time of the call was known (1490) remained approximately constant throughout all trimesters (511, 513 and 466, respectively). Of the intentional exposures with trimester information at the time of the call, the number and the number of exposures with suicidal intentions (in total 359 and 215, respectively) decreased from the first to the third trimester (180 and 97, 105 and 76, 74 and 42).

**Route of exposure**

Figure 2 shows that the main route of exposure was oral (1524/2871, 53.1%), followed by inhalation (874/2871, 30.4%), dermal (229/2871, 8.0%) and by other routes of exposure (244/2871, 8.5%), including animal bite/sting, intravenous, intramuscular, subcutaneous, paravenous, sublingual, ocular, nasal, rectal, vaginal and transplacental). For intentional exposures, oral intake was by far the most prevalent route (405/471, 86.0%), whereas for accidental exposures, the oral route was closely followed by inhalation (1054/2297, 45.9%; 846/2297, 36.8%). From the 846 accidental inhalations, 603 occurred at home and 179 in an occupational setting (71.3% and 21.2%, respectively).

**Agents**

Leading to approximately one third of all calls, household products were the frontrunner among agents involved (791/2871, 27.6%), closely followed by medications (733/2871, 25.5%). Ranking third and fourth were technical and industrial agents (387/2871, 13.5%) and food and beverages (299/2871, 10.4%), followed by agricultural and gardening products, plants, poisonous animals, hygiene products, mushrooms, recreational drugs, veterinary drugs and other agents (shown in figs 1 and 2). When the medication subclass was analysed according to the Anatomic Therapeutic Chemical (ATC) classification system [13], two

**Figure 1:** Types of agents reported by the different parties who contacted Tox Info Suisse on agent intake during pregnancy (n = 2871)

Agent	General public										Physicians										Others					All agents	
	Period of pregnancy					n	%	Period of pregnancy					n	%	Period of pregnancy					n	%						
	Trimester			PP	UK			Trimester			PP	UK			Trimester			PP	UK								
	1	2	3			1	2	3			1	2	3														
Household chemicals	122	133	138	2	280	675	33.2	28	28	21	0	23	100	13.6	3	4	4	0	5	16	15.5	791	27.6				
Medications	87	50	44	6	87	274	13.5	167	97	64	16	71	415	56.6	19	7	4	1	13	44	42.7	733	25.5				
Technical and industrial agents	62	63	55	3	95	278	13.7	29	21	13	3	22	88	12.0	5	4	0	2	10	21	20.4	387	13.5				
Food and beverages	58	64	59	0	100	281	13.8	3	5	3	0	4	15	2.0	1	1	0	0	1	3	2.9	299	10.4				
Agricultural and gardening products	29	24	24	1	26	104	5.1	8	5	5	1	3	22	3.0	2	1	0	0	2	5	4.9	131	4.6				
Plants	17	20	15	0	29	81	4.0	3	5	3	2	0	13	1.8	1	0	0	0	1	2	1.9	96	3.3				
Poisonous animals	5	14	14	0	25	58	2.9	3	2	0	0	2	7	1.0	0	1	0	0	1	2	1.9	67	2.3				
Hygiene products	11	18	12	0	8	49	2.4	5	0	3	1	3	12	1.6	0	0	0	0	0	0	0.0	61	2.1				
Mushrooms	3	5	8	0	14	30	1.5	2	3	6	0	3	14	1.9	0	0	0	0	0	0	0.0	44	1.5				
Recreational drugs	6	5	4	1	4	20	1.0	7	4	2	2	4	19	2.6	0	1	0	1	1	3	2.9	42	1.5				
Veterinary drugs	2	5	3	0	4	14	0.7	1	0	1	0	0	2	0.3	0	1	1	0	1	3	2.9	19	0.7				
Other agents	33	42	37	3	56	171	8.4	9	3	3	1	10	26	3.5	0	1	2	0	1	4	3.9	201	7.0				
Total (n)	435	443	413	16	728	2035	100	265	173	124	26	145	733	100	31	21	11	4	36	103	100	2871	100				
% of total*	21.4	21.8	20.3	0.8	35.8	100	36.2	23.6	16.9	3.5	19.8	100	30.1	20.4	10.7	3.9	35.0				100		100				
% of total*						70.9								25.5									100				

PP = postpartum; UK = unknown. Data are shown for all pregnancy periods taken together (all) and then distinguished by the time of the call (trimester 1, 2 or 3, or postpartum). \* Total within a given calling party; † Total for all pregnancy periods together (including postpartum and unknown).

Reading example: 13.8% of the general public calls (281/2035) concerned exposure to food and beverages. Of these, 58 calls took place during the first pregnancy trimester, 64 in the second, 59 in the third. In addition to the general public calls on food and beverages, there were 15 and 3 calls from physicians and others, respectively, on food and beverages; this means that a total of 299 calls were due to food and beverages, which corresponds to 10.4% of the total number of calls (2871).

main groups were identified: remedies for the nervous system (265/733, 36.2%) and the genitourinary system (74/733, 10.1%).

Members of the general public contacted Tox Info Suisse most frequently owing to exposure to household chemicals (675/2035, 33.2%), followed by food and beverages (281/2035, 13.8%), technical and industrial agents (278/2035, 13.7%), and medications (274/2035, 13.5%). Physicians called most often to check medications (415/733, 56.6%), household products (100/733, 13.6%), and technical and industrial agents (88/733, 12.0%). The prevalence of the two most frequent agent groups changed according to the trimester of pregnancy when the call took place: during the first trimester, calls about exposures to medications were more numerous than calls about household products (273/731, 37.3% vs 153/731, 20.9%), whereas this changed in the second (154/637, 24.2% vs 165/637, 25.9%) and the third trimesters (112/548, 20.4% v. 163/548, 29.7%).

The agents involved in accidental exposures were more heterogeneous than those in intentional exposures (fig. 2). Household products represented a third of all accidental exposures (762/2297, 33.2%), followed by technical and

industrial agents (373/2297, 16.2%), and medications (283/2297, 12.3%). In contrast, three quarters of intentional exposures involved medications (363/471, 77.1%). Of the two most frequently mentioned types of agents, household products were most often inhaled (367/791, 46.4%; 35 thereof in an accidental occupational setting), whereas medications were mostly taken orally (609/733, 83.1%).

**Questions posed by callers**

A total of 3507 questions were asked (fig. 3). The question posed most frequently was whether the situation was dangerous in general (1377/3507, 39.3%), followed by the question whether the situation was dangerous specifically for the unborn child (904/3507, 25.8%) and what measures should be taken (582/3507, 16.6%). Only a small number of queries were about specific danger to the mother (82/3507, 2.3%). Questions about abortion were very rare and comparable in intentional and in accidental exposures (total 13/3507, 0.4%; 6 vs 4, respectively).

Within the calling parties “general public” and “physicians”, the question posed most frequently was how dangerous the situation was (1044/2426, 43.0% of all ques-

**Figure 2:** Intake of various types of agents during pregnancy according to intake intention and route of exposure (n = 2871).

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Agent	Accidental				n	%	Intentional				n	%	Other				n	%	All agents			
	Route of exposure						Route of exposure						Route of exposure						n	%	n	%
	Oral	Inhaled	Dermal	Other			Oral	Inhaled	Dermal	Other			Oral	Inhaled	Dermal	Other						
Household chemicals	283	361	85	33	762	33.2	21	6	1	0	28	5.9	1	0	0	0	1	1.0	791	27.6		
Medications	211	12	21	39	283	12.3	337	2	4	20	363	77.1	61	1	6	19	87	84.5	733	25.5		
Technical and industrial agents	54	251	32	36	373	16.2	1	8	0	2	11	2.3	0	2	0	1	3	2.9	387	13.5		
Food and beverages	275	7	5	2	289	12.6	8	0	0	0	8	1.7	1	0	0	1	2	1.9	299	10.4		
Agricultural and gardening products	36	70	12	6	124	5.4	3	2	0	1	6	1.3	1	0	0	0	1	1.0	131	4.6		
Plants	74	3	7	3	87	3.8	8	0	0	0	8	1.7	0	0	1	0	1	1.0	96	3.3		
Poisonous animals	6	2	15	44	67	2.9	0	0	0	0	0	0.0	0	0	0	0	0	0.0	67	2.3		
Hygiene products	16	12	16	4	48	2.1	7	1	3	1	12	2.5	0	0	1	0	1	1.0	61	2.1		
Mushrooms	43	0	0	1	44	1.9	0	0	0	0	0	0.0	0	0	0	0	0	0.0	44	1.5		
Recreational drugs	8	0	1	2	11	0.5	17	5	0	9	31	6.6	0	0	0	0	0	0.0	42	1.5		
Veterinary drugs	4	1	11	2	18	0.8	1	0	0	0	1	0.2	0	0	0	0	0	0.0	19	0.7		
Other agents	44	127	7	13	191	8.3	2	1	0	0	3	0.6	1	0	1	5	7	6.8	201	7.0		
<b>Total (n)</b>	<b>1054</b>	<b>846</b>	<b>212</b>	<b>185</b>	<b>2297</b>	<b>100</b>	<b>405</b>	<b>25</b>	<b>8</b>	<b>33</b>	<b>471</b>	<b>100</b>	<b>65</b>	<b>3</b>	<b>9</b>	<b>26</b>	<b>103</b>	<b>100</b>	<b>2871</b>	<b>100</b>		
% of total <sup>†</sup>	45.9	36.8	9.2	8.1	100	86.0	5.3	1.7	7.0	100	63.1	2.9	8.7	25.2	100	3.6	100	100				
% of total <sup>*</sup>																						

\* Total within a given intake intention; † Total for all types of intake taken together

**Figure 3:** Focus of questions posed to Tox Info Suisse by the different calling parties, according to intake intention (n = 3507).

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Question	General public				n	%	Physicians			n	%	Other			n	%	All questions				
	Circumstances			n			%	Circumstances				Circumstances					n	%	n	%	
	Accidental	Intentional	Other					Accidental	Intentional			Other	Accidental	Intentional							Other
Dangerous situation	982	48	14	1044	43	143	135	6	284	29.3	36	12	1	49	43.4	1377	39.3				
Dangerous for unborn child	686	32	19	737	30.4	84	57	5	146	15.1	19	2	0	21	18.6	904	25.8				
What measures should be taken	255	21	7	283	11.7	104	160	14	278	28.7	13	8	0	21	18.6	582	16.6				
Dangerous for pregnancy	118	7	3	128	5.3	35	32	4	71	7.3	5	2	0	7	6.2	206	5.9				
Symptoms explained by exposure	46	9	3	58	2.4	18	10	16	44	4.5	2	0	0	2	1.8	104	3.0				
Teratogen	23	3	4	30	1.2	27	27	12	66	6.8	0	4	0	4	3.5	100	2.9				
Information about agent	52	5	1	58	2.4	14	12	5	31	3.2	7	1	0	8	7.1	97	2.8				
Dangerous for mother	56	5	1	62	2.6	8	12	0	20	2.1	0	0	0	0	0.0	82	2.3				
Other questions	15	2	1	18	0.7	3	7	2	12	1.2	1	0	0	1	0.9	31	0.9				
Need for interruption	2	1	0	3	0.1	2	5	3	10	1.0	0	0	0	0	0.0	13	0.4				
Breast feeding possible	4	1	0	5	0.2	1	2	3	6	0.6	0	0	0	0	0.0	11	0.3				
<b>Total (n)</b>	<b>2239</b>	<b>134</b>	<b>53</b>	<b>2426</b>	<b>100</b>	<b>439</b>	<b>459</b>	<b>70</b>	<b>968</b>	<b>100</b>	<b>83</b>	<b>29</b>	<b>1</b>	<b>113</b>	<b>100</b>	<b>3507</b>	<b>100</b>				
% of total <sup>†</sup>	92.3	5.5	2.2	100	86.0	45.4	47.4	7.2	100	73.5	25.7	0.9	100	3.2	100						
% of total <sup>*</sup>																					

\* Total within a given calling party; † Total considering all calling parties together

tions from the general public, and 284/968, 29.3% of all physician-posed questions). In contrast, the second most frequently posed question differed: members of the general public asked 737 times if the situation was dangerous for the unborn child (737/2426, 30.4%), whereas physicians asked 278 times what measures should be taken (278/968, 28.7%).

During the different trimesters, the ranking of the questions remained similar to that for the overall total, except that the questions concerning teratogenicity were remarkably more frequent in the first trimester than in the second or third, or postpartum (50, 20, 6 and 4, respectively). The question about teratogenicity was most often posed by physicians (66/100, 66%).

After both accidental and intentional exposures, the question about the danger of the situation was the one posed most frequently (1161/2761, 42.0% of all questions asked after an accident and 195/622, 31.4% of all questions asked after intentional exposure). However, the second most frequently posed question differed: after an accident, the callers were more concerned about the danger to the unborn child (789/2761, 28.6%) and after an intentional exposure more often about what measures should be taken (189/622, 30.4%).

**Symptoms and severity**

Among all 2871 calls, 905 (31.5%) cases with symptoms and 684 (23.8%) without symptoms were recorded. No documentation on symptoms was available for the remaining 1282 calls (44.7% of the total). In 742 of the 905 cases with documented symptoms (742/905, 82.0%), the correlation between the symptoms and the known effects of the agent was evaluated as likely.

As shown in figure 4, a total of 1268 symptoms were recorded. The four organ systems affected the most were the gastrointestinal with 423 symptoms (33.4%), the neu-

rological with 264 symptoms (20.8%), the otorhinolaryngeal with 165 symptoms (13.0%) and the dermatological system with 139 symptoms (11.0%). Furthermore, symptoms related to the respiratory (89), ophthalmological (60), cardiovascular (31), hepatic (7), metabolic (4), muscular (3), urological (2) and blood (1) systems, as well as 55 symptoms not assignable to an organ system, were recorded. Gynaecological-obstetric problems were seldom reported, and comprised 6 cases of vaginal bleed, 5 cases of uterine contractions, 2 cases of threatened abortion and 12 abortions (note that threatened abortions are listed in figure 4 as pregnant women's symptoms, classified as severe).

Around 800 symptoms were classified as mild (820/1268, 64.7%), 144 as moderate (144/1268, 11.4%), 24 as severe (24/1268, 1.9%; including 12 abortions) and further 280 symptoms could not be specified concerning severity (280/1268, 22.1%) (fig. 4). In all organ systems except gynaecological-obstetric (0 mild, 0 moderate, 2 severe, 11 not further specified, 12 abortions) and muscular systems (only 2 moderate), the predominant symptom severity was mild, followed by moderate. Severe symptoms occurred only in the neurological, dermatological and in the gynaecological-obstetric systems (in fig. 4 mentioned under "others"). In 19 children, unborn or postpartum, a total of 28 symptoms and two premature deliveries were recorded (data not shown). The symptoms recorded in the children were mild in 5, moderate in 7, severe in 5 and not further specified in 11 cases. The symptoms were: decreased intrauterine movement and malformation (4 of each), respiratory insufficiency (3), mild somnolence, bradycardia and no appetite (2 of each), cramps, reduced tone, symptoms of withdrawal, tachypnoea, metabolic acidosis, aspiration, hypothermia, thrombopenia, ascites, hepatosplenomegaly and hearing loss (all 1 each).

Among the various types of agents to which the women were exposed, medications were most often associated

**Figure 4:** Maternal symptoms after exposure to various agents during pregnancy in relation to the affected organ system, according to their severity (n = 1268).

Agent	Gastrointestinal				Neurological				Otorhinolaryngeal				Dermatological				Others				All												
	Severity				Severity				Severity				Severity				Severity																
	Mild	Moderate	Severe	NS	n	%	Mild	Moderate	Severe	NS	n	%	Mild	Moderate	Severe	NS	n	%	Mild	Moderate	Severe <sup>†</sup>	NS	n	%	n	%							
Medications	44	9	0	31	84	19.9	97	14	4	7	122	46.2	1	0	0	0	1	0.6	7	2	0	3	12	8.6	33	7	2	26	68	24.5	287	22.6	
Household chemicals	47	11	0	13	71	16.8	28	3	0	10	41	15.5	78	0	0	0	78	47.3	16	8	0	4	28	20.1	37	3	2	19	61	22.0	279	22.0	
Technical and industrial agents	28	2	0	7	37	8.8	20	4	0	10	34	12.9	54	0	0	0	54	32.7	14	1	0	6	21	15.1	23	1	5	19	48	17.3	194	15.3	
Food and beverages	45	19	0	29	93	22.0	5	2	0	0	7	2.7	1	0	0	0	1	0.6	4	3	1	0	8	5.8	5	1	0	2	8	2.9	117	9.2	
Plants	23	6	0	19	48	11.3	2	1	0	0	3	1.1	1	0	0	0	1	0.6	5	0	1	1	7	5.0	5	1	0	2	8	2.9	67	5.3	
Mushrooms	17	11	0	18	46	10.9	3	0	0	1	4	1.5	0	1	0	0	1	0.6						0	0.0	4	0	0	0	4	1.4	55	4.3
Poisonous animals	1	0	0	0	1	0.2	0	0	0	0	0	0.0	0	0	0	0	0	0.0	27	13	0	6	46	33.1	3	0	0	0	3	1.1	50	3.9	
Agricultural and gardening products	6	0	0	4	10	2.4	8	0	0	1	9	3.4	4	0	0	0	4	2.4	4	1	1	0	6	4.3	7	1	3	2	13	4.7	42	3.3	
Recreational drugs	2	2	0	3	7	1.7	3	3	0	1	7	2.7	0	0	0	0	0	0.0		0	0	0	0	0	0.0	3	1	2	0	6	2.2	20	1.6
Hygiene products	1	0	0	0	1	0.2	3	0	0	2	5	1.9	2	0	0	0	2	1.2	2	0	1	2	5	3.6	2	0	0	4	6	2.2	19	1.5	
Veterinary drugs	1	0	0	0	1	0.2	1	0	0	0	1	0.4	0	0	0	0	0	0.0	1	0	0	0	1	0.7	0	1	0	1	2	0.7	5	0.4	
Other agents	17	3	0	4	24	5.7	22	4	0	5	31	11.7	23	0	0	0	23	13.9	4	1	0	0	5	3.6	26	4	2	18	50	18.0	133	10.5	
Total (n)	232	63	0	128	423	100	192	31	4	37	264	100	164	1	0	0	165	100	84	29	4	22	139	100	148	20	16	93	227	100	1268	100	
% total*	55	15	0	30	100		73	12	2	14	100		99	0.6	0	0	100		60	21	2.9	16	100		53	7	5.8	34	100				
% total†					33.3						20.8						13.0						11.0						21.8			100	

NS = not specified; \* Total within a given organ system; † Total considering all organ systems together; ‡ Including 12 cases of abortion

with the occurrence of symptoms (fig. 4). In 733 cases where medications were involved, 205 (205/733, 28%) patients developed symptoms. The sum of all symptoms was 287, of which 182 were mild, 32 moderate, 4 severe and 67 not further specified; moreover, 2 abortions were detected. Three out of the four severe symptoms were caused by medications for the central nervous system and one by a medication for the respiratory system. Of the two abortions, one was associated with hormonal medication and the other with an intake of a dietary supplement.

After medications, household chemicals caused the most frequent occurrence of symptoms (195/791, 24.7% symptomatic exposures in all cases exposed to household products). As shown in figure 4, these exposures led to 279 symptoms, of which the majority was mild (206), followed by moderate (25), severe (2, including an abortion) and not further specified (46).

### Measures

In 374/2871 (13.0%) of all cases, some measures had already been taken before Tox Info Suisse was contacted. Among these cases, a total of 385 measures were taken, of which the two most popular actions were exposure interruption (e.g., airing the room, stopping application of the agent), which was carried out 150 times, and active decontamination measures (rinsing of eyes, cleaning of skin, etc.), carried out 144 times.

In 1867/2871 (65%), a total of 2331 measures were recommended. These measures were divided into two groups: immediate measures, which had to be taken unconditionally, and conditional measures, the execution of which was linked to a certain condition in clinical development or diagnostic result. The top two of the immediate measures (total 1961) were exposure interruption (412) and forwarding to another institution (345) mostly to an embryo toxicological centre (88). A considerable proportion of the conditional measures recommended consisted of administration of medication (119/370).

Two hundred and seventy-four of all members of the general public (274/2035, 13.5%) took autonomous measures before contacting Tox Info Suisse. In 1193 cases (1193/

2035, 58.6%), Tox Info Suisse recommended further measures. Of these, the three most common immediate measures were exposure interruption (365), non-pharmaceutical decontamination (212) and contacting another institution (109). The physicians took slightly fewer measures (87/733, 11.9%), but more frequently obtained advice for further immediate measures (599/733, 81.7%). These involved contacting another institution in 218 cases, surveillance measures in 164 and medicinal decontamination measures (e.g., activated charcoal) in 10.

### Follow-up reports from health professionals

The in-house database of Tox Info Suisse included 314 follow-up reports from health professionals; in 265 of these, the symptom's relationship with the agent in question was considered certain or likely, or no symptoms occurred at all. A variety of agents was involved in these 265 cases. In the present analysis, only exposures with agents involved in at least 5 cases were considered (9 agents; 70 exposures). As shown in figure 5, a total of 137 symptoms were considered to be caused by these agents. In the majority of the cases, medications were involved (56/70, 80.0%). Paracetamol was the agent most often involved (15), followed by mefenamic acid (9) and the household product sodium hypochlorite (9). Mostly, the symptoms were mild (122/137, 89.1%), a few were moderate (10), one was severe and four could not be further specified. Among the various organ systems affected, the nervous system showed the most symptoms (46), followed by the gastrointestinal system (23). In total, 25 decontamination measures were taken, of which the application of a single dose of activated charcoal was the most frequent (10) (fig. 6). Fifteen specific therapies were initiated, of which the administration of N-acetyl cysteine was most frequent (10). A total of 48 different symptomatic therapies were applied (fig. 6).

### Discussion

Between 1995 and 2015, Tox Info Suisse recorded an annual average of 137 calls due to agent exposure during pregnancy. This suggests that agent exposure during preg-

**Figure 5:** Symptoms caused by the nine most frequently mentioned agents in cases with professional feedback.

Agent	Cases (n)	Blood	Gastro-intestinal	Hepatic	ORL	Cardiac	Metabolic	Neurological			Ophthalmological	Respiratory		Gynaecological	Others	Total symptoms		
		Anaemia, leucocytosis	Nausea, vomiting, corrosion oesophagus, other	Necrosis liver cell, cholestasis	Irritation, hoarseness, other	Bradycardia, tachycardia, hypotonia, other	ECG changes	Hypokalaemia, alkalosis	Hypokalaemia	Somnolence, dysarthria, anti-cholinergic reaction, other	Coma, gen. epileptic seizures, anti-cholinergic reaction, other	Coma	Miosis, impaired vision	Dys- and tachypnoea, cough, hypersensitivity, other	Apnoea		Contraction, other	Stomach pain, headache, chest pain, other
Severity		Mild	Mild	Mild	Mild	Mild	NS	Mild	Moderate	Mild	Moderate	Severe	Mild	Mild	Moderate	Mild	Mild	
Paracetamol	15		4	1		3	1			4							10	23
Mefenamic acid	9		2			2				4	2						1	11
Sodium hypochlorite	9		6		5								3				6	20
Diphenhydramine	7		4			3	2			5	1					2		17
Lorazepam	7	1	2	1		3		1		6	1		1				1	17
ASA	7	1	4			1	2			3	1			5			3	20
Bromazepam	6					1				7	1		1				1	11
Ethanol	5		1			1				3	1	1		1				9
Zolpidem	5					1	1			5	1							9
Total (n)*	70	2	23	2	5	15	4	2	1	37	8	1	2	9	1	2	23	137
Total / organ-system†		2	23	2	5	19		3		46		2		10		2	23	137

ORL = otorhinolaryngeal; \* Total within a given organ system; † Total considering all organ systems together

nancy is not rare. The strengths of the present study are the high number of calls analysed and the access to data that are otherwise not available. Still, and for various reasons (lack of looking for help, contacting other institutions, language limitations, etc.) the documented exposures are likely to represent only part of all exposures taking place in Switzerland. A further limitation of the present study is that the database was not specifically designed to answer the questions addressed. Moreover, the purpose of Tox Info Suisse implies a high heterogeneity of cases and limits data clustering. In the case of calls by members of the general public, some medical and technical information might not be complete. Finally, the information on most recorded cases reflects a brief time period.

The great majority of calls were made by members of the general public, implying that uncertainty about how to handle such situations is widespread in the population. These uncertainties mostly concerned exposures to agents such as household products, technical and industrial agents, and food and beverages. One quarter of all calls were made by physicians, showing that even for health professionals this issue remains challenging [14]. They were most frequently concerned with exposures to medications, and such exposures were most often associated with symptomatic cases. Besides wanting to know how dangerous the situation was, physicians also wanted to find out what measures should be taken to protect both mother and unborn child in such unfamiliar and particularly challenging circumstances.

Awareness of agent teratogenicity is crucial [15] and the malformation risk associated with agent exposure during pregnancy is perceived as high in the general population [10]. Accordingly, members of the general public frequently asked about the wellbeing of the unborn child, but teratogenicity was even more often an issue when physicians contacted Tox Info Suisse than when members of the general public did. This is in line with the comparatively high frequency of physicians' queries in the first trimester. Both observations can be explained by the professionals' knowledge that the risk of teratogenicity after agent exposure is highest during the first 8 gestational weeks [16]. The fear of long-term damage can also explain why a considerable number of phone calls were made 24 hours after the exposure – or even later – when acute symptoms are usually waning and queries about exposures in non-preg-

nant persons seldom occur. In contrast to these fears, the number of symptoms that occurred in children were low compared with the number of symptoms developed by the mothers (28 vs 1268 in 2871 primary calls; 0 vs 137 in the 70 follow-up reports from health professionals that were analysed). Four cases of malformation were observed in our primary calls, and none in the follow-up reports from health professionals. The causal correlation of the reported 12 abortions with the substance to which the pregnant women had been exposed was classified as possible in two cases. In one case, a technical/industrial product was involved (glue for foam material); in the other case, a recreational drug (cannabis) could have played a role.

The relatively low number of malformations and abortions seem to suggest that the first concern when confronted with agent exposure during pregnancy should be the mother's wellbeing. Furthermore, our finding corroborates previous studies in which, after drug overdose, no higher rate of malformations were found [4, 7]. Schaefer et al. stated that the acute treatment of intoxications during pregnancy should not differ from procedures for non-pregnant women [9]. We feel that concern about teratogenicity was almost excessive compared with other possible – rather immediate – dangers through agent exposures, such as direct effects on the mother. The majority of symptoms the mothers experienced after accidental and intentional exposures were mild. Comparable observations were reported by Sein Anand et al., who investigated a case series of self-poisonings, in which the clinical courses were mostly mild or moderate [17].

More than half the intentional exposures occurred with suicidal intent. This finding is consistent with a previous evaluation of hospital admissions of pregnant women due to self-intoxications, which showed that 68.6% were attempted suicides [18]. Earlier work further showed that attempted suicides during pregnancy do not seem to induce a higher prevalence of structural birth defects [4] and completed suicides are seldom caused by medication overdose, especially as compared to deaths by violent acts [19]. We observed that medications in general and, among these, medications for the nervous system were the agents mainly involved in intentional exposures, which again is in line with previous work [20, 21]. The latter reported that the highest incidence of suicidal attempts is within the first trimester, which our data confirm. Generally, pregnancy is

**Figure 6:** Measures taken to minimise and/or treat symptoms caused by the nine most frequently mentioned agents in cases with professional feedback.

Agent	Cases (n)	Total symptoms	Decontamination			Specific therapy			Symptomatic therapy								
			Activated charcoal	Gastric lavage	Other	N-acetyl cysteine	Flumazenil	Naloxone	Hospitalisation/surveillance	Intubation	Inhalation water vapour	Hydration/electrolyte solution	Propulsives	GORD/PPI	Psychiatric therapy	Caesarean section	
																	Single dose
Paracetamol	15	23	1	1	5	10			5	1		1				2	1
Mefenamic acid	9	11	2		1	1			1				1		1	1	
Sodium hypochlorite	9	20									1				1		
Diphenhydramine	7	17	2	1								1					
Lorazepam	7	17	2						5				2				4
ASA	7	20	2	1					2			1		1			
Bromazepam	6	11	1		1				2	1							
Ethanol	5	9									5		1				
Zolpidem	5	9		1		1			1								
Total (n)*	70	137	10	5	2	8	10	4	1	28	1	1	6	2	2	7	1
Total / type of measure†		137	25			15			48								

GORD/PPI = gastro-oesophageal reflux disease / proton-pump inhibitors  
 \* Total for a given type of measure  
 † Total considering all measures of one type together

a protective factor against suicide [22], but it is known that almost 80% of all suicide attempts during pregnancy are carried out for the first time [17]. Our data clearly show that suicide attempts during pregnancy in Switzerland – especially during early pregnancy – cannot be ignored. Most available feedback concerned exposure to medications. This correlates with the most frequent reason for the first calls from physicians (medications in 56.6%). Easily accessible analgesic drugs (paracetamol, mefenamic acid, acetylsalicylic acid) showed the highest incidence (31), followed by benzodiazepines and Z-drugs (18; lorazepam, bromazepam, zolpidem), which are available only on prescription. The symptoms caused by these exposures were however mostly mild. In Switzerland, 16.7% of all women use mental-health services during the perinatal period [23], implying that mental issues appear with high frequency in this period and hence such medications are present in a considerable proportion of households. As to be expected from the types of agents involved, the decontamination measure initiated most frequently was the application of activated charcoal, which inhibits gastrointestinal absorption of agents [24], and the specific treatment with N-acetyl cysteine, which is the antidote to paracetamol. Our results on agent exposure during pregnancy have implications for Tox Info Suisse, for several professional groups and for public health. For Tox Info Suisse, the present work means that special attention should be paid to pregnancy, and that cooperation with institutions dedicated to issues of teratogenicity should be intensified. These institutions include the Swiss Teratogen Information Service (STIS), the Federal Office of Public Health (“Bundesamt für Gesundheit”, BAG), the Swiss Working Group for Perinatal Pharmacology (“Schweizerische Arbeitsgemeinschaft für Perinatale Pharmakologie, SAPP), maternity and gynaecological hospitals and universities. The prevalence of occupational exposure was considerable, and twice as high as that for other women in the same age range contacting Tox Info Suisse (data not shown). Since exposure can be relevant as early as during the first trimester, protective measures established before pregnancy occurs are likely to be more effective and could contribute to reducing situations of insecurity. Employers, especially those from work domains involving exposure to possibly toxic chemical agents, should invest in information for women of reproductive age. Moreover, since current warning notices about (toxic) household products are not fully effective in preventing unintentional exposures, the manufacturers concerned should re-think their warning texts. Physicians directly confronted with agent exposure during pregnancy should be aware that most immediate consequences will affect the mother, and only a few the unborn child. Therefore, it is important to prioritise the treatment of symptoms affecting the pregnant woman. At the same time, it appears reasonable to reduce the distress caused by fear of miscarriage and/or teratogenicity. Since stress during pregnancy is *per se* associated with poor perinatal outcomes, this would contribute to a healthier pregnancy course [25]. Furthermore, physicians and other health professionals involved in antenatal care should be aware that suicide attempts during pregnancy do occur. Since a considerable proportion of the suicide attempts during pregnancy are first time events, an especially careful evaluation

of the suicidal status of the pregnant woman is needed. Appropriate counselling of women facing difficult situations during pregnancy, including possible involvement of close social contacts might reduce the rate of attempted suicides. Pregnancy remains a particularly challenging period in a women’s life. From the public health point of view, multiple efforts should be made to support and reassure pregnant women. Several professional groups and the society in general should be sensitised for this need and motivated to participate in those efforts thereby contributing to improve the future health of both mothers and their offspring.

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