Results: Of 152,762 reports to STIC, 55 involved OD with thiopurines (n = 39), MMF (n = 14), or SIR (n = 2). Of these, 32 were with suicidal intent, 19 accidental, and 4 iatrogenic errors. Eleven (31%) thiopurine, 4 (31%) MMF, and 1 (50%) SIR ODs had attributable symptoms. The majority of symptoms were minor, although 1 case of sustained thiopurine OD caused agranulocytosis, 1 case of a 9-fold MMF OD caused biphasic hypotension (possibly reflecting enterohepatic circulation), and 1 case of SIR OD in a child caused tremor, raised liver enzymes, and gastroenteritis. Symptoms were observed in patients taking 1.5 and 2.4 times or greater than their usual dose (or the maximum licensed dose in patients not usually taking medication) for thiopurines and MMF, respectively. Decontamination measures were undertaken in 10 thiopurine ODs (9 activated charcoal, 1 gastric lavage). The OR for the development of symptoms after gastrointestinal decontamination in these ODs was 0.14 (95% CI, 0.01–1.5) compared with cases without decontamination. Charcoal was given primarily to children. The mean age of cases managed with charcoal was 8 (10) versus 30 (15) years for cases managed without ($P < 0.0001$).

Conclusion: Acute toxicity with thiopurines appears to only be significant with a prolonged exposure to high drug concentrations. MMF ODs seem to be well tolerated. Physicians should be aware, however, that patients who develop hypotension shortly after oral OD may relapse some hours later. It seems that SIR is highly toxic in young children even at modest degrees of overdose. Gastrointestinal decontamination with activated charcoal appeared to reduce symptom development after overdose of thiopurines. Thiopurine, MMF, and SIR OD patterns, outcomes, and management require continued study and transplant and poisons centers should be encouraged to actively seek follow-up data on the cases with which they are involved.

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Disclosure of Interest: None declared.

PP232—ACUTE TOXICITY PROFILE OF PIPAMPERONE IN OVERDOSE: A CONSECUTIVE CASE SERIES

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Introduction: Pipamperone (PIP) is a mild to moderately potent butyrophenone neuroleptic. Its mechanism of action is thought to be the antagonism of serotonin 5-HT2A and dopamine D4 receptors. The aim of the study was to analyze the clinical features of PIP poisoning because information on patterns of toxicity of this substance in overdose is scarce and limited to case reports.

Patients (or Materials) and Methods: Retrospective consecutive review of acute PIP monointoxications reported by physicians to the STIC between August 1974 and November 2012.

Results: Thirty-two adults, 3 teenagers, and 3 children could be included. Mean age of the group with adults and teenagers was 41 years (range, 14–90), and the ingested dose in this group ranged between 60 and 2400 mg (mean, 638). Five (14%) patients remained asymptomatic, 21 (60%) showed minor, 8 (22%) moderate, and 1 severe symptoms according to Poisoning Severity Score. There was no fatality. Minor symptoms occurred after ingestion of 60 to 1200 mg PIP (mean, 578), moderate symptoms after 160 to 2400 mg (mean, 950), and severe symptoms after 1200 mg. Signs and symptoms predominantly involved the central nervous and the cardiovascular systems (**Table**). An ECG was available in 20 patients, and 8 showed a prolonged QTc interval (455–505 ms) after ingestion of 400 to 1600 mg. A previously healthy woman developed a generalized seizure after ingestion of 1600 mg. Coma occurred after intake of 1200 mg in an adult, and 360 mg in a 4.5-year-old child. Two children (2- and 4-year-old) remained asymptomatic after ingestion of 10 and 80 mg, respectively.

Table. Symptoms/signs with classification according to severity (Poisoning Severity Score).

	Severity		
Symptom/Sign	Minor n (%)	Moderate n (%)	Severe n (%)
Somnolence	15 (39)		
Coma		2 (5.2)	2 (5.2)
Dystonic reactions	3 (7.9)	1 (2.6)	
Seizures		1 (2.6)	
Disorientation		1 (2.6)	
Agitation	1 (2.6)	1 (2.6)	
Tachycardia	6 (15.8)		
Hypotension	5 (13.1)	1 (2.6)	
QTc prolongation	8 (18.4)	1 (2.6)	
AV block I		1 (2.6)	
Xerostomia	3 (7.9)		
Gastrointestinal symptoms	3 (7.9)		
Urinary retention		1 (2.6)	

Conclusion: The severity of poisoning was related to the ingested PIP dose. Overdose was associated mostly with mild to moderate, neurologic and cardiovascular signs/symptoms. There was 1 acute single convulsive episode, which has not been previously described in literature. The remarkable frequency of QTc prolongation deserves particular attention, since a case of torsades de pointes has been previously described.[1] The relevance of this phenomenon could increase in the near future because a fixed combination of low-dose PIP and citalopram, which has also QT prolonging potential, is investigated in a Phase III study. Poisoned patients should be monitored for central nervous system depression, dysrhythmias and QTc prolongation.

Disclosure of Interest: None declared.

Reference

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PP233—CYP1A ACTIVITY AFTER CHRONIC EXPOSURE TO DIOXINS FROM A WASTE INCINERATOR

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Introduction: Inhabitants of Melun and vicinities have been exposed to a waste incinerator (1974–2002) emitting high concentrations of dioxins (226 ng I-TEQ/Nm3) up to 2000-times the maximal recommended values. This constitutes a case of unique and well-identified source of pollution. Dioxin (TCDD) is a well-described CYP1A inducer in vitro but in vivo studies are, however, rare. CYP1A has a role in the activation of some environmental and food-borne carcinogens and metabolic ratio of paraxanthine (17X) and caffeine (1,3,7-trimethylxanthine, 137X) is used as a measure of its activity. The aim of the study was to assess the exposed population through

an epidemiologic questionnaire and measure CYP1A activity as a putative biomarker of chronic exposure to dioxins.
Patients (or Materials) and Methods: Volunteers living in Melun area for at least 5 years (between 1974 and 2002) were included in the study. A questionnaire was designed to assess source and length of exposure, risk and confounding factors, and environmental sources of variability in CYP1A activity. The following items were systematically assessed: place of habitation, place and type of work, other sources of pollution, food questionnaire, smoking, caffeinated drinks and alcohol consumption, and medications (CYP1A inhibitors/inducers). They had a full medical history and physical examination with a special focus on skin lesions. CYP1A activity was assessed 2 hours after the ingestion of a drink containing caffeine through measurement of the ratio (MR) of 17X/137X by liquid chromatography mass spectrometry. CYP1A activities were compared with the phenotypes of healthy volunteers and to the acute dioxin intoxication of Victor Yushchenko described by Sorg et al. (Lancet 2009; 374:1179-85.)
Results: Forty-eight volunteers (age, 11–78) were included in the study (25 men, 23 women). A high frequency of dysthyroidism and cancer was noticed in the population. Eleven had a history of thyroid disease (23%) and 7 (14.5%) had a cancer. Skin lesions were described in 13 patients (27%). Mean CYP1A activity of the exposed population was comparable to the healthy volunteers (17X/137X MR of 0.250 SD 0.08 and 0.273 SD 0.12, respectively). However, 8 exposed volunteers (16%) had a 17X/137X MR above 0.4, indicating that CYP1A is induced (maximal 17X/137X MR of 0.649). CYP1A activity was not correlated with the presence of thyroid disease, cancer, or skin lesions. After acute dioxin intoxication, CYP1A was more strongly induced (maximal 17X/137X MR of 1.9). Induction was still persistent 2 years after acute exposure.
Conclusion: A high frequency of dysthyroidism (23%) and cancer (14.5%) was noticed in a sample population of Melun area exposed chronically to dioxins from a waste incinerator. CYP1A was induced in 16% of the population but without significant association with thyroid disease, cancer, or skin lesions. After acute dioxin intoxication, the magnitude of CYP1A induction was 3- to 6-fold higher.
Disclosure of Interest: None declared.

PP234—INTOXICATION WITH ATYPICAL ANTIPSYCHOTICS IN YOUNG CHILDREN: A MULTICENTRE ANALYSIS OF POISONS CENTRES DATA

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Introduction: Although accidental poisoning with atypical antipsychotics in children is 1 of the most important causes of morbidity after accidental ingestion of medications, the number of studies that have assessed the effects of acute exposure to this class of drugs is very limited. The aim of this study was to achieve a better characterization of the acute toxicity profile in young children of the common atypical antipsychotics clozapine, olanzapine, quetiapine, and risperidone.
Patients (or Materials) and Methods: Multicenter retrospective analysis of cases with atypical antipsychotics intoxication in children <6 years, reported by physicians to German, Austrian, and Swiss Poisons Centres between January 1, 2001, and December 31, 2009.
Results: A total of 106 cases of intoxication (31 clozapine, 29 olanzapine, 12 quetiapine, and 34 risperidone) were analyzed. Mean age was 2.6 years (range, 0.8–5.5). There were 52 (49%) females, 43 (40.6%) males, and in 11 (10.4%) cases gender was not reported. No correlation between age and number of ingested pills was found (Spearman correlation coefficient, 0.16). Concerning the number of ingested pills, there was no significant difference between males and females (Wilcoxon test, $P = 0.39$). Overall toxicity was rated as severe in 2 (1.9%), moderate in 28 (26.4%), and minor in 47 (44.3%) cases according to the Poisoning Severity Score. Twenty-eight (26.4%) cases were asymptomatic. No fatalities were recorded. Neurological and cardiovascular symptoms were predominating. Minor reduction in vigilance (Glasgow Coma Scale score >9) (62.3%) was the most frequently reported symptom, followed by miosis (12.3%) and mild tachycardia (10.4%). Extrapyramidal motor symptoms were observed in 1 case (0.9%) after ingestion of 2 mg (0.1 mg/kg) of risperidone. Electrocardiography was performed in 32 (30.2%) children: 3 (2.8%) showed extrasystoles, and in 1 (0.9%) case a prolonged QTc interval (468 ms) was recorded after the ingestion of 150 mg (13.6 mg/kg) of quetiapine. For clozapine, the lowest dose causing objective symptoms or signs was 0.8 mg/kg, resulting in aggressiveness, ataxia, dysarthria, and somnolence; for olanzapine, 0.4 mg/kg resulting in ataxia and somnolence; for quetiapine, 3.1 mg/kg resulting in ataxia and somnolence; and for risperidone, 0.05 mg/kg resulting in somnolence and mild tachycardia. In most cases, surveillance and supportive care were sufficient to achieve a good outcome, and all children made a full recovery.
Conclusion: Most children poisoned with the atypical antipsychotics clozapine, olanzapine, quetiapine, and risperidone had a benign clinical course without sequelae. Extrapyramidal side effects were rare, and the only case reported was caused by risperidone. Symptomatic patients should be monitored for central nervous system depression, and an electrocardiogram should be obtained.
Disclosure of Interest: None declared.

PP237—EVALUATION OF THE EFFECT OF DIMETHOATE INTOXICATION ON MALE RAT REPRODUCTIVE PERFORMANCES

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Introduction: Oranophosphorus compounds are widely used in industry, agriculture, and for public health purposes. The aim of this work was to study the effect of dimethoate on fertility in adult male rats and the possible underlying mechanism of action.
Patients (or Materials) and Methods: The study was conducted on healthy, sexually mature male Wistar albino rats weighing between 250 and 300 g. Animals were assigned randomly into 4 groups, each of 6 rats as follows: Group 1, control, orally administered with 1 mL of corn oil. Groups 2, 3, and 4 received dimethoate at a dose equivalent to 7, 10.5, and 21 mg/kg body weight, respectively. Commercial formulation of dimethoate was used. Radioimmunoassay (RIA) kits for determination of testosterone, lutenizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin hormone. For total cholesterol determination, available kit was used. Fertility test: Each male was allowed to undergo mating with 2 females (3–4 months old) of proven fertility during the last 10 days of the experiment. Serum and organ collections for determination of acetylcholinesterase activity and for histopathologic evaluations using light and electron microscopic study.