



PRESIDENZA DEL CONSIGLIO DEI MINISTRI
Dipartimento Politiche Antidroga



SISTEMA NAZIONALE DI ALLERTA PRECOCE
NATIONAL EARLY WARNING SYSTEM - N.E.W.S.



In collaborazione con

R.I.S. - Arma dei Carabinieri

New Drugs 2013

Pavia, 7 ottobre 2013

UPDATE SULLE NUOVE SOSTANZE PSICOATTIVE

Aspetti clinico-tossicologici delle Nuove Sostanze Psicoattive - NSP

Carlo Locatelli

National Early Warning System
Centro Antiveleni di Pavia – Centro Nazionale di Informazione Tossicologica
IRCCS Fondazione Maugeri, Pavia



Istituto Superiore di Sanità
Dipartimento del Farmaco

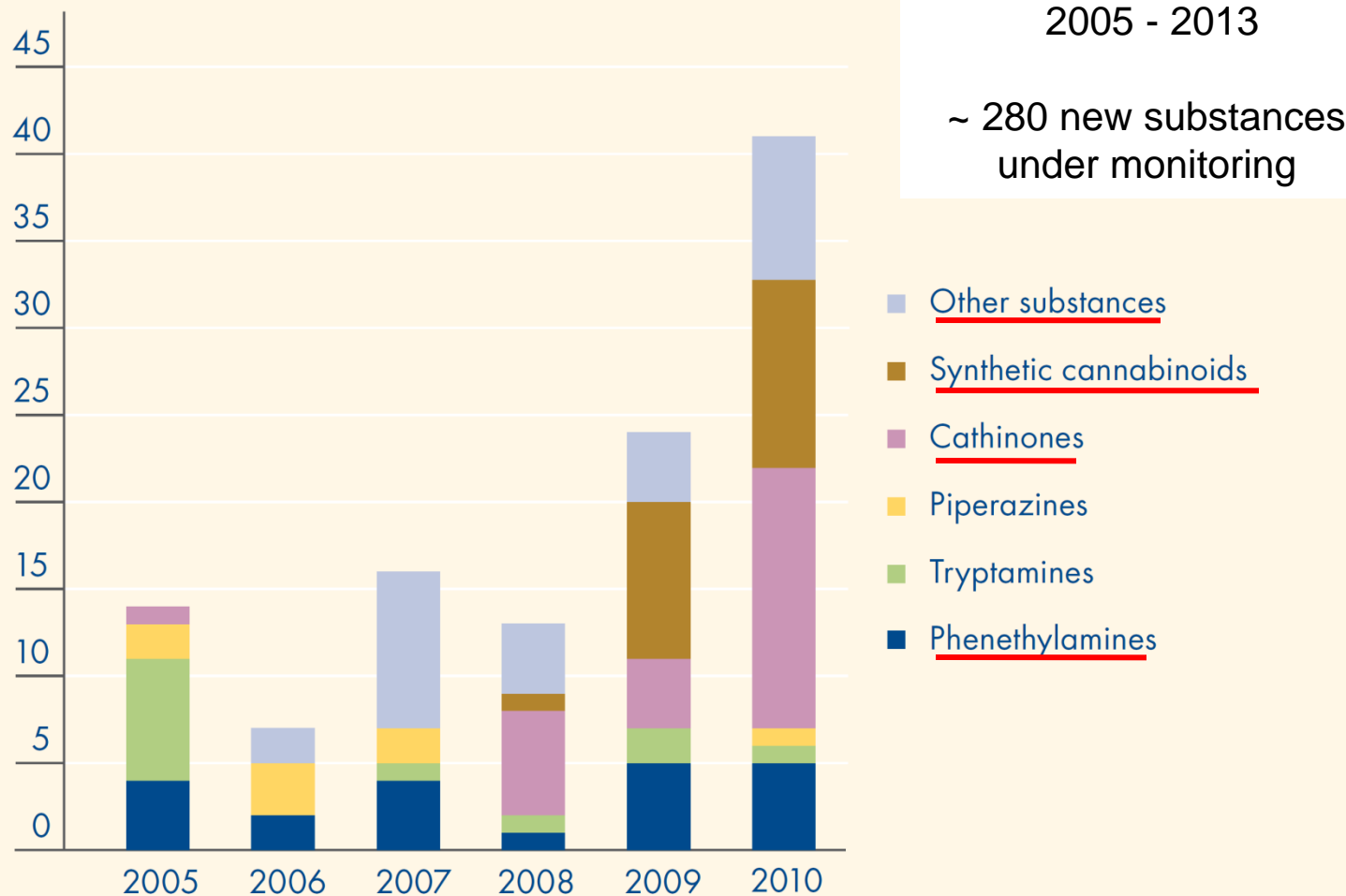


Regione del Veneto - Azienda ULSS 20
Dipartimento delle Dipendenze



IRCCS - Fondazione S. Maugeri
Centro Antiveleni Pavia

New psychoactive substances reported in EU



rilevanza NSP

- dati epidemiologici
 - EMCDDA
 - NEWS
 -
- sequestri / identificazione analitica
- salute → effetti clinici
 - intossicazioni acute / croniche / decessi
 - dipendenza / tolleranza / astinenza
 - conseguenze a breve / medio / lungo termine

rilevanza NSP

letteratura scientifica

anni	Synthetic cannabinoid(s)	Synthetic cathinon(s)	Benzofury - APB	Methoxetamine
1969-2003	158	56	-	-
2004-2009	204	31	-	-
2010	51	17	-	-
2011	74	24	-	1
2012	107	51	-	11
2013 (settembre)	32	14	1	6
Tot uomo (preclinico)	594 (739)	180 (244)	1 (1)	18 (7)

62.000
evenextraospedalieri
nel corso del 2009
ti

11,5%

**Pazienti soccorsi con ipotesi
diagnostica psichiatrica e
alterazioni comportamentali da
abuso di sostanze**

■ **22% con ipotesi
diagnostica
psichiatrica**

■ **78% alterazioni
comportamentali
da abuso di
sostanze**

**45% abuso
di alcool**

**55% abuso
altre sostanze non
Medicamentose**
(tra cui THC, cocaina,
oppiacei e derivati,
droghe sintetiche)

*Emergenza comportamentale e psichiatrica:
L'intervento del SSUEm 118 di Como*

Quadri clinici in pronto soccorso / DEA / TI

- intossicazione / overdose
 - eroina
 - sindrome simpaticomimetica / eccitatoria
 - paziente agitato
 - paziente allucinato
 - paziente con **quadro misto**
 - allucinazione + agitazione
 - allucinazione + depressione SNC
 - agitazione + depressione SNC
 -



Problematiche diagnostiche nel *setting* dell'urgenza

- assunzione in assenza di “dipendenza” nota
- anamnesi incompleta / errata
- uso “ricreazionale”, saltuario
- uso di sostanze stupefacenti o psicotrope di difficile (o al momento impossibile) identificazione
 - di sintesi
 - “smart” (“droghe furbe”, vegetali, naturali, etniche, etnobotaniche, naturali, “biodroghe”)
- effetti di sostanze da taglio o in “co-formulazione”
- co-assunzione di più sostanze d'abuso, farmaci, (benzodiazepine, SSRI, calcio-antagonisti, ...) e alcool
- traumi / incidenti e NSP
- interventi chirurgici in urgenza e NSP
-

Aspetti decisionali-gestionali

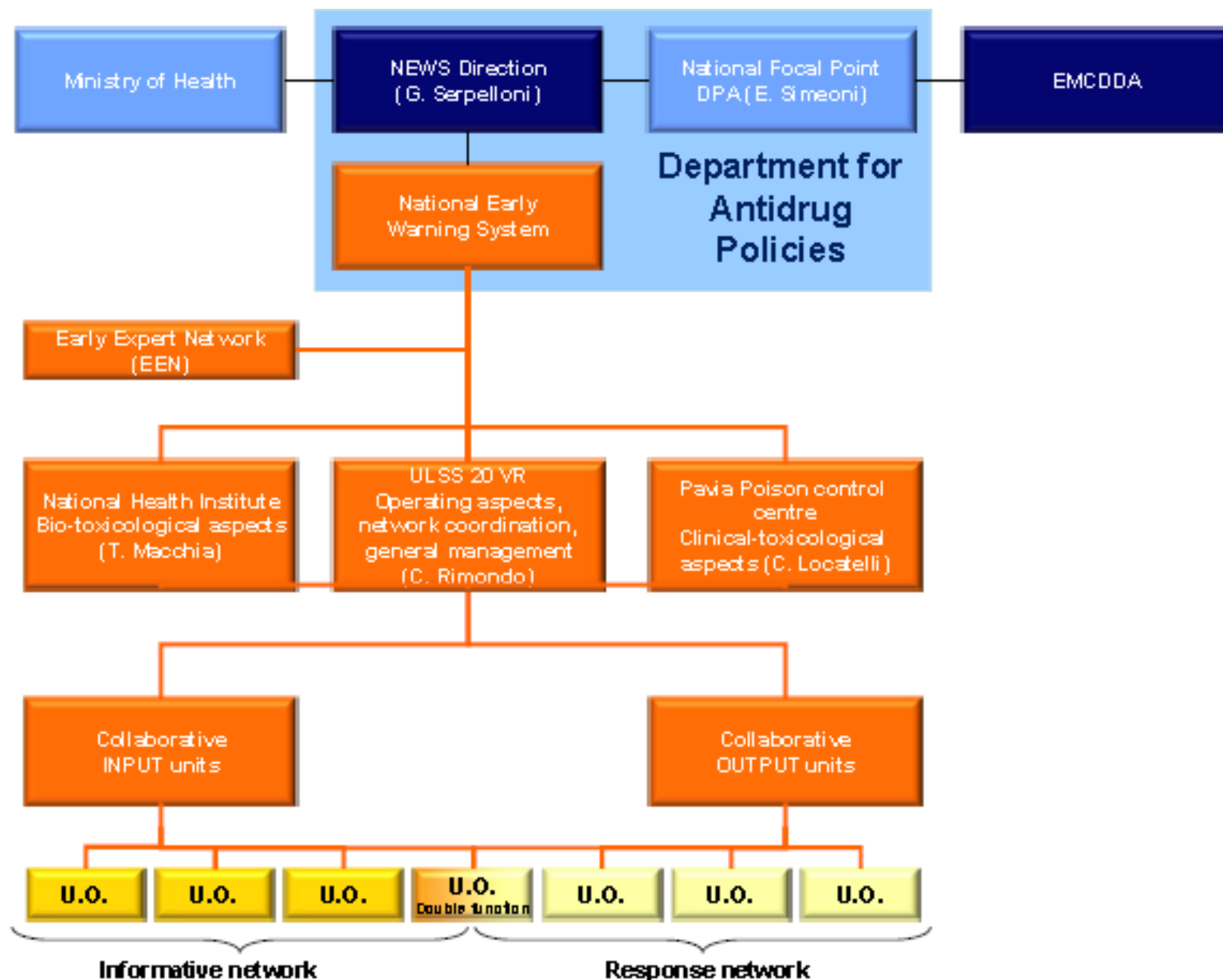
possibili criticità

- priorità gestionali nelle prime fasi
 - stabilizzazione, decontaminazione, impiego di farmaci, eventuale trattamento antidotico
- diagnosi tossicologica specifica (clinica e analitica)
- scelta del monitoraggio più indicato (clinico e/o strumentale)
- tipo di ricovero
 - osservazione breve
 - medicina d'urgenza
 - SPDC
 - altri reparti
- trasferibilità presso reparti a minore intensità di cura o dimissione

Inquadramento clinico

Valutazioni specifiche

- insufficiente/assente caratterizzazione degli effetti tossici acuti e post-acuti o cronici (es. tipologia, gravità, durata) per molte delle NSP
- elevata frequenza di co-assunzione di sostanze d'abuso «misurabili» e di alcol (→ **diagnosi incomplete ed errate**)
- possibile somministrazione di sostanze incapacitanti per scopi illeciti (es. violenza sessuale)
- scarsa consapevolezza da parte del consumatore di ciò che assume



Attività dei Centri Antiveleni

- consulenza specialistica (tossicologica)
- trattamento dei pazienti con intossicazione
- documentazione
- prevenzione
- tossico- e farmaco-vigilanza
- antidoti
- formazione, aggiornamento e training
- tossicologia analitica
- ricerca tossicologica ed epidemiologica
-

Centro Antiveleni di Pavia

Centro Nazionale di Informazione Tossicologica

IRRCCS Fondazione Maugeri

- servizio (CAV di 2° livello) dedicato a
 - SSN (attività e funzioni previste dall'Accordo Stato-Regioni 2008)
 - Amministrazioni dello Stato
 1. Sostanze d'abuso – [NEWS aspetti clinici](#) (Dipartimento Politiche Antidroga - Presidenza del Consiglio dei Ministri)
 2. Emergenze chimiche (Dipartimento Protezione Civile - Presidenza del Consiglio dei Ministri)
 3. NBCR (Difesa civile – Ministero della Salute)
- Strutturazione/organizzazione per emergenze e problematiche tossicologiche maggiori, ricerca
 - disponibilità analitico-tossicologiche in urgenza (attraverso laboratori di riferimento nazionale) per la diagnosi di intossicazioni / emergenze chimiche
 - personale specializzato / specificamente addestrato

Centro Antiveneni di Pavia – Centro Nazionale di Informazione Tossicologica

Personale che partecipa alle attività del NEWS

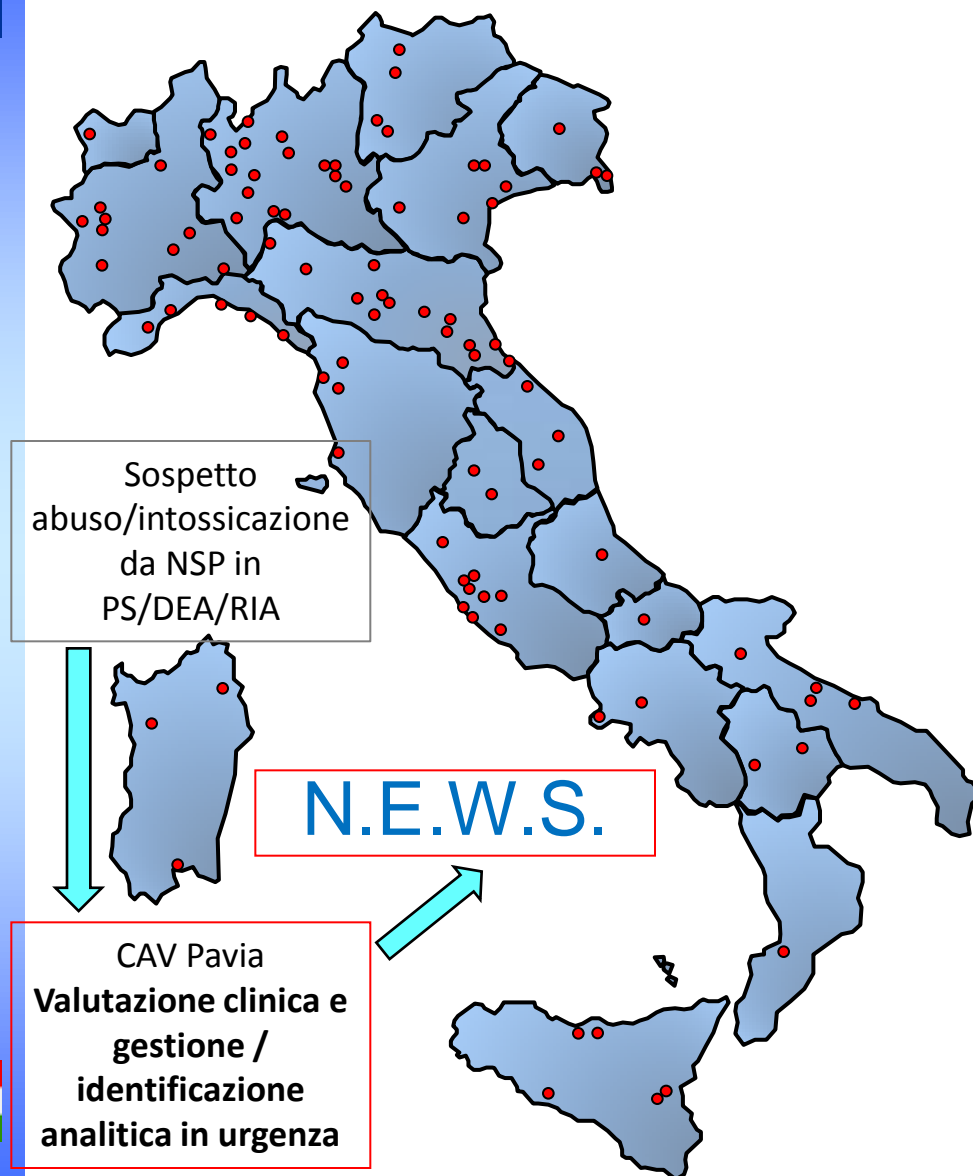
- medici → n. 7 / 9
 - 24/24, 7/7 front-office → diagnosi e trattamento (WHO, 1997)
 - Identificazione/selezione dei casi atipici/sentinella
- farmacisti → n. 3
- tecnici informatici: n. 1
- amministrativo: n. 1
- Laboratorio di tossicologia analitica di 1° livello (+ attività di ricerca)
 - biologi: n. 2
 - tecnici di laboratorio: 2
- Laboratorio di tossicologia clinica-analitica di 2° livello (convenzionato, IRCCS Policlinico San Matteo, Pavia - attività in urgenza + ricerca)
 - biologi: n. 5

Centro Antiveneni di Pavia – Centro Nazionale di Informazione Tossicologica organizzazione, strutture e procedure per le attività del NEWS

- data-base interno dei casi
- attività clinica dedicata
 - diagnosi / trattamento
 - → follow-up completo dei casi
- collezione di campioni biologici
 - gestione inter-ospedaliera
 - trasporto
 - in urgenza per casi gravi (118, altro)
 - dilazionato 1-3 gg (corriere)
 - stoccaggio e trasferimento ai LabTox
- laboratori → procedure analitiche / attività



Network dei DEA/PS (n. 144) e CAV Pavia



Identificazione, raccolta e valutazione delle intossicazioni da NSP a livello nazionale

- variazione nel pattern dei consumi
 - nuove sostanze coinvolte
 - Incidenza degli avvelenamenti
 - casi sentinella
 - quadri clinici di presentazione (identificazione di «sindromi» tossiche)
 - percorsi diagnostico-terapeutici
 - nuove necessità analitiche utili nel setting dell'urgenza
 - conseguenze post-acute
 - individuazione precoce di fenomeni potenzialmente pericolosi per la salute pubblica → NEWS → allerte
 -
- vantaggi
 - osservatorio nazionale
 - procedure standardizzate
 - un sistema, un metodo

Selezione dei pazienti nei servizi d'urgenza

criteri di inclusione

- soggetti noti/non noti come dipendenti/abusatori
- soggetti che riferiscono uso “ricreazionale” (frequente/occasionale) di una/alcune sostanze nuove / non note / sconosciute (sintetiche, naturali) o di “prodotti”
- soggetti che riportano uso di sostanze al momento non identificabili in PS (indipendentemente dalla positività/ negatività dei test per sostanze comuni)
- effetti clinici gravi dovuti a
 - co-assunzione di sostanze nuove e/o classiche
 - nuove sostanze da taglio

Selezione dei pazienti nei servizi d'urgenza

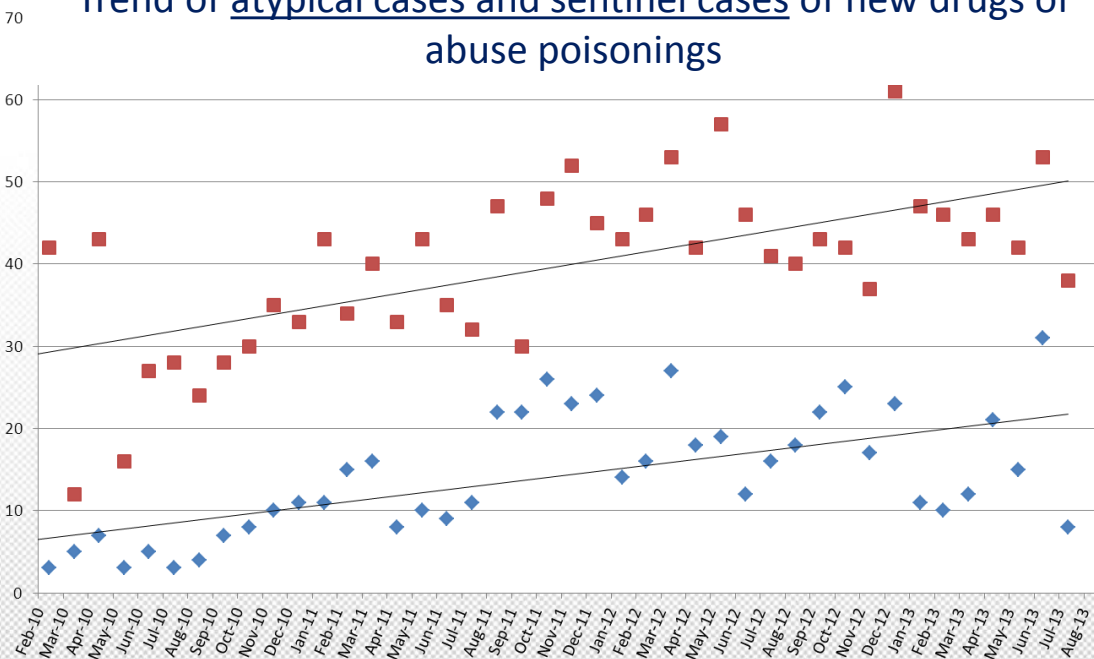
criteri di inclusione → quadro clinico

- casi “atipici”
 - uso **sospetto** di nuove sostanze
 - presentazione clinica **non tipica/inusuale**
- casi “sentinella”
 - uso **accertato** di nuove sostanze d'abuso, o
 - **effetti clinici che non correlano con le sostanze riferite e/o con il test rapido urinario** per le sostanze classiche*, o
 - **effetti clinici gravi molto probabilmente correlati a sostanze nuove o ancora non note** (stimolanti / eccitanti / allucinogeni), anche se non riferiti all'anamnesi
- *sostanze “classiche”
 - cocaina, oppioidi (eroina, metadone), cannabis, amfetamine / metamfetamine

Specialist consultation → cases of poisoning by substances of abuse
(Pavia PCC activity from February 2010 to August 2013)
 $n = 5593$

Ethanol abuse + body-packers
(stuffers) cases

Trend of atypical cases and sentinel cases of new drugs of abuse poisonings



“atypical” cases
 $n = 1723$

“sentinel” cases
 $n = 604 / 1723 (35\%)$

NSP analizzabili in urgenza nei Lab-Tox di Pavia

Screening 1 - CS

1. JWH-200
2. JWH-073
3. JWH-302
4. JWH-250
5. JWH-007
6. JWH-081
7. JWH-098
8. JWH-398
9. JWH-147
10. JWH-016
11. JWH-018
12. JWH-307
13. JWH-122
14. JWH-019
15. AM-2233
16. AM-2201
17. AM-694
18. MAM-2201
19. WIN-55212
20. WIN-48,098
21. RCS4
22. RCS8

Screening 2

1. ketamine
2. metoxyetamine
3. atropine
4. scopolamine
5. mephedrone
6. butylone
7. dimethylcathinone
8. dimethylmetcathinone
9. bufedrone
10. etcathinone
11. 4-fluormetcathinone
12. pentedrone
13. metedrone
14. etilone
15. pentilone
16. 1-naphyrone

17. MDPV
18. 4-MEC
19. 5-APB/6-APB
20. dimethyltriptamine
21. 2-C-I
22. 2-C-T7
23. 2-C-B
24. DOB

Screening 3

1. 4-fluoroamhetamine
2. MDAI
3. PMMA-PMA

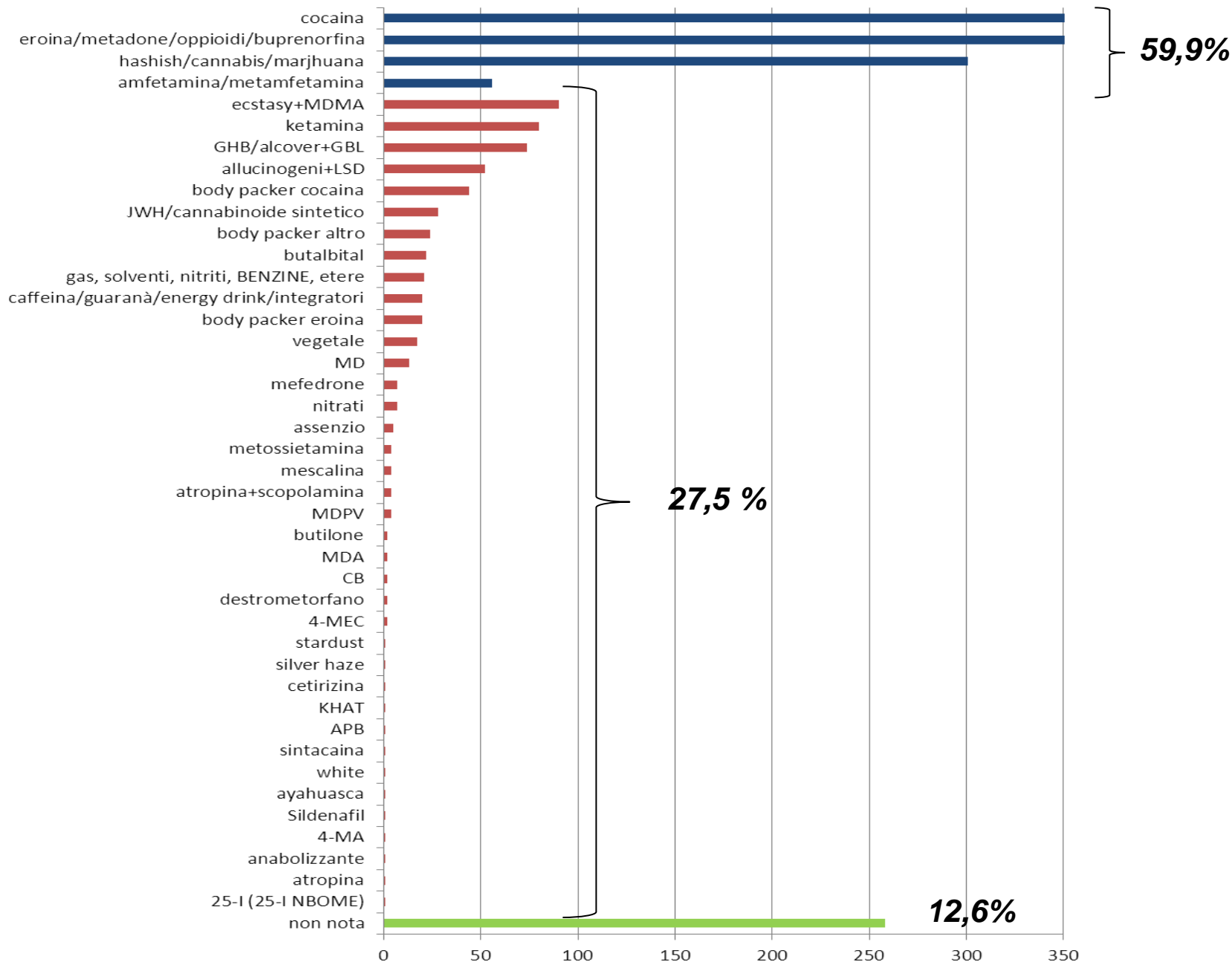
Screening 4

1. eroina/morfina
2. 6-MAM
3. cocaina
4. THC
5. amfetamine
6. MDMA
7. etanolo

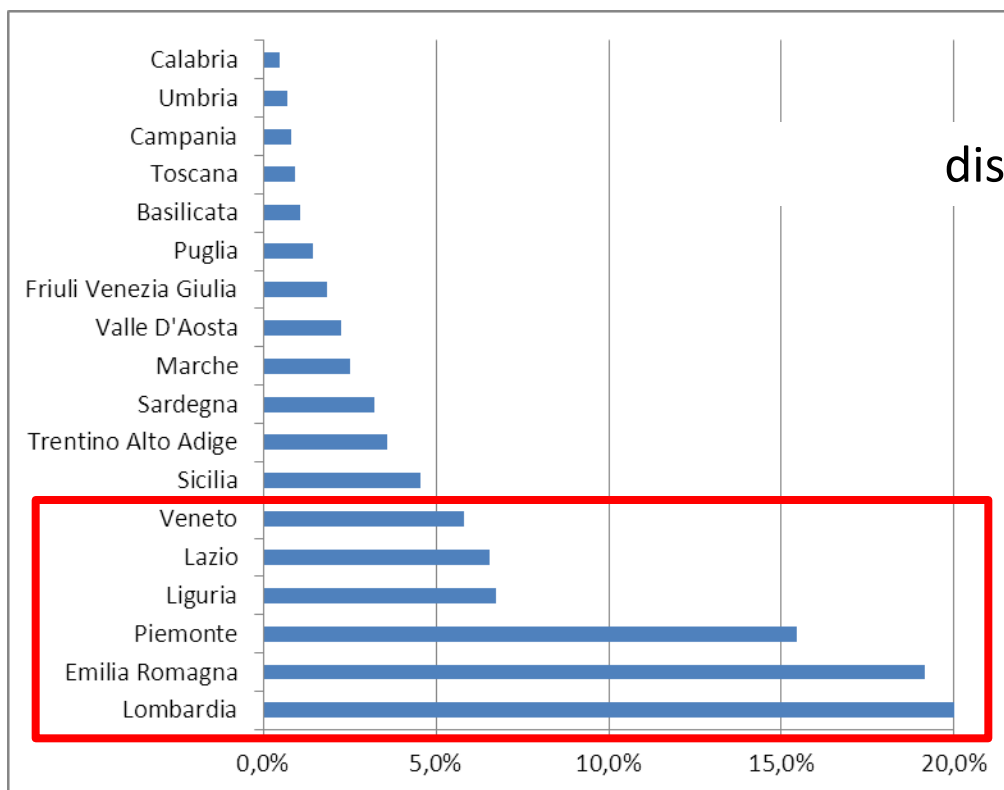
Screening 5

1. .. altro, su richiesta
2.

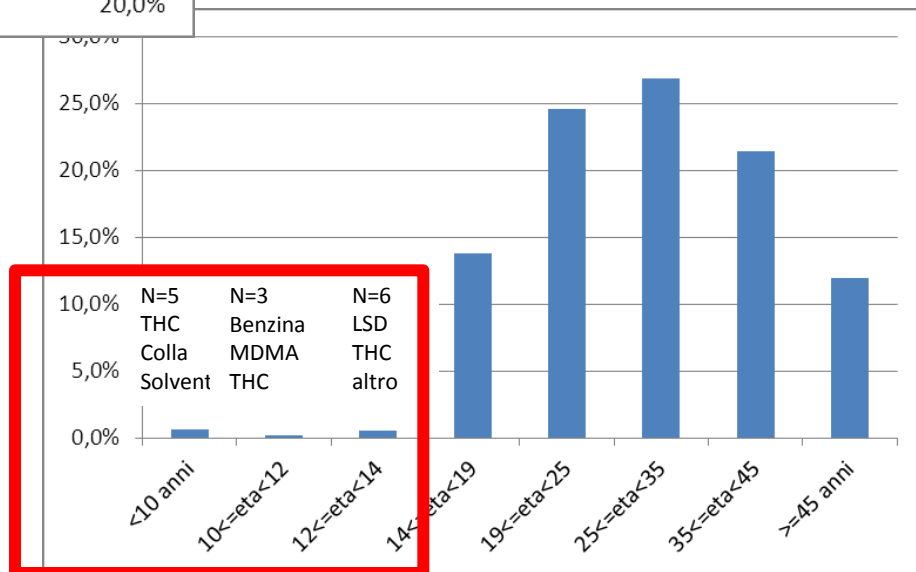
1723 casi "atipici" di intossicazione → sostanze identificate



Risultati: 1723 casi atipici di intossicazione da sostanze d'abuso



distribuzione per età



“sentinel” cases
n = 604

Analytical test not achieved: n = 56 (~ 9 %)

- samples collection
- sample preservation
- sample consignment

1st and 2nd level toxicological testing
n = 548 (sample from 186 hospitals of 161 cities)
NON emergency transportation (express courier) n = 450 (82,1%)

negative analytical tests = 171 (31%)

- really negative
- unavailability of the standard
- collection time (late)
- urine / blood
-

Positive analytical tests for NPSs
n = 375 → 68%



“new” hallucinogenic/stimulants/psychoactive drugs (NPSs) analytical confirmation in 604 «sentinel» cases

most frequent

- synthetic cannabinoids
- synthetic cathinones
- ketamine → synthetic ketamines (e.g. metoxyetamine)
- caffeine (+ cocaine and/or heroin)
- GHB / GBL
- anticholinergic agents (seeds, atropine, scopolamine)
- amphetamines-type substances (PMA/PMMA, 4-FA, ...)

less frequent

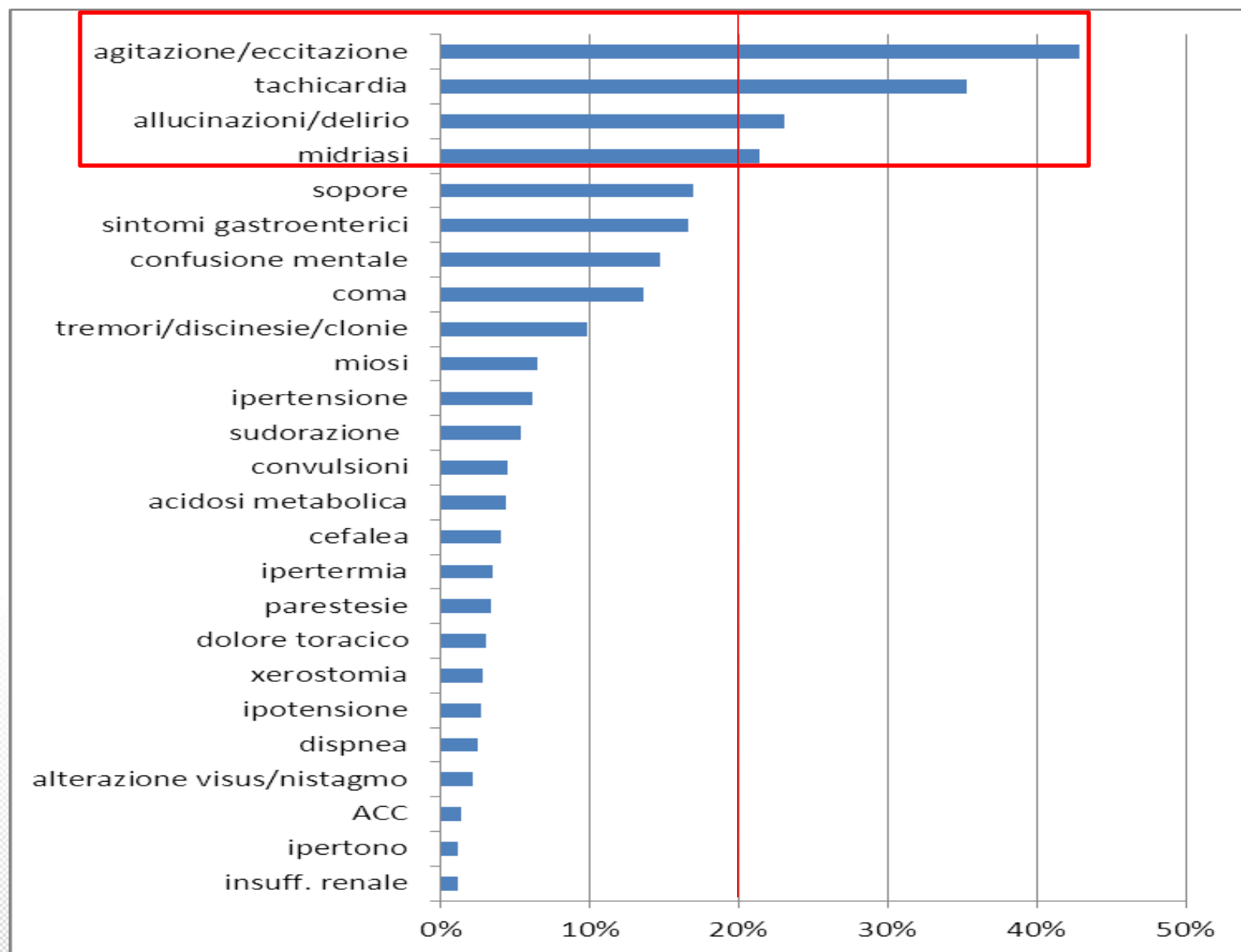
- myristic acid (nutmeg)
- ergine
 - *Rivea corymbosa* (seeds)
 - *Argyreia nervosa* (Hawaiian Baby Woodrose seeds)
 - *Ipomea violacea* (Morning glory)
- ayahuasca (dimethyltryptamine + harmine)
- benzofurans (APB isomers)
- 2C-E
- 2-CB
- 5-IT
- performing agents
- anorectic agents (e.g. sybutramine)
- bupropion
-

Risultati

Manifestazioni cliniche dei casi «sentinella» (n= 604) in PS



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Dipartimento Politiche Antidroga

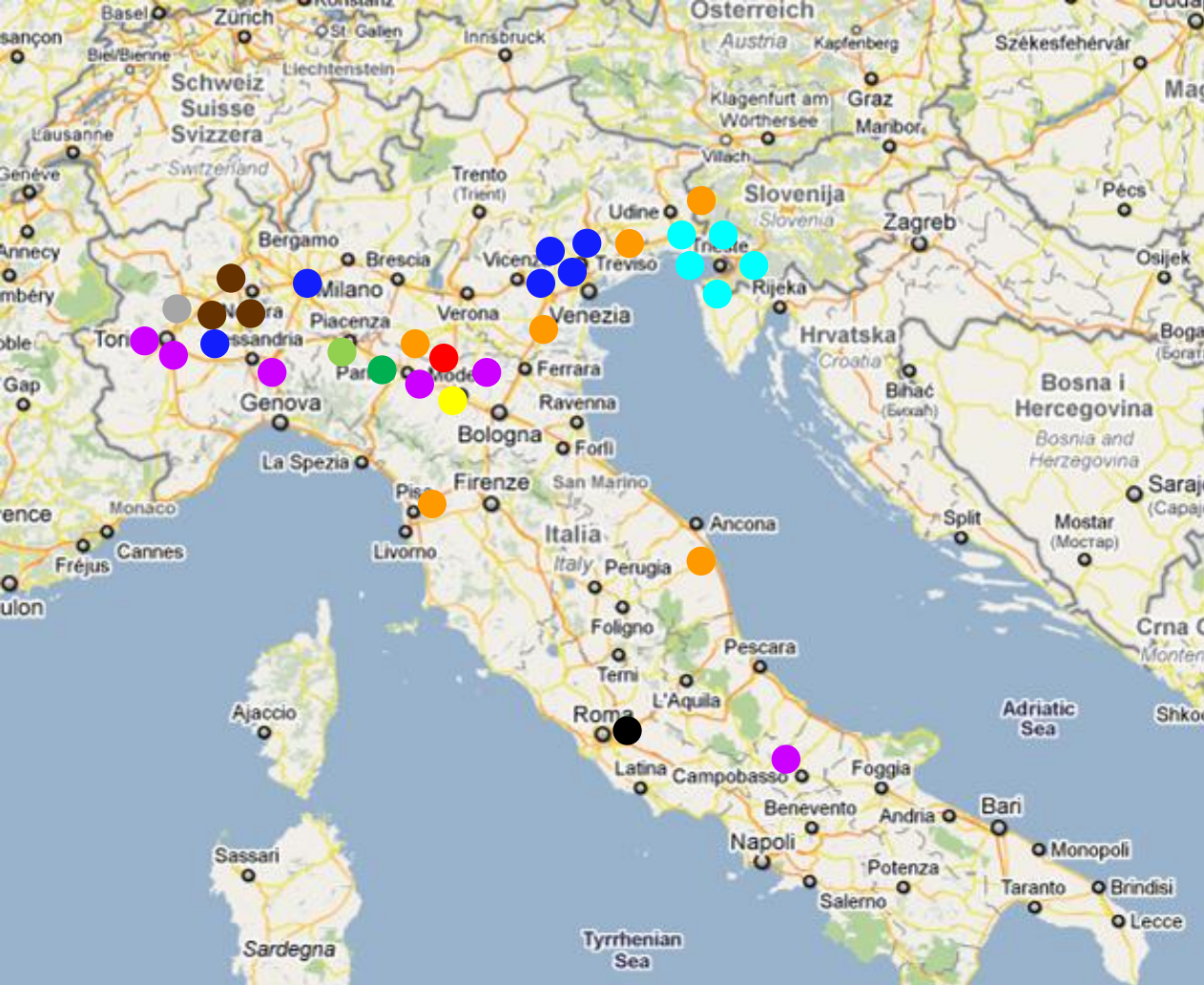


Synthetic cannabinoids clinical and/or lab-confirmed cases (Jan 2010- 29 Feb 2012)

33 cases

PRODUCT'S NAME

- 6 n-Joy (JWH-018)
- 1 Spice
- 3 Forest Green (JWH-122; JWH-250)
- 6 Jungle Mystic Incense (JWH-122)
- 6 Bonzai (JWH-122; JWH-018)
- 1 Genie
- 1 Orange Oxana
- 1 Amnesia
- 1 Atomic bomb (JWH-018)
- 1 Ocean Burst Red (JWH-122; JWH-018; JWH-073)
- 6 Generic herbal blend (JWH-122; JWH-018; JWH-073)



Age 14-55 years (23,33 ± 9,83)

- ✓ 14-21 years 22/33 66,6%
- ✓ 22-35 years 8/33 24,4%
- ✓ 36-55 years 3/33 9%

Source: Italian National Early Warning System



Trade name	Cannabinoids	Controlled subst	Trade name	Cannabinoids	Controlled subst
Genie	JWH-018	YES	Ketama Gold	JWH-250	NO
N-Joy	JWH-018	YES	Jungle Mystic Incense	JWH-122	NO
Spice Artic Synergy	JWH-018 JWH-073	YES	Jamaican Spirit	JWH-250	NO
Amazonas	JWH-250	NO	Start of Fire	JWH-250	NO
Orange Iilia	JWH-018 JWH-073	YES	<u>Bonzai</u>	JWH-250	NO
Orange Oxana	JWH-073 delta-9-THC	YES	<u>Bonzai Citrus</u>	JWH-018	YES
Jamaican Gold	JWH-018	YES	Blaze	JWH-018	YES
Jamaican Spirit	JWH-250 JWH-081	NO	Smoke	JWH-018	YES
Jamaican Spirit	JWH-250	NO	Blaze	JWH-018	YES
Mojo	JWH-018	YES	<u>Bonzai</u>	JWH-018	YES
Infinity	JWH-073	YES	<u>Bonzai Citrus</u>	JWH-081	NO
<u>Bonzai</u>	JWH-018	YES	Creme Supreme Incense	JWH-250	NO
Sencation	JWH-073 metil derivato	NO	Gejnie	JWH-018	YES
<u>Bonzai Citrus</u>	JWH-081	NO	Jamaica Spirit	JWH-081 JWH-250	NO
Afghan Incense	JWH-018	NO	King B	JWH-073 JWH-073 metil derivato	YES NO
<u>Bonzai Winter Boost</u>	JWH-250	NO	Original Diamond	JWH-073	YES
New Jamaican Gold	JWH-081	NO	Original Diamond Spirit	JWH-073	YES
Blaze	JWH-081	NO	Spice Artic Synergy	JWH-018 CP 47,497 (C8)	YES NO
Blaze	JWH-250	NO	Spice Diamond	CP 47,497 (C8)	NO
Jamaican Spirit	JWH-200+JWH-081	NO	Spice Diamond Spirit	JWH-018	YES
Forest Green	JWH-250+tracce di JWH-122	NO	Spice Gold	CP 47,497 (C8)	NO
Forest Green	JWH-122	NO	Spice Tropical Synergy	JWH-018 CP 47,497 (C8)	YES NO
Intensive Shot	JWH-250	NO	Yucatan Fire	JWH-018	YES



JWH-210; JWH-022; AM-2201

EWS 211/12, 03/02/2012



Trade names of herbal blends reported to the National Early Warning System and synthetic cannabinoids identified. Source: National Early Warning System, 2010.



M, 16 non-competitive sporting activities

ED: chest pain (lasting 3 days)

EKG ST elevation (inferior-lateral) – TN 3 (n.v. <0.4 ng/ml)

normal echocardiography

24 hrs later: clinical and EKG worsening; increase of TN to 25
coronary angiography : normal

Assumption of K2 → 24 hrs before the onset of symptoms

Marijuana → 3 weeks before



M, 16

ED: chest pain (lasting 7 days): heart “discomfort”, 30 minutes episodes

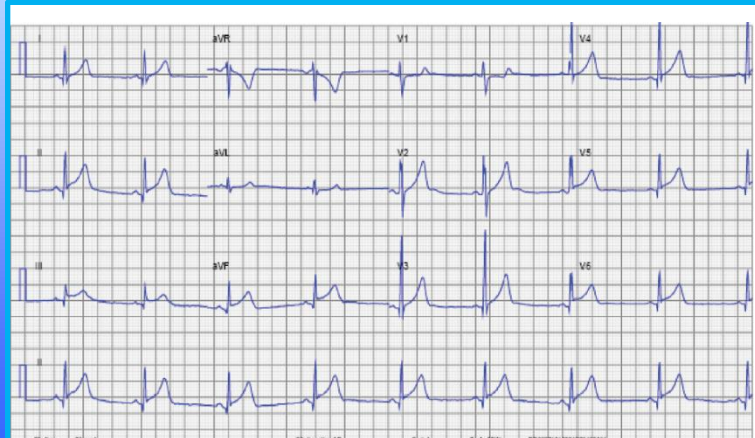
EKG ST elevation (inferior-lateral) – TN 11.6

Normal echocardiography

coronary angiography : normal

Assumption of K2 → 3 days before the onset of symptoms

Marijuana → 2 weeks before



M, 16

ED: chest pain (lasting 3 days): retrosternal, episodic (1-2 hrs / episode)

EKG: ST elevation (inferior-lateral) – TN 7

normal echocardiography

24 hrs later: worsening of EKG and increase of TN to 12

Assumption K2 → 7 days before the onset of symptoms

Negativity (urine) for JWH-018 e -073

Letters to the Editor

Psychiatric Sequelae of Spice, K2, and Synthetic Cannabinoid Receptor Agonists

TO THE EDITOR: Spice and K2 are among the plethora of herbal smoking blends available at smoke shops and via the internet. These otherwise inert herbal mixes are adulterated with synthetic cannabinoid receptor agonists, which are responsible for their psychoactive effects. Users may manifest a variety of neuropsychiatric symptoms.¹ Here, we describe the case of a patient using these products who presented with symptoms of psychosis.

Mr. A was a 20-year-old honors college student who presented to the emergency department with severe anxiety and paranoia. Work-up was negative for any acute medical problem and urine toxicology screening was negative. Psychiatric consultation was requested to evaluate for new onset psychosis.

Examination revealed a healthy appearing man who was anxious, tachycardic, and diaphoretic, with halting speech and avoidant eye contact. He described a gradual increase in anxiety over the previous 6 months, acutely worse over the last 2 weeks with development of paranoia and both auditory and visual hallucinations. He noted that this acute exacerbation of his symptoms coincided with his new daily habit of smoking marijuana (that had started 3 weeks prior to his Emergency Department presentation), which he had hoped would assuage his anxiety, but Δ^9 -tetrahydrocannabinol (THC) was not detected in his urine. On further questioning, he clarified that he had actually

been smoking Spice purchased from a local smoke shop.

It was unclear if Mr. A was experiencing a drug-induced psychosis or exacerbation of a nascent primary psychosis. He declined voluntary psychiatric admission. He was counseled to stop smoking Spice; immediate outpatient psychiatric follow-up was arranged.

Synthetic cannabinoid receptor agonists, such as JWH-018 and HU-210, have become popular alternatives to marijuana since they can be obtained legally in many parts of the United States and via the internet (although a number of jurisdictions have recently passed legislation outlawing their sale).¹ JWH-018 (the active agent in Spice) is a potent agonist of cannabinoid receptor 1 (CB₁), whereas THC is postulated to only be a weak agonist.² While little information exists on the association between synthetic cannabinoids and psychosis, there are data to suggest that cannabis use is associated with the development or worsening of psychosis.³ Given similar receptor activity and possible greater potency, it is plausible that synthetic cannabinoids may also be associated with psychosis.

Unlike marijuana, synthetic cannabinoids are not detected by conventional urine drug tests,¹ thus clinicians should familiarize themselves with the names of these products available in their area and ask patients specifically about their use. Anecdotal reports of hypokalemia associated with the use of these substances may provide an objective diagnostic clue.¹ In this case, Mr. A admitted to using marijuana despite a negative urine drug screen, prompting a more detailed discussion about the type of "marijuana" he was

smoking. Unfortunately, other patients may not be quite so forthcoming.

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References

1. Vearrier D, Osterhoudt C: A teenage with agitation: higher than she should have climbed. *Pediatr Emerg Care* 2010; 26: 462–465
2. Atwood BK, Huffman J, Straiker A, et al: JWH018, a common constituent of 'spice' herbal blends, is a potent and efficacious cannabinoid CB1 receptor agonist. *Br J Pharmacol* 2010; 160:585–593
3. Every-Palmer S. Warning: Legal synthetic cannabinoid-receptor agonists such as JWH-018 may precipitate psychosis in vulnerable individuals. *Addiction* 2010; 105:1859–1860

Products containing synthetic cannabinoids and psychosis

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DOI: 10.1177/0004867411433974

To the Editor

In June 2011, products containing synthetic cannabinoids were banned in Western Australia (Sydney Morning Herald, 2011; Daily Telegraph, 2011). Elsewhere, they are sold in tobacco

shops and are widely available (Sydney Morning Herald, 2011; Daily Telegraph, 2011). These products are most commonly known as 'kronic' or 'kronic black' in Western Sydney, but are also known as 'spice', 'K2', 'purple haze', 'kaos', 'dream', and 'voodoo'. Often these products are sold as mixtures of herbs and they are of particular relevance to Australian mining communities where they are not detected by urine drug testing (Sydney Morning Herald, 2011). There have been several case reports published internationally associating these products with psychosis (Muller et al., 2010; Johnson et al., 2011; Schneir et al., 2011; Simmons et al., 2011).

Although these products are reported to have been available in Australia for the last 2 years (Daily Telegraph, 2011), only in recent months has the problem of synthetic

cannabis products and psychosis been recognized in patients presenting to Nepean hospital, Sydney. In these cases, psychosis has been associated with more agitation than would be expected from cannabis alone. This has been reported in case reports (Muller et al., 2010; Schneir et al., 2011; Simmons et al., 2011) and has been hypothesized to be related to differences in its chemical structure and in particular the absence of cannabidiol (CBD) which in itself is presumed to have antipsychotic potency (Every-Palmer, 2011).

Synthetic cannabinoid products are associated with psychosis, more prominent agitation, and are not detected by routine drug testing. Clinicians should consider screening for synthetic cannabinoid use when interviewing patients presenting with psychosis or agitation.

Toxicological Findings of Synthetic Cannabinoids in Recreational Users

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²Division of Drug Research, Linköping University, Linköping, Sweden

In recent years, several synthetic cannabinoid compounds have become popular recreational drugs of abuse because of their psychoactive properties. This paper presents toxicological findings of synthetic cannabinoids in whole blood from some cases of severe intoxication including quantitative data from recreational users and a fatal intoxication. Samples were analyzed by liquid chromatography–tandem mass spectrometry in a scheduled multiple reaction mode after a basic liquid extraction. Twenty-nine synthetic cannabinoids were included in the method. In our data set of ~3000 cases, 28% were found positive for one or more synthetic cannabinoid(s). The most common finding was AM-2201. Most of the analytes had median concentrations of <0.5 ng/g in agreement with other published data. The emerging drugs MAM-2201 ($n = 151$) and UR-144 ($n = 181$) had mean (median) concentrations of 1.04 (0.37) and 1.26 (0.34), respectively. The toxicity of the synthetic cannabinoids seems to be worse than that of natural cannabis, probably owing to the higher potency and perhaps also to the presence of several different cannabinoids in the smoked incense and the difficulties of proper dosing. The acute toxic effects may under certain circumstances contribute to death.



Catinoni identificati in UE

(in blu quelli identificati in Italia)

- **MDPV, MDPK** (3,4-methilenediossiprovalerone)
- **α-PPP, PPP** (alfapirrolidinopropiofenone)
- **alfa-PVP** pirrolidinovalerofenone
- **Pirovalerone**
- **MPPP** (4'-metil-α-pirrolidinopropiofenone)
- **MPBP** (4'-metil-α-pirrolidinobutirrofenone)
- **MDPBP** (1-(3,4-Metilenediossifenil)-2-pirrolidinilbutan-1-one)
- **Propanone**
- **Pentanone**
- **Metilone**
- **Butilone, bk-MBDB**
- **dibutilone , bk-MMBDB**
(2-dimetilamino-1-(3,4-metilenediossifenil)butan-1-one)
- **bk-MDMA, metilone** (3,4-metilendiossimetcatinone)
- **N-Etilcatinone**
- **Mefedrone**
- **4-FMC** (Flefedrone)
- **Etcatinone e iso-Etcatinone**
- **Pentilone**
- **BMDB** (2-benzilamino-1-(3,4-metilenediossifenil)butan-1-one)
- **BMDP** (2-benzilamino-1-(3,4-metilenediossifenil)propan-1-one)
- **bk-MDDMA** 3,4 metilenediossimetanfetamina
- **bk-PMMA**, metedrone (4-Methoxymethcathinone)
- **3-FMC, 3-Fluorometcatinone**
- **4-MBC** (4-metil-N-benzilcatinone)
- **4-EMC** (4-etilmetcatinone)
- **4-BMC**, Brefedrone, 4-Bromometcatinone
- **3,4-DMMC** (3,4-dimetil-metcatinone)
- **Pentedrone** (α-metilamminovalerofenone)
- **iso-pentedrone**
- **4-MEC** (4-metiletcatinone)
- **β-etil-metcatinone** (2-metilamino-1-fenil-1-pentanone)
- **Bufedrone**
- **NEB** (N-etilbufedrone)
- **3,4-DMMC** (3,4-dimetilmetcatinone)
- **Nafirone** (1-naphthalen-2-yl-2-pyrrolidin-1-yl-pentan-1-one)
- **Iso-nafirone** (1-naftalen-1-il-2-pirrolidin-1-il-pentan-1-one)
- **4-metiletcatinone** (2-etilamino-1-(4-metilfenil)-1-propanone)

Catinoni identificati 2010-2012



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	2010	2011	2012	molecola	Italia	altro paese
1	√	√		Mefedrone	√	
2	√			Nafirone		Svezia
3	√			Isoetcatinone		Irlanda
4	√	√	√	4-MEC	√	Regno Unito
5	√	√	√	MDPV	√	
6	√	√	√	Butilone	√	Austria
7	√	√	√	Metilone	√	
8	√			MPBP		Bulgaria
9	√			Isomero Nafirone		Regno Unito
10	√			MPPP		Regno Unito
11	√			Pentilone		Regno Unito
12	√	√	√	β-etilmetcatinone (Pentedrone)	√	Austria
13	√			3,4-DMMC		Ungheria
14	√			MDPBP		Regno Unito
15	√			βk-MMBDB (dibutilone)		Finlandia
16		√		BMDB		Regno Unito
17		√		BMDP		Regno Unito
18		√	√	3-FMC	√	
19		√		4-FMC	√	
20		√	√	α-PVP	√	Francia
21		√		N-etilbufedrone (NEB)		Danimarca
22		√		4-BMC (Brefedrone)		Finlandia
23		√		Isopentedrone		Austria
24		√		Pirovalerone	√	
25		√	√	Etilcatinone	√	
26		√	√	Bufedrone	√	
27		√		4-EMC		Svezia
28		√		βk-MDDMA		Finlandia
29		√		4-Me-MABP (4-metilbufedrone)		Olanda
30			√	α-pirrolidino-butilrofenone		Finlandia
31			√	3-fluoroisometcatinone(3-FiMC)		Rep. Ceca
32			√	1-fenil-2(piperidin-1-il)-butan-1-one		Spagna
33			√	2,4,5-trimetilmetcatinone (TMMC)		Germania
34			√	MPHP		Svezia

Catinoni: casi di intossicazione acuta 2010-2012

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anno	Sesso, età	sostanza dichiarata	Esami Tossicologici (sangue=S e urine=U)	Altre positività e negatività agli esami tossicologici (sangue=S e urine=U)
2010	M, 36	GHB Mefedrone (fertilizzante)	non eseguiti	non eseguiti
2011	M, 20	3 capsule bianche	<u>Butilone e MDPV (U)</u>	<u>THC: positivo (U)</u> LSD, atropina, scopolamina, mefedrone: negativo (U)
2011	M, 18	cannabis	<u>4-MEC (U)</u>	Ketamina, atropina, scopolamina, mefedrone, levamisolo: negativi (U) cannabinoidi sintetici: negativi (S)
2011	M, 24	concime (droga sintetica)	<u>Butilone (U)</u>	Ketamina, atropina, scopolamina, mefedrone, levamisolo: negativi (U) cannabinoidi sintetici: negativi (S)
2012	M, 37	6-APB (Benzofuria)	4-MEC e 6-APB (prodotto) 4-MEC negativo (U e S)	<u>6-APB: positivo (S e U)</u> THC, cocaina, metadone, oppiacei, amfetamine, MDMA: negativo (U). Alcolemia: negativo
2012	M, 34	mefedrone	<u>4-MEC (U e S)</u>	Ketamina, atropina, scopolamina, levamisolo, mefedrone, butilone, metossietamina, APB (isomeri), 4-FA, MDAI: negativo (U)
2012	M, 25	Ketamina, ecstasy, cocaina, popper	<u>Mefedrone (U)</u> <u>pentedrone (U)</u>	<u>Ketamina/norketamina, levamisolo, cocaina, amfetamine, ecstasy in urina: positivi (U)</u> Atropina, scopolamina, butilone, 4-MEC, PMA, PMMA, metossietamina, APB (isomeri), 4-FA, MDAI: negativo (U)
2012	M, 38	MDMA, Energy, Crystal, mefre	<u>MDPV (U e S)</u>	Ketamina, atropina, scopolamina, levamisolo, mefedrone, butilone, 4-MEC, metossietamina, APB (isomeri), 4-FA, MDAI: negativo (U)

Clinical survey in the emergency setting for fentanyl (Jan 2007- Aug 2012)

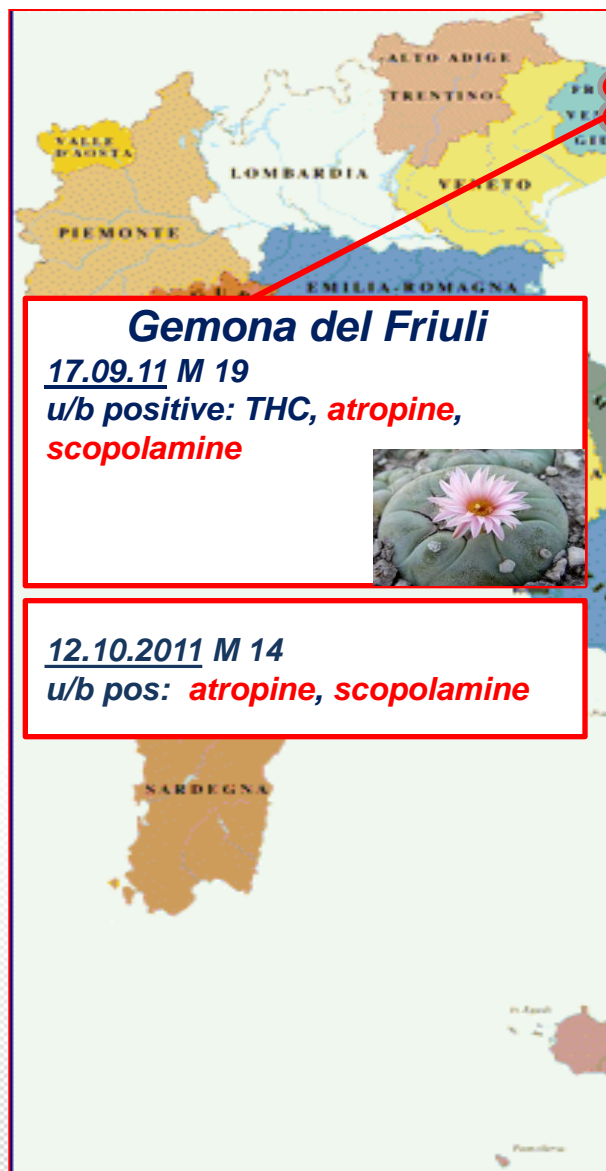
10 cases

- 6 “White” or “China white”
- 2 medications
- 2 medications (transdermal)

Age: 20-49 years

Male / female → 8/2

- young people
- geographical and temporal distribution
- symptomatology → a “toxidrome”
- antidotic treatment → physostigmine



Tolmezzo

25.09.11 M 19

u/b positive: THC, **atropine**,
scopolamine

25.09.11 M 16

u/b positive: THC, **atropine**,
scopolamine

Gemona del Friuli

17.09.11 M 19

u/b positive: THC, **atropine**,
scopolamine



12.10.2011 M 14

u/b pos: **atropine**, **scopolamine**

San Benedetto d Tronto

06.11.11 M 16

u/b positive: **atropine**,
scopolamine



11.11.2011 M 18

u/b positive: **atropine**,
scopolamine



21/02/2011
Prot. EWS 141/11

AD USO INTERNO DEI CENTRI COLLABORATIVI DEL N.E.W.S.

Alla c.a.
 Ministero della Salute
 Assessorati alla Sanità
 Assessorati alle Politiche Sociali
 Referenti regionali
 Servizi per la tossicodipendenza
 Comunità terapeutiche
 Pronto soccorso
 Centri Collaborativi del N.E.W.S.

oggetto: Pre-allerta "Registrato caso di intossicazione acuta a seguito di assunzione di eroina con elevate concentrazioni di caffeina"

A. Segnalazione ricevuta

Fonte della segnalazione: Laboratorio di Tossicologia Clinica Analitica, IRCCS Policlinico San Matteo di Pavia e Centro Antiveneni di Pavia, IRCCS Fondazione Salvatore Maugeri di Pavia

Data: 11 febbraio 2011

Tipic:

☐ osservazionale

☒ supportata da dati

☒ di laboratorio

☒ clinici

☐ anamnestici/comportamentali

☐ epidemiologici

Contenuto sintetico: Il Laboratorio di Tossicologia Clinica Analitica e il Centro Antiveneni di Pavia hanno segnalato un caso di intossicazione acuta legato all'assunzione di eroina contenente un'elevata percentuale di caffeina. Casi analoghi sono stati registrati negli ultimi mesi anche in altri Paesi europei.

Supervisione tecnico scientifica della presente "Informativa":
 T. Macchia – Istituto Superiore di Sanità, Dipartimento del Farmaco
 C. Locatelli – Fondazione "S. Maugeri", Centro Antiveneni di Pavia

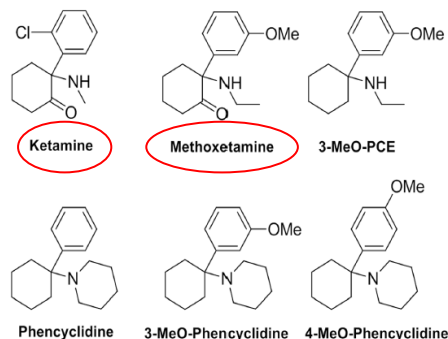


Cases requiring differential diagnosis for meningoccephalitis or septicemia

sex , age	CNS	body temp (°C)	other signs and symptoms	treatment	invasive tests for diagnosis	substances	Lab result*
M, 33	Severe psychomotor agitation, seizure,	39	Miosis, 200 BPM, metabolic acidosis (pH 7.26; lactate 14), rhabdomyolysis (62300 U/l), AST 1724, LDH 5035, renal impairment	fluids, urine alkalinisation, benzodiazepines, chlorpromazine	Cerebral CT scan	Cocaine, other (?)	Cocaine, levamisole
M, 30	confusion, severe psychomotor agitation	38	xerostomia, mydriasis, muscle rigidity, 140 BPM, rhabdomyolysis (3300 U/l)	fluids, benzodiazepines, orotracheal intubation	Cerebral CT scan	unknown	Atropine/ scopolamine
M, 40	confusion, severe psychomotor agitation	39.3	mydriasis, muscle rigidity, 140 BPM, metabolic acidosis, rhabdomyolysis (24000 U/l)	fluids, urine alkalinisation, benzodiazepines, orotracheal intubation, CRRT	Cerebral CT scan	Meth (ice)	amph, caffeine (product assumed)
F, 21	Coma, seizure, severe psychomotor agitation, respiratory failure	39.1	tachycardia, metabolic acidosis	fluids, urine alkalinisation, benzodiazepines, orotracheal intubation	Cerebral CT scan	unknown	THC (serum and urine)
M, 40	severe agitation, coma	39.2	mydriasis, profuse sweating, 167 BPM, diffuse clonus, rhabdomyolysis (2592 U/l)	Fluids , intravenous midazolam, propofol, ceftriaxone and acyclovir	cerebral-MRI and CT-scan, CSF analysis	Benzofury (APB, 4-MEC)	MDMA and amph (urine); APB-isomers

*lab analysis: JWH-200, JWH-073, JWH-302, JWH-250, JWH-007, JWH-081, JWH-098, JWH-398, JWH-147, JWH-016, JWH-018, JWH-307, JWH-122, JWH-019, AM-2233, AM-2201, AM-694, MAM-2201, WIN-55212, WIN-48,098, RCS4,RCS8 – ketamine, atropine/scopolamine, levamisole, mefedrone, butilone, dimetilcatinone, dimetilmecatinoe, bufedrone, etcatinone, 4-fluormecatinoe, Pentedrone, Metedrone, Etilone, Pentilone, 1-naphyrone, MDPV, MXE, 4-MEC, 5-APB/6-APB, dimetiltriptamina, 2-C-I, 2-C-T7, 2-C-B, DOB - 4-fluoroamfetamina, MDAI, PMMA-PMA.

Ketamine vs methoxetamine



Criteria	KET	MXE
Chemical name	2-(2-chlorophenyl)-2-(methylamino)cyclohexanone	2-(3-methoxyphenyl)-2-(amino)cyclohexanone
Chemical class	PCP derivative	PCP derivative
Molecular weight	237.73 g/mol	283.79 g/mol
Pharmacological class	Dissociative anesthetic	Dissociative anesthetic
Receptors	NMDA, σ , and μ	NMDA, σ , and μ
Routes of administration	IV, IM, intranasal, and oral	Intranasal, oral, sublingual, rectal, IM, and very rarely IV
Dosage	10–250 mg	<u>10–100 mg</u>
Onset of action	30 second–30 min	<u>30–90 min</u>
Duration of action	3 h 0 min 0 second	<u>5–7 h</u>
Desired effects	Depersonalization and out-of-the-body experiences, including near-death experiences; stimulation	<u>Euphoria, empathy, coziness, pleasant sensory experience, dissociation, derealization, vivid hallucinations, introspection, antidepressant, dissociation from body ("M-hole")</u>
Risk of re-dose	No	<u>Yes</u>
Tolerance	Yes	<u>Yes</u>
Dependence	Yes	<u>Yes</u>
Known adverse effects	Confusion, vivid dreams, hallucination, flashbacks, referential thinking, panic attack, agitation, cardiovascular issues, depression, dissociation, apnea	Confusion, dizziness, time distortion, aphasia, synesthesia, cardiovascular issues, acute cerebellar toxicity, and psychomotor agitation
Bladder toxicity	<u>Yes</u>	<u>Not confirmed</u>
Cerebellar toxicity	Not reported	<u>Anecdotaly reported</u>

MXE abuse: case series in Italy



12 MXE confirmed intoxications in 1 year

(Feb 2012 – Feb 2013)

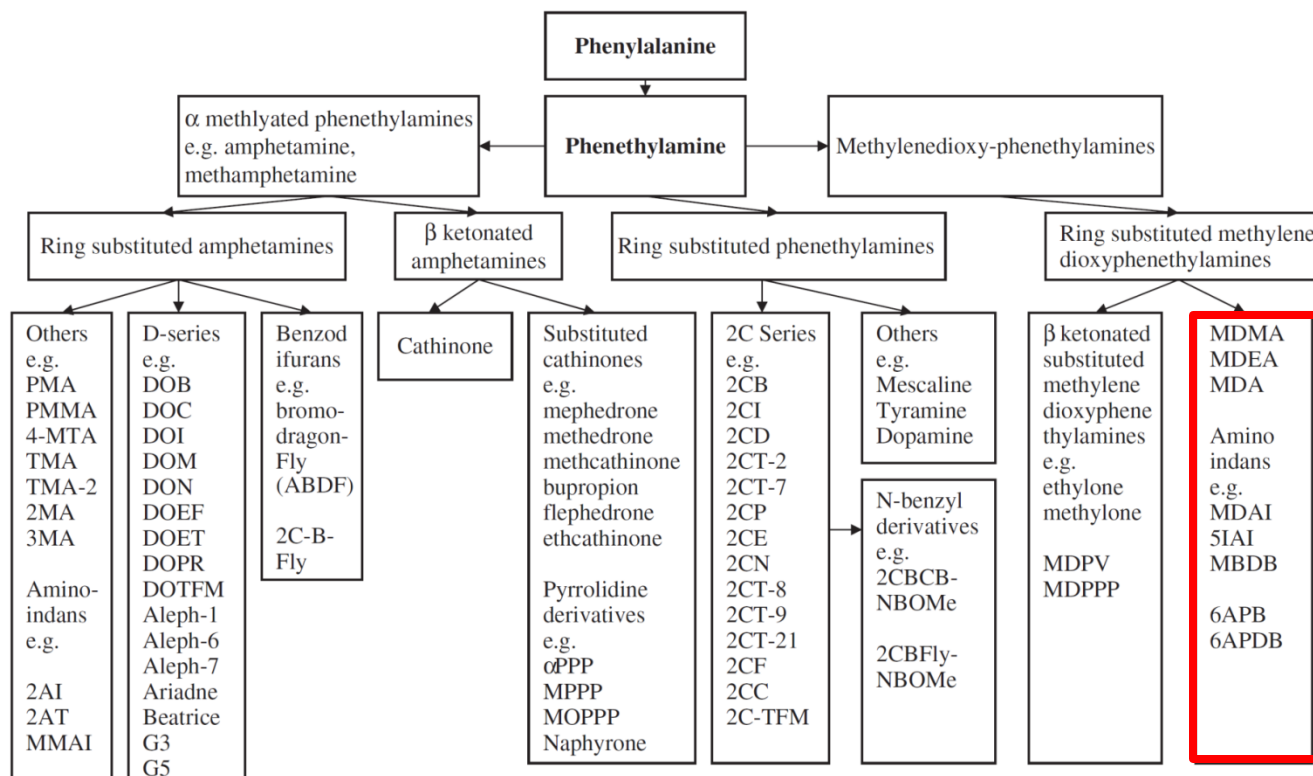


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Age, sex	Substances	Clinical manifestations	treatment	Lab results (positivity)
27, M	Dextromethorphan, mxe	<u>severe psychomotor agitation</u> , hallucinations confusion, tachycardia (120 BPM)	benzodiazepines, valproic acid, haloperidol	MXE (product) and biological samples(167 mcg/ml urine, 0,2 mcg/ml serum). Methorphan urine
17, M	MDMA, 1 blue pill and ketamine	<u>severe psychomotor agitation</u> , hallucinations, mydriasis	fluids and benzodiazepine	MXE (198 ng/ml serum e 9000 ng/ml urine), ketamine/nork, MDMA, MDA, amphetamine, THC (urine)
24, M	Unknown	<u>severe psychomotor agitation</u> , hallucinations, mydriasis, tachycardia (150 BPM)	benzodiazepine, betablocker (metoprolol) e calcium channel blockers (diltiazem)	MXE , APB-isomers , levamisole, methadone, benzoilecgonine, ecsatsy (urine); ethanol (2,7 g/L)
38, M	Unknown and ethanol	<u>severe psychomotor agitation</u> , aggressive, mydriasis, hypertension (150/90 mmHg)	fluids	MXE (167 ng/ml serum e 7400 ng/ml urine), APB-isomers (164 ng/ml), amphetamine and MDMA urine
23, M	Ethanol, unknown (red liquid contained in 3 vials)	confusion, drowsiness, rhabdomyolysis (CPK 1400 U/L)	symptomatic	MXE , levamisole, benzoilecgonine, THC e opiates (urine)
23, M	THC and ketamine	coma, dyspnoea, (Sat O ₂ 90%)	naloxone 0.2 mg, fluids	MXE , ketamine and norketamine (urine)
22, M	THC and ketamine	<u>severe psychomotor agitation and</u> hallucinations, dissociative state, mydriasis	symptomatic	MXE , ketamine/norketamine (urine)
16, F	Ethanol and unknown	<u>severe psychomotor agitation</u> , confusion, amnesia	G/E decontamination, fluids	MXE e THC (urine)
17, F	unknown	<u>severe psychomotor agitation</u> , confusion hallucination and amnesia, miosis,	G/E decontamination, fluids	MXE , THC, ketamine/norketamine (urine)
23, M	ethanol and ketamine	drowsiness, tachycardia, vertical nistagmus, SatO ₂ 93%	G/E decontamination, fluids	MXE , benzoilecgonine, levamisole (urine)
22, F	ethanol, ketamine, heroin	drowsiness, hypertension	G/E decontamination, fluids, naloxone	MXE , benzoilecgonine, levamisole (urine)
18, F	Ketamine and LSD	tremors, chest pain, myalgia	benzodiazepines, fluids	MXE (urine)

MXE assumption has never been declared in the history

Benzofurans



Hill et al., 2011

Common Name	Chemical Name	Chemical Structure
Butylone	1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one	
Dimethylcathinone	(RS)-2-methylamino-1-phenylpropan-1-one	
Ethcathinone	(RS)-2-ethylamino-1-phenylpropan-1-one	
Ethylone	(RS)-1-(1,3-benzodioxol-5-yl)-2-(ethylamino)propan-1-one	
3-Fluoromethcathinone	(RS)-1-(3-fluorophenyl)-2-methylamino)propan-1-one	
4-Fluoromethcathinone	(RS)-1-(4-fluorophenyl)-2-methylamino)propan-1-one	
Mephedrone	(RS)-2-methylamino-1-(4-methylphenyl)propan-1-one	
Methcathinone	α-methylamino-propiphenone	
Methedrone	(RS)-1-(4-methoxyphenyl)-2-(methylamino)propan-1-one	
Methylenedioxypropylverone (MDPV)	(RS)-1-(Benzodifur[1,3]dioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one	
Methylone	(±)-2-methylamino-1-(3,4-methylenedioxyphenyl)propan-1-one	
Pyrovalerone	(RS)-1-(4-methylphenyl)-2-(1-pyrrolidinyl)pentan-1-one	

Prosser et al.,
2011



Collaborative centres

- Dipartimento Politiche Antidroga – Presidenza del Consiglio dei Ministri
- *Tossicologia Forense - Università Cattolica del Sacro Cuore, Roma*
- *Centro Antiveleni - Centro Nazionale di Informazione Tossicologica, IRCCS Fondazione Maugeri e Università degli Studi, Pavia*
- 85 enrolled (...-June 2013)



GHB rape-drug

euphoria, disinhibition, anxiolysis,
enhanced sensuality, emotional
warmth, **short-term amnesia**

colorless, inodour



Triage urine

Sostanza

rilevabilità (giorni)

✓	oppioidi/morfina	2
✓	amfetamine	2
✓	cocaina (metaboliti)	2 - 5
✓	cannabinoidi/THC uso moderato	5
	uso elevato	10
	cronico	20
✓	metadone	3
✓	ecstasy	0,5 - 1
✓	benzodiazepine dose terapeutica	3
	dose sovraterapeutica	4 – 8
✓	ADT	3
✓	barbiturici	2

Problemi diagnostici

- Quadro clinico complesso, poco specifico, NON noto agli operatori dell'urgenza → ruolo CAV
- Sindromi / non sindromi
- anamnesi potenzialmente inaffidabile → scarsa consapevolezza della reale molecola assunta (spesso genericamente indicata come ecstasy o “pasta”)
- inattendibilità del triage urine e degli esami di laboratorio presenti nella routine ospedaliera
 - ✓ sostanze misurabili → vetuste
 - ✓ laboratorio capacità specifiche per sostanze poco comuni → h 24 / risposta rapida in urgenza (metodi *ad hoc*)
 - trauma ?
 - psicosi acuta ?





Analyte	% Cross reactivity
JWH-018	100
JWH-018 6-hydroxyindole	215
JWH-018 N-5-hydroxypentyl	184
JWH-073	135
JWH-200	127
5-hydroxy JWH-018	130
AM2201	119
JWH-018 N-pentanoic acid	85
JWH-018 5-hydroxyindole	56
JWH-019	35
JWH-018 4-hydroxyindole	23
JWH-398	12
JWH-122	10
WIN 55,212-3 mesylate	3
JWH-015	3
3-(1-naphthoyl)-1H-Indole	3
JWH-007	2

Synthetic Cannabinoids (Spice) ELISA



Features:

- A rapid, cost effective screening solution
- Highly sensitive and accurate assay
- Save time and money on extraction by eliminating negatives prior to chromatographic analysis
- The ability to routinely screen for these drugs
- Applications for urine and blood
- Automated ELISA micro plate reader and washer package available

Synthetic Cannabinoid Drug Testing

NEW URINE LAB TEST

- First lab to offer synthetic cannabinoid urine metabolite test.
- Identifies the parent synthetic cannabinoids (JWH-018 and JWH-073) and their metabolites in human urine
- Precise urine metabolite detection, significantly more reliable than only testing for parent-drug
- Presence of metabolites confirms ingestion; following a single low dose the window of detection is up to 72 hours. In case of chronic use the detection window could be longer.
- Performed on QTrap LC/MS/MS equipment; providing definitive synthetic cannabinoid biomarker test results

NEW ORAL FLUID LAB TEST

- First lab to offer synthetic cannabinoid oral fluid parent drug test
- Quantitatively identifies the parent drugs JWH-018, JWH-073 & JWH-250 in human oral fluid/saliva
- Detects recent abuse more accurately than urine; ideal for monitoring current and recent ingestion
- Presence of parent drug in saliva confirms recent ingestion; average detection window up to 24-48 hours
- Performed on LC/MS/MS equipment; providing definitive synthetic cannabinoid biomarker test results

SYNTHETIC CANNABINOID SALIVA TEST

Are they abusing "synthetic marijuana"?

Synthetic Cannabinoid Oral Fluid testing — a convenient, gender-neutral solution, ideal for recent use detection. You need to know. We'll find out.

HERBAL SMOKING BLENDS HAVE GAINED INCREASING ATTENTION AS AN ALTERNATIVE TO MARIJUANA.

RTI - Oral collector with saliva volume indicator.



New designer drug of abuse: 3,4-Methylenedioxypyrovalerone (MDPV). Findings from apprehended drivers in Finland

Pirkko Kriikku^{a,*}, Lars Wilhelm^b, Olaf Schwarz^b, Janne Rintatalo^c

^a Vita Health Care Services Ltd., Vita Laboratory, Laivakatu 5 F, 00150 Helsinki, Finland

A B S T R A C T

Starting in 2008 a new designer drug, 3,4-methylenedioxypyrovalerone (MDPV) appeared among users of illegal drugs in Finland. Since then there have been several seizures of MDPV by police and customs and it has been connected to many crimes of different types. In this study the incidence and impact of the use of MDPV in drivers suspected of being under the influence of drugs (DUID) in Finland was assessed.

Since autumn 2009, blood samples from drivers suspected of DUID in Finland have been analysed for the presence of MDPV. A new LC–MS/MS method for the determination of MDPV in serum was established. In order to assess the impact of MDPV on driving performance, drug and alcohol findings of positive MDPV cases were compared with data from the clinical examination carried out while the suspect was under arrest. In a period of one year there were 259 positive MDPV cases from apprehended drivers (5.7% of all confirmed DUID cases). In 80% of the cases in which MDPV was found, amphetamine was also present. Benzodiazepines were also frequently found together with MDPV, which was to be expected since in Finland, in our experience, stimulants are very often used together with benzodiazepines.

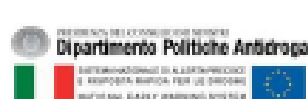
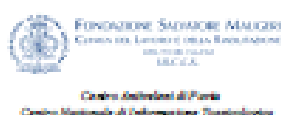
In most cases it remained unclear whether the observed psycho-physical achievement deficiency was induced by MDPV because the concentrations of other drugs, especially other stimulants, were often high. However, in some subjects, MDPV, or MDPV in combination with other substances was the most probable cause of the impairment. The concentrations of MDPV varied from 0.016 mg/L to over 8.000 mg/L.

Little is known about the pharmacology of MDPV. However, based on our findings it is clear that MDPV has a serious impact on traffic safety in Finland.

Oggetto: Allerta grado 2 "Registrati 2 casi di intossicazione acuta correlati al consumo di fenetilammine"

B. Dati rilevati - descrittiva

1. Ad aprile, il Centro Antiveleni di Pavia ha segnalato al Sistema Nazionale di Allerta Precoce 2 casi di intossicazione acuta correlati al consumo di due diverse fenetilammine.
 2. Il primo caso, avvenuto in Liguria, è relativo a un ragazzo di 17 anni accompagnato da parenti presso un Pronto Soccorso perché a casa si presentava catatonico, a tratti non contattabile, delirante ed estremamente agitato. Alla prima valutazione medica il paziente mostrava midriasi, rallentamento psicomotorio e stato confusionale. All'anamnesi il paziente ha dichiarato di aver consumato quattro ore prima 1-2 pasticche di "mescalina" insieme ad amici; ha riferito inoltre di aver utilizzato in passato THC ed "MD".
 3. Lo screening tossicologico sulle urine effettuato in loco è risultato positivo a THC e negativo ad oppiacei e amfetamina; l'etanolemia è risultata negativa (parametri confermati anche dai primi accertamenti effettuati presso il Laboratorio di Tossicologia – Centro Antiveleni di Pavia).
 4. Le analisi tossicologiche sulle urine eseguite presso il Laboratorio di Tossicologia Clinica Analitica della Fondazione Policlinico San Matteo, mediante LC-MS e GC-MS, hanno evidenziato positività analitica compatibile con la molecola 2,5-dimetossi-4-etil-fenetilamina (2C-E) - metodo: gascromatografia-spettrometria di massa full-scan, su estratto di urina analizzato tal quale e dopo derivatizzazione (TMS derivato e acil-derivato). La conferma del risultato e le eventuali analisi quantitative non sono state effettuate per assenza dello standard di riferimento. La ricerca nelle urine di atropina, scopolamina, ketamina, norketamina, butilone, mefedrone, MDPV, 4-MEC, PMA, PMMA, 4-FA, MDAI, 5/6 APB, DMT, 2-CB, 2-C I, 2C-T7 è risultata negativa (metodo: LC-MS; LOD 10 ng/ml).
- b) Risulta essere già stata segnalata da parte del Reparto Carabinieri Investigazioni Scientifiche di Parma che ne ha eseguito il sequestro nell'area di Bolzano a settembre 2010 (Prot. EWS 149/11 del 28/03/2011).
- c) In Italia, essa non risulta inclusa nella Tabella I del D.P.R. 309/90 e s.m.i.



DISPONIBILITÀ DI ANALISI TOSSICOLOGICHE IN URGENZA-EMERGENZA A SCOPO CLINICO SUL TERRITORIO ITALIANO (inclusi alcuni parametri ambientali)

Questionario da compilare on-line sul sito www.cavpavia.it entro il 15 giugno 2012

Per informazioni rivolgersi a

Centro Antiveleni di Pavia - Centro Nazionale di Informazione Tossicologica
IRCCS Ospedale Fondazione Maugeri - Via Maugeri, 10 - 27100 Pavia
telefono urgenze: 0382 24444 - telefono segreteria 0382 26261 dalle ore 9:30 alle ore 17:30
fax: 0382 24605 - email: cnit@fsm.it - www.cavpavia.it

Scopo del questionario è conoscere le capacità analitico-tossicologiche a scopo clinico e la loro disponibilità in urgenza.

Ciò costituirà la premessa per la creazione di un network nazionale di servizi analitici in grado di rispondere in tempi rapidi a esigenze analitico-tossicologiche su tutto il territorio nazionale.

Il presente studio si riferisce ad analisi tossicologiche eseguite esclusivamente a scopo clinico e senza valenza o finalità medico-legale.

Le sostanze oggetto di indagine (e presenti nel questionario on-line) sono riportate nell'allegato 1 suddivise in 11 gruppi in modo che sia più semplice selezionare quelle di interesse per il proprio laboratorio:

1. sostanze chimiche di interesse industriale
2. agenti non convenzionali/armi chimiche
3. farmaci
4. sostanze d'abuso
5. metalli
6. agrofarmaci/fitosanitari/pesticidi
7. tossine naturali
8. altre analisi (non comprese nelle liste precedenti)
9. test di screening
10. markers di intossicazione
11. dosimetria/radionuclidi

306 □ Lamotrigina	344 □ Paroxetina	382 □ Tranilcipromina	2-metossifenil 1-pentil-1H-indol-3-il metanone	444 □ DMC	478 □ Pseudoefedrina
307 □ Levetiracetam	345 □ Perfenazina	383 □ Trazodone	409 □ 2C-B-FLY	445 □ DMMA	479 □ RCS-4(C4)
308 □ Levodopa	346 □ Periciazina	384 □ Triesifenidile	410 □ 2C-B-FLY	446 □ Etafedrina	480 □ Scopolamina TMA-6
309 □ Levomepromazina	347 □ Pindololo	385 □ Trifuoperazina	411 □ 2C-C-MBOMe	447 □ Etaqualone	481 □ (trimetossiamfetamina)
310 □ Levosulpiride	348 □ Piroxicam	386 □ Trimetoprim	412 □ 2-feniletilamina	448 □ Etilfenidato	482 □ Tropicamide
311 □ Lidocaina	349 □ Posaconazolo	387 □ Triprolidina	413 □ 3C-B-FLY	449 □ Fenazepam	483 □ WIN serie
312 □ Litio	350 □ Pralidossima	388 □ Venlafaxina	414 □ 3-FMA	450 □ Fenciclidina	484 □ Yoimbina
313 □ Loratadina	351 □ Pregabalin	389 □ Veralipride	415 □ 3-Metifentaniil	451 □ Fentanil	485 □ β-Me-PEA
314 □ Maprotilina	352 □ Primidone	390 □ Verapamil	416 □ 4-acetoxi-N,N-dimethyltryptamine	452 □ Fluorotropacocaina (p-FBT)	Altro:
315 □ Meflochina	353 □ Procainamide	391 □ Vigabatrin	417 □ 4-AcO-MET	453 □ GBL (gamma-butirolattone)	
316 □ Mepivacaina	354 □ Promazina	392 □ Voriconazolo	418 □ 4-APB	454 □ HU serie	
317 □ Metaqualone	355 □ Prometazina	393 □ Warfarin	419 □ 4-Fluoroamfetamina	455 □ JWH serie	5. METALLI
318 □ Metformina	356 □ Propafenone	394 □ Zolpidem	420 □ fluorometamfetamina (4-FMA)	456 □ Kratom	486 □ Alluminio
319 □ Metoclopramide	357 □ Propifenazone	Altro:	421 □ 4-MeO-PCP	457 □ M-ALPHA	487 □ Antimonio
320 □ Metoprololo	358 □ Propranololo		422 □ 4-metilamfetamina	458 □ MDA	488 □ Argento
321 □ Mianserina	359 □ Quetiapina	4. SOSTANZE D'ABUSO	423 □ 5-HTTP	459 □ MDAI	489 □ Arsenico
322 □ Miofenolato	360 □ Ranitidina	395 □ Amfetamine e Metamfetamine ANTIDEPRESSIVI	424 □ 5IAI	460 □ Metanandamide	490 □ Bario
323 □ Minoxidil	361 □ Reboxetina	396 □ TRICICLICI (qualitativo o quantitativo)	425 □ 5-MeO-DPT	461 □ Metorfano	491 □ Berillio
324 □ Mirtazapina	362 □ Ribavirina	397 □ BARBITURICI (qualitativo o quantitativo)	426 □ 6APB	462 □ Metossietamina	492 □ Bismuto
325 □ Nadololo	363 □ Rifabutina	398 □ BENZODIAZEPINE E ANALOGHI (qualitativo o quantitativo)	427 □ 6-MAM	463 □ MPA (Metipropamina)	493 □ Boro
326 □ Nafazolina	364 □ Rifampicina	399 □ Buprenorfina	428 □ AM serie	464 □ N,N-dimetilamfetamina	494 □ Bromo
327 □ Naproxene	365 □ Risperidone	400 □ Cocaina	429 □ Atropina	465 □ N,N DMT	495 □ Cadmio
328 □ Nebivololo	366 □ Ropivacaina	401 □ Etanolo	430 □ Benzidamina	466 □ N,N-dimetilfenetilamina	496 □ Cerio
329 □ Niaprazina	367 □ Salicilati	402 □ GHB (acido gamma-idrossibutirrico)	431 □ Benzilpiperidina	467 □ N-benzil-1-fenetilamina	497 □ Cesio
330 □ Nicardipina	368 □ Scopolamina	403 □ Ketamina	432 □ Bromo-Dragonfly	468 □ N-etilamfetamina	498 □ Cobalto
331 □ Nicotina	369 □ Sertralina	404 □ LSD	433 □ Caffaina	469 □ OMMA (orto-metossiamfetamina)	499 □ Cromo
332 □ Nifedipina	370 □ Sertalimus	405 □ MDMA (ecstasy)	434 □ Camfetamina	470 □ ORG serie	500 □ Ferro
333 □ Nimesulide	371 □ Sotalolo	406 □ Metadone	435 □ CATINONI	471 □ Ostarina	501 □ Gadolinio
334 □ Nimodipina	372 □ Sulpiride	407 □ Oppioidi	436 □ Colofonia	472 □ Para-Metossiamfetamina (PMA)	502 □ Iodio
335 □ Olanzapina	373 □ Sultopride	408 □ THC/Cannabinoidi	437 □ CP serie	473 □ Para-metossimetilamfetamina (PMMA)	503 □ Litio
336 □ Omeprazolo	374 □ Tacrolimus	Altro:	438 □ CRA-13	474 □ Petidine (o Meperidina, Demerol)	504 □ Manganese
337 □ Orfenadrina	375 □ Teofillina		439 □ Desomorfina ("crocodile")	475 □ PIPERAZINE	505 □ Mercurio
338 □ Oseltamivir	376 □ Tiapride		440 □ Desossipipradrolo (2-DMP)	476 □ Piperonale	506 □ Nichel
339 □ Ossicodone	377 □ Ticlopidina		441 □ Destropropossifene	477 □ Poppers (alchil nitriti)	507 □ Oro
340 □ Oxatomide	378 □ Tioridazina		442 □ Dipipanone		508 □ Piombo
341 □ Oxcarbazepina	379 □ Tolbutamide		443 □ DMAA		509 □ Platino
342 □ Oxprenololo	380 □ Topiramato				510 □ Rame
343 □ Paracetamolo	381 □ Tramadol				511 □ Rubidio

Nuove sostanze d'abuso

Survey / patients selection in the emergency setting

Limitation in the collection of data

- only a part of the Italian EDs (1/6) is involved as collaborative centre
- compliance of all the emergency physicians working in the EDs of the network as collaborating centres
 - use of PCC only for special / severe cases
 - generally a “rapid solution” of the case is preferred to a complex pathway
- overload of patients in the ED
- momentary overload of the lines of the PCC
- incompleteness of data due to lack of knowledge of NPS-related
 - *prise en charge* in addiction treatment services and in psychiatric ward
 - deaths



Clinical survey in the emergency setting

Advantages

- collection of clinical cases → relevant data regarding
 - assumed product (street product, medications, ...)
 - characteristic of abuse
 - clinical effects related to abuse → evaluation / identification of the
 - toxidromes
 - severity of poisoning
 - treatments
- prevention of mortality (rapid identification → treatments)
- more confident evaluation of the prevalence
- promptness in alerting the national health system → early warning system
-

Allerte NEWS (Jan 2010 - Sep 2013)

2010

- Eroina
- Eroina / Bacillus Anthracis
- N-Joy / JWH-018*
- N-Joy / JWH-073*
- Mefedrone
- MDPV
- Forest Green / JWH-250*
- Jungle Mystic Incense / JWH-122*

2011

- Ketamina*
- eroina con caffeina*
- decessi droga-correlati
- PMMA decessi
- decessi droga-correlati
- overdose non letali
- PMMA decessi
- JWH-210, JWH-019 *
- decessi droga-correlati
- eroina tipo "brown sugar" e "white" con metorfano, decessi

2012-settembre 2013:

- overdose da oppiacei
- cannabinoidi sintetici *
- overdose da oppiacei
- JWH-022, AM-2201 *
- Metossietamina *
- JWH-073
- 4-MEC, metilone, bufedrone
- Eroina/Bacillus Anthracis
- 4-metilamfetamina decessi
- 6-APB *
- Eroina/Bacillus anthracis
- RCS-4, AM-2233, JWH-307 *
- 5-IT
- catinoni sintetici*
- Eroina/Bacillus anthracis
- PMA/PMMA *
- Metossietamina*
- 25I-NBOMe, 2C-B, 2C-H
- 2C-B, 2C-E*
- 4-MA
- Metossietamina*

* Casi identificati da CAV Pavia

- growing popularity of NPSs → (“recreational”) use of NPS appears to be an emerging public health problem for the (acute and chronic) toxic effects
- patient history is frequently false / incorrect
 - the patients is uninformed about the substances used in more than 40-50% of the cases
- the same product may vary in the composition in a little period of time
- co-assumption of more than two substances is frequent
- the severity of poisoning differs among the diverse cannabinoids/cathinons/other NPS
- toxic effects (severity, duration) of several new substances are mostly unknown at this time
- the easy evaluation of the behavioural toxic effects may lead to underestimation of severe cardiovascular complications
- the knowledge of the substances available in a period of time in a specific region can help physicians in the diagnostic process

- analytical tests usually available in EDs are insufficient to characterize the actual pattern of abuse → a need in emergency care
 - only in less than 10 % of our “sentinel” cases there is relation between reported substance and analytical results
- specifically organized PCC and clinical-toxicology labs are the clinical services that more rapidly can
 - notice changes and news in this field → help EDs
 - correctly evaluate and demonstrate the relationships between the clinical effects and the analytical data (→ patients)
 - → several NPS → included in the Italian list of controlled substances in 2010-2013 thanks also to this activity
 - identify the analytical needs (e.g. point of care testing) for the emergency setting lined up the new trends of abuse
 - → stimulus for the industrial production of new methods/test/...

Toxicovigilance on NPSs → the Italian NEWS clinical experience

- a National Early Warning System should include a specific network of one (or more) specialist PCC connected to emergency medical services (e.g. EDs, psychiatric wards, ICUs) and to clinical toxicology labs,
- this network can efficiently contribute to the increase of
 - the “perception” of this new health problem
 - the knowledge of new substances for abuse in the National Health System
 - developing clinical and lab responses in the emergency setting to the phenomenon
- Main general results of the toxicovigilance system
 - enhanced reporting of specific intoxications (non fatal and fatal) with analytical confirmation → medical action → care of patients
 - correct evaluation and demonstration of relationships between clinical effects (→ patients) and analytical data
 - prompt detection of sentinel cases / signal of toxicity → alerts on new emerging toxicological problems
 - unique collection of new / original information/data on clinical toxicology of NPSs