Common toxidromes in movement disorder neurology

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ABSTRACT

Background Physicians can come across patients who are exposed to certain prescription drugs or toxins that can result in adverse effects and complications which have high rates of morbidity and mortality.

Objective To summarise the key clinical features and management of the common movement disorder toxidromes relevant to physicians (with an interest in neurology).

Methods We searched PUBMED from 1946 to 2016 for papers relating to movement toxidromes and their treatment. The findings from those studies were then summarised and are presented here.

Results The key features of 6 of the common movement disorder toxidromes and their treatment are tabulated and highlighted. The management of toxidromes with the highest mortality like neuroleptic malignant syndrome and serotonin syndrome are discussed in detail.

Conclusion There are several toxidromes that have the potential to become a serious life-threatening emergency if there is a delay in recognition of key clinical features and instituting the appropriate treatment at the earliest is crucial.

INTRODUCTION

A toxidrome or toxic syndrome can be defined as a constellation of findings that are evident either from the physical examination of the patient or from ancillary testing, which may result from drug overdose, or withdrawal or exposure to a toxin.¹ Understanding of the pathophysiology of these disorders along with a high index of suspicion in the relevant clinical context is the key to recognition, for example, a patient with high fever and rigidity on antipsychotics with dopamine receptor blocking potential could be suffering from a neuroleptic malignant syndrome (NMS) while a patient with myasthenia gravis on an anticholinesterase medication such as pyridostigmine with excess salivation or perspiration can be recognised by the clinician to be experiencing a cholinergic toxidrome.

This article is focused on a discussion of toxidromes relevant to general neurology and a more detailed discussion of toxidromes resulting from chemical and animal neurotoxins relevant to emergency medicine practice is beyond the scope of this article and the reader is referred elsewhere for a comprehensive account. Neurological emergencies that have at their heart an underlying toxidrome are elaborated here along with the appropriate clinical context. The description that follows is that of single agent toxidromes and multiagent toxidromes can show a combination of signs and symptoms or

additional problems but are not described here^{1 2}(table 1).

Anticholinergic toxidrome

Central anticholinergics such as trihexyphenidyl have traditionally been used in the treatment of Parkinson's disease⁸ though with the advent of dopaminergic therapies⁹ and the cognitive side effects of anticholinergics¹⁰ their use is now declining. Other uses have included generalised dystonia,¹¹ rhythmic-oscillatory movements of brainstem-cerebellar origin (palatal myoclonus, pendular nystagmus, facial myokymia)¹² and various types of tremor including rubral tremor.¹³ Antipsychotics, tricyclic antidepressants and many first-generation antihistamines also have prominent anticholinergic activity. The salient features of an anticholinergic toxidrome are described in table 1 and its differentiation from a cholinergic toxidrome in table 2. Additional features that may be seen include restlessness, visual hallucinations, dysarthric speech, mydriasis, urinary retention, fever, tachycardia and red, dry skin.¹⁴

Central anticholinergic syndrome (CAS) is not often considered in the differential diagnosis of delirium but should strongly be suspected in patients with a recent history of anticholinergic medication administration as morbidity is high. Moreover, CAS can occur even after only a single dose of an anticholinergic agent, as an idiosyncratic phenomenon.³

Drug-induced parkinsonism

Drug-induced parkinsonism (DIP) is the second most common cause of an akinetic rigid syndrome in the Western world and its prevalence is increasing due to the rise of polypharmacy. DIP was initially reported as a complication of neuroleptic medication use in psychiatric patients, but it can also be caused by several other classes of drugs including antiemetics, antidepressants, calcium channel antagonists, antiarrhythmics and antiepileptics. Although traditionally considered to be a completely reversible condition, DIP may persist long after drug withdrawal. At least 10% of patients with DIP develop persistent and progressive parkinsonism in spite of the discontinuation of the offending agent that represents unmasking of a preclinical neuronal dopaminergic deficit. The best treatment of DIP therefore is caution when prescribing drugs with a potential to cause this problem carefully weighing benefits and risks of such a prescription particularly for psychiatric patients when their state of mind does not allow them to make a rational decision based on information provided; nevertheless there will be a case

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Table 1 Salient features of the toxidromes relevant to neurology practice

Toxidrome	Salient features
Adrenergic toxidrome	Agitation, confusion, tachycardia, hypertension, dilated pupils, paranoid psychosis
Anticholinergic toxidrome	Confusion, dry flushed skin and mucous membranes, fever, mydriasis, sluggish bowel movements, urinary retention ³
Benzodiazepine toxidrome	Depressed consciousness*, impaired motor coordination, slurred speech, blurry vision, erratic behaviour, respiratory depression ²
Cholinergic toxidrome	Diaphoresis, hypersalivation, fasciculation, lacrimation, miosis, increased frequency of bladder and bowel movements, decreased consciousness or agitation, acute respiratory failure ⁴
Drug-induced parkinsonism	Tremor, bradykinesia and rigidity that is usually symmetrical but can be asymmetrical
Neuroleptic malignant syndrome	Altered mental status ranging from agitation to coma, fever, rigidity, bradykinesia, tremor, high creatine kinase (↑↑CK), autonomic hyperactivity and respiratory depression
Parkinson hyperpyrexia syndrome	Clinical features are identical to the neuroleptic malignant syndrome
Opioid toxidrome	Depressed consciousness*, respiratory depression, miosis, sluggish bowel movements or constipation ⁵
Serotonin syndrome	Agitation, bradykinesia, fever, rigidity, hyper-reflexia, autonomic hyperactivity, increased bowel movements, confusion ⁶
Tardive (antidopaminergic) syndromes	Various phenotypes of tardive syndromes can exist singly or in combination
a. Tardive dyskinesia	Choreiform movements—oral, buccal and lingual
b. Tardive dystonia	Focal dystonia> segmental dystonia> generalised dystonia
c. Tardive tremor	Postural and kinetic that persist despite DRBA withdrawal
d. Tardive myoclonus	Myoclonic jerks in isolation or combination with tardive dystonia or akathisia
e. Tardive akathisia	Inner and manifest restlessness
f. Tardive complex	Three or more tardive movement disorders in the same patient
Tricyclic antidepressant toxidrome	Dry mouth, blurred vision, dilated pupils, sinus tachycardia, pyramidal neurological signs, and depressed consciousness, convulsions, respiratory depression, hypotension and prolongation of the PR and QT intervals ⁷

*This exists on a continuum of drowsiness, stupor and coma.
DRBA, dopamine receptor blocking agent.

Table 2 Clinical differentiating features between cholinergic and anticholinergic toxidromes¹⁵

Characteristics	Cholinergic toxidrome	Anticholinergic toxidrome
Pupils	Constricted	Dilated
Temperature	Normal	Hyperthermia
Heart rate	Bradycardia	Tachycardia
Skin	Increased perspiration	Dry skin
Mucous membranes	Sialorrhoea, rhinorrhoea, lacrimation, bronchorrhoea	Dry secretions
Bladder	Urinary frequency	Urinary retention
Bowel	Increased peristalsis	Constipation

where such medications will be required by the patient's clinical condition but the doses should be kept at the lowest possible required.¹⁶

Neuroleptic malignant syndrome

This toxidrome is mainly characterised by hyperthermia, altered mental state, haemodynamic dysregulation, elevated serum creatine kinase and rigours. It has been associated with multisystem organ failure potentially leading to rhabdomyolysis, acute respiratory distress syndrome and disseminated intravascular coagulation.¹⁷ It can be associated with exposure to dopamine receptor blocking agents (DRBAs) (table 3) and also with the sudden withdrawal of dopamine agonists when it is referred to as neuroleptic malignant-like syndrome or the parkinson hyperpyrexia syndrome (PHS).

An international consensus study of NMS has proposed diagnostic criteria reflecting a broad consensus among an international multispecialty panel of physicians (table 4).¹⁸

Permanent neurological injury may occur if there is a delay in recognition or treatment.

Table 3 Drugs associated with the neuroleptic malignant syndrome

Class	Drugs
Typical antipsychotics	Chlorpromazine, droperidol, fluphenazine, haloperidol, mesoridazine, molindone, loxapine, perphenazine, pimozide, thiothixene, trifluoperazine, thioridazine
Atypical antipsychotics	Clozapine, olanzapine, risperidone, quetiapine, ziprasidone, aripiprazole
Others	Metoclopramide, prochlorperazine, promethazine

The differential diagnosis includes heatstroke, idiopathic malignant catatonia, malignant hyperthermia with inhalational anaesthetics such as halothane, CAS and serotonin syndrome (SS).

Neuroleptic-induced catatonia and mild forms of NMS share parkinsonian features, catatonic symptoms and low grade fever, and have been described in patients receiving antipsychotic agents. Some consider the overlapping features as a continuum on a 'neuroleptic toxicity spectrum'.¹⁹ Woodbury and Woodbury²⁰ describe five stages in this spectrum from an 'extra-pyramidal reaction' (Stage 1) to severe NMS (Stage 5) (table 5).

Parkinson hyperpyrexia syndrome

PHS in the past has been referred to with its alternative name acute dopamine depletion syndrome.²¹ Fatal hyperpyrexia with a severe akinetic rigid syndrome can occur following acute levodopa withdrawal. The clinical features are the same as those of NMS, and this can include any combination of fever, parkinsonian rigidity, confusion and raised creatine kinase; the distinction being that no neuroleptic is involved. The rapid decrease in dopaminergic activity may be important in causing the syndrome, therefore, if dopaminergic medications require withdrawal this should be achieved gradually rather than suddenly.²²

Table 4 Diagnostic criteria for neuroleptic malignant syndrome according to an international consensus study.¹⁸

Criteria	Findings
Essential criteria	Exposure to dopamine antagonist or dopamine agonist withdrawal in past 72 hours
Clinical features	Hyperthermia, >100.4°F or > 38.0°C on at least two occasions BP elevation ≥25% above baseline BP fluctuation ≥20 mm Hg (diastolic) or ≥25 mm Hg (systolic) change within 24 hours HR ≥25% above baseline RR ≥50% above baseline
Laboratory features	CK >4× normal
Exclusion criteria	Other central nervous system, systemic and toxic causes of hyperthermia

BP, blood pressure; CK, creatine kinase; RR, respiratory rate.

Additional features can include generalised stimulus-sensitive myoclonus and myoglobinuric renal failure.^{23 24}

Although withdrawal of levodopa is the most common cause of PHS, sudden withdrawal of other agents, including amantadine, dopamine agonists and catechol-O-methyltransferase inhibitors can also cause this syndrome. Patients with Parkinson's disease are susceptible to PHS due to its inherent dopamine-depleted state, but PHS has also been reported in patients with atypical parkinsonism, for example multiple system atrophy and progressive supranuclear palsy.^{25 26}

Serotonin syndrome

SS is an iatrogenic condition caused by exposure to drugs that have effects on serotonergic transmission in the brain. It was first recognised in the 1960s in depressed patients exposed to monoamine oxidase inhibitors (MAOIs).²⁷ This syndrome has also been referred to in the literature as the serotonin behavioural or hyperactivity syndrome. Although initial reports concerned patient exposure to either MAOI or selective serotonin reuptake inhibitors (SSRIs), exposure specifically to these classes of drugs is not required for this syndrome to develop and several other drugs can also cause this syndrome (table 6). The development of the SS is unpredictable as it can develop at therapeutic doses but co-prescription of these two drug classes is a contraindication. The salient features are described in table 1 and although it is

Table 6 Drugs associated with the serotonin syndrome^{6 28 30 31}

Class	Drugs
SSRI	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
SNRI	Venlafaxine
Serotonin receptor antagonist	Trazodone
Amphetamines	3,4-methylenedioxymethamphetamine (Ecstasy), dextroamphetamine, methamphetamine, sibutramine
MAOI	Phenelzine, moclobemide*
Opioids	Meperidine (pethidine), fentanyl, tramadol
Others	Lithium, sodium valproate,

*Several MAOIs are not in clinical use and are not listed here.

MAOI, monoamine oxidase inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

often described as a clinical triad of mental-status changes, autonomic hyperactivity and neuromuscular abnormalities, not all of these findings are consistently present in all patients with the disorder.²⁸ Additional problems include seizures, QT prolongation, arrhythmias and the syndrome of inappropriate antidiuretic hormone secretion.²⁹

Two different sets of criteria have been proposed for the recognition of SS in clinical settings (figure 1, table 7).

The clinical differentiation of SS from NMS is crucial as treatments are different. There are some physical signs that can help in making this distinction (bold type in table 8), thereby aiding treatment decisions.

Tardive syndromes

As opposed to acute toxidromes, chronic exposure to DRBAs can cause a variety of movement disorders that develop gradually although acute toxicity can also occur in the form of sudden dystonic reactions and oculogyric crises.³³ The various phenotypes of dopamine receptor blockade related tardive syndromes are described in table 1.

Other tardive complications that have been reported include tardive dystonia of the pharynx causing dysphagia³⁴ and respiratory irregularities with audible involuntary respiratory noises that may be accompanied by prominent gasping and episodes of aspiration pneumonia.³⁵

Table 5 Stages of 'neuroleptic induced toxicity spectrum'²⁰

Stages	Muscle rigidity	Autonomic instability	Temperature
Stage 1 (EPR)	Mild-moderate	Nil	Normal
Stage 2 (NIC)	Mild-moderate + cog-wheel rigidity	HR: 70–90 RR: 18–28 BP: 120/70–140/80 mm Hg	Normal
Stage 3 (Mild NMS)	Mild-moderate + cog-wheel rigidity	HR: 90–110 RR: 25–30 BP: 130/80–150/90 mm Hg	38–39°C
Stage 4 (Moderate NMS)	Moderate-severe + lead-pipe rigidity	HR: 110–130 RR: 25–30 BP: 140/100–210/110 mm Hg	39–40°C
Stage 5 (Severe NMS)	Severe lead-pipe rigidity	HR: 130–150 RR: 30–36 BP: 140/100–210/110 mm Hg	39–42°C

BP, blood pressure; EPR, extrapyramidal reaction; HR, heart rate; NIC, neuroleptic-induced catatonia; NMS, neuroleptic malignant syndrome; RR, respiratory rate.

Figure 1 Hunter serotonin toxicity criteria proposed by Dunkley (adapted from Dunkley *et al* [32]).

EVALUATION

History

A carefully obtained history from the patient is crucial to correctly identifying the toxidrome under consideration. However, under certain circumstances, such as when dealing with a comatose patient who has taken an overdose of SSRIs where the depressed level of consciousness is a manifestation of the toxidrome, getting a first-hand account may not be possible but information gleaned from attendants, carers and family members about medications, comorbidities and exposure to toxins can lead the clinician to the correct diagnosis. Recording the chronology of events, the *tempo* of development of clinical features and a detailed medication history are first steps in hypothesis generation by the clinician which can be further confirmed by a methodical clinical examination.

A distinction between acute toxidromes such as NMS from exposure to dopamine receptor blockers from chronic tardive syndromes such as tardive chorea arising from exposure to the same class of drugs is as much historical as it is based on clinical examination findings.

Examination

A general physical examination assessing for vital signs including temperature, skin, mucous membranes, and cardiovascular examination and abdominal examination may help provide clues. For example, a patient with fever, dry mucous membranes, tachycardia and sluggish bowel sounds on auscultation could point towards a diagnosis of an anticholinergic toxidrome if substantiated by a history of prescription of drugs with anticholinergic side effects.

Table 7 Sternbach's criteria for diagnosis of serotonin syndrome⁶

1.	Recent addition or increase in a known serotonergic agent
2.	Absence of other possible aetiologies (infections, substance abuse)
3.	No recent addition or increase of a neuroleptic agent
4.	At least three of the following symptoms:
	Mental status changes (confusion, hypomania)
	Agitation
	Myoclonus
	Hyper-reflexia
	Diaphoresis
	Shivering
	Tremor
	Diarrhoea
	Incoordination
	Fever

Table 8 Differentiating features between neuroleptic malignant syndrome (NMS) and serotonin syndrome (SS)^{27 29}

Characteristics	NMS	SS
Precipitant	Dopamine antagonist	Serotonergic drugs
Temperature	Febrile, tachycardic, flushed	Febrile, tachycardic, flushed
Mental status	Depressed consciousness*	Depressed consciousness* or agitated confusion
Eye signs	Normal pupils	Dilated pupils, ocular clonus
Parkinsonism	Tremor, rigidity	Tremor, rigidity
UMN signs	Normal reflexes	Hyper-reflexia, clonus, extensor plantar responses
Gastrointestinal symptoms	Normal	Diarrhoea

*This exists on a continuum of drowsiness, stupor and coma.
UMN, upper motor neurone.

A focused neurological examination for the most part complements the findings of a general physical examination and must be directed to look at pupillary responses, fundi, tone, deep tendon reflexes and gait if the patients is mobile but in most cases of significant overdose the patient's state of alertness, cognition and behaviour may not allow a detailed examination where cooperation is desired. Eliciting upper motor neuron signs in a febrile, rigid comatose patient may be crucial in distinguishing NMS from SS (table 8) when a full drug history is not accessible.

DIAGNOSTIC TESTS

Many of the clinical features described above such as mydriasis, fever, rigidity even when they are part of a constellation can be due to several medications or toxins and therefore confirmatory tests are sometimes required. For example, an awake and alert patient who presents with torticollis after an injection of metoclopramide, a dopamine receptor antagonist, can be easily recognised as an iatrogenic drug reaction. Blood and urine drug testing may be helpful in certain circumstances positively identifying the culprit drug and helping to start definitive treatment where one is available or required. However, the drawbacks of waiting for the availability of test results from a referral centre, false positives and false negatives can lead to delays in instituting treatment. Life-saving and emergency treatments in such a scenario can be empirical and necessary but clinical judgement in

analysing historical data and examination findings can guide the clinician to the correct course of action.

Reaching the correct diagnosis early is essential to the successful management of a life-threatening toxidrome. That NMS can be misdiagnosed as SS illustrates the perils of making an incorrect diagnosis as the management is very different.

MANAGEMENT

The Airway, Breathing, Circulation, Disability, Exposure (ABCDE) approach is applicable in all clinical emergencies for immediate assessment and treatment.³⁶ Once the first three components (airway, breathing and circulation) have been assessed and secured, standard treatment follows to stabilise the deranged physiological parameters in order to preserve life and prevent harm. Not all the treatment recommendations provided here are based on evidence obtained from high quality clinical trials; where such evidence is lacking clinical judgement and consensus opinion among physicians is the next best option in what can be uncharted territory.

General measures for all the toxidromes discussed include withdrawal of the offending agent and providing supportive care which may include rehydration with intravenous fluids, cooling measures if patients are febrile and instituting corrective measures to stabilise vital signs such as low blood pressure. Specific therapy however will depend on the correct identification of the underlying toxidrome, for example, dopamine agonists can be used for the treatment of NMS but can exacerbate the problems in someone with SS. Herein lies the importance of using clinical acumen and the power of observation to differentiate between syndromes that may bear a superficial resemblance to one another. The intensity of therapy in general will depend on the severity of illness. A treatment outline of several toxidromes is shown in table 9 and a more detailed description of the potentially life-threatening toxidromes NMS and SS is as follows:

Managing a case of suspected NMS

The most important first step is to recognise the clinical features of this syndrome and stop further exposure to neuroleptics that block dopamine receptors.⁵³ Supportive therapy such as intravenous rehydration in patients who are unwell, febrile and comatose and restoring electrolyte balance are the next steps.⁵⁴ This may require admission to an intensive care unit. Medications with anticholinergic effects prevent sweating which may lead to further elevation of temperature and should be avoided. The specific treatment of NMS should be individualised based on the severity of the syndrome. Long-acting benzodiazepines such as lorazepam 1–2 mg administered intravenously or intramuscularly every 4–6 hours may be all that is required for mild cases of NMS.⁴³ Traditionally dantrolene has been advocated for severe cases (table 8). Others have suggested the use of glutamate receptor antagonists such as amantadine⁵⁵ and intravenous levodopa⁵⁶ to treat NMS. For patients with prominent catatonic features when other therapies have been ineffective, electroconvulsive therapy may be considered.⁵⁷

Managing a case of suspected SS

The first step in the management of SS is to recognise the clinical signs and symptoms, and distinguish them from mimics, such as NMS. Discontinuation of all serotonergic agents is the next step, following which supportive care to control agitation, hyperthermia and autonomic dysfunction must be instituted. In mild cases, supportive care and administration of benzodiazepines (eg, diazepam 5 mg intravenously), if the patient is

Table 9 Treatment outlines for the common toxidromes in neurological practice

Toxidrome	Treatment
Adrenergic toxidrome	Agitation may be treated with benzodiazepines, psychosis with haloperidol and hypertension with phentolamine, supraventricular tachyarrhythmias with β -blockers. ³⁷
Anticholinergic toxidrome	Agitation can be treated with benzodiazepines, dexmedetomidine an α_2 -adrenergic agonist approved by the US Food and Drug Administration for the sedation of adults who are intubated on mechanical ventilation and in non-intubated adults who are undergoing surgical procedures, has been used in adolescent cases. ³⁸ If life-threatening such as cardiac arrhythmias occur, the cholinesterase inhibitor physostigmine can reverse the abnormality. Initial dose: 0.5–2 mg intravenously (slow push)*. ³⁹
Benzodiazepine toxidrome	Flumazenil intravenous/intramuscular. Initial dose: 0.1–0.3 mg (bolus) intravenously*. ⁴⁰
Cholinergic toxidrome	Atropine intravenously for any evidence of significant toxicity such as symptomatic bradycardia. Initial dose: 0.5 mg (bolus) intravenously*. ⁴¹
Drug-induced parkinsonism	Recognition and withdrawal of the offending drug. ⁴²
Neuroleptic malignant syndrome	Cooling measures, rehydration, bromocriptine or other dopamine agonists orally (or via NG), consider dantrolene intravenously for severe cases. Initial doses: bromocriptine 2.5–5 mg orally (or via NG) 8 hourly, dantrolene 1–2.5 mg /kg intravenously 6 hourly for 48 hours. ⁴³
Parkinson hyperpyrexia syndrome	Reinstitute treatment with levodopa or dopamine agonist orally (or via NG). ⁴⁴ If due to suspected DBS battery failure, confirm by interrogating device and get battery replaced. ⁴⁵
Opioid toxidrome	Naloxone intravenous/intramuscular/subcutaneous/intranasal. Initial doses: 0.2 mg (bolus) intravenously, 0.4 mg intramuscular, 0.8 mg subcutaneous; 2 mg intranasal*. ^{46 47}
Serotonin syndrome	Withdrawal of the offending agent and supportive care. Benzodiazepines may be used to treat agitation and tremor. Oral (or via NG tube) cyproheptadine may be used as an antidote. Initial dose: 4–8 mg orally (or via NG). ^{48 49}
Tardive (antidopaminergic) syndromes	Early recognition and stopping the offending drugs is important as tardive syndromes can be highly resistant to drug treatment. Calcium channel blockers, β -blockers, benzodiazepines have been tried but there is little evidence to support their use. ⁵⁰ Tetrabenazine is effective in some cases. ⁵¹
Tricyclic antidepressant toxidrome	Gastrointestinal decontamination. Activated charcoal (1 gm orally or via NG) adsorbs TCAs. Intravenous fluids, cardiovascular and respiratory support. Administration of sodium bicarbonate intravenously might be beneficial for patients with severe or life-threatening TCA toxicity if there is a prehospital protocol for its use. ⁵²

*Repeat dosing may be required if response is inadequate or symptoms recur.

DBS, deep brain stimulation; NG, nasogastric tube; TCA, tricyclic antidepressants.

agitated, may be adequate.^{58 59} In moderate and severe cases, administration of 5-HT_{2A} antagonists can be useful.⁶⁰ Cyproheptadine and chlorpromazine have been used but there are no clinical trials to support their use in such a scenario. Case reports of treatment with cyproheptadine have been reported with no major adverse effects^{49 61} and recovery can be within hours of cyproheptadine prescription when other therapies have failed.⁶²

CONCLUSION

Prompt recognition and correct identification of toxidromes is vital in managing potential emergencies in neurology practice that can have high morbidity and mortality. Prevention can be a part of the approach to dealing with these problems and some toxidromes can be avoided by a combination of education and modifications to prescribing practices.

Main messages

- Movement disorder toxidromes can such as neuroleptic malignant syndrome (NMS) and serotonin syndrome (SS) can represent medical emergencies and a basic knowledge for recognising these conditions is essential for clinicians.
- Differentiating NMS from SS is important because treatments for these conditions, which can have some overlapping features, are different.
- Mortality and morbidity of some of these toxidromes can be high so instituting treatments, both generic and specific, in a timely manner is of paramount importance.

Current research questions

- The treatment for tardive movement disorder syndromes is suboptimal as recovery from these conditions can be delayed for months and years, and almost always never complete. Research into underlying molecular mechanisms and better treatments would be invaluable for patients.
- There is a lot of variation in the phenotypical manifestations and severity of patients developing movement disorder toxidromes even when exposed to similar doses of medications. The mechanisms for this heterogeneity remain largely unexplained.
- Preventive treatments are largely non-existent at present for most toxidromes apart from avoiding the exposure to the culprit drug but some of these drugs have important therapeutic value for treating the conditions that they are indicated and licensed for. Finding molecules and drugs that can prevent the development of certain toxidromes that can be anticipated when prescribing a particular class of drugs to patients would be useful.

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