Supplementary Online Content

Orlova Y, Rizzoli P, Loder E. Association of coprescription of triptan antimigraine drugs and selective serotonin reuptake inhibitor or selective norepinephrine reuptake inhibitor antidepressants with serotonin syndrome. *JAMA Neurol.* Published online February 26, 2018. doi:10.1001/jamaneurol.2017.5144

eTable. Clinical Details of 17 Cases of Clinically Suspected Serotonin Syndrome

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable. Clinical Details of 17 Cases of Clinically Suspected Serotonin Syndrome

Case	Synopsis, including medications prescribed at the time of diagnosis	Satisfies criteria for serotonin syndrome?	Exposure to co-prescription during year of event?	Definite* or Possible** diagnosis at the time of exposure to co-prescription (triptan and SSRI/SNRI)
1	Male in his 40s on chronic opioid therapy. History of brain tumor resected in childhood; hydrocephalus with ventriculoperitoneal shunt; nonfunctioning occipital nerve stimulator for chronic daily headache. Admitted for confusion attributed to shunt malfunction. Serotonin syndrome documented in past medical history but clinical notes contain no corroborating information. Medications: Amantadine Cholecalciferol Cyanocobalamin Diazepam Docusate Sodium Dronabinol Esomeprazole Famotidine Ketamine Labetalol Hcl Methadone Oxycodone Controlled Release Oxycodone Oxymorphone Extended Release Polyethylene Glycol Promethazine Hcl Quetiapine	Sternbach: Not enough information to assess Hunter : Not enough information to assess	NO	NA

2	Female in her 30s with migraine, chronic back pain on opiates and anxiety reports palpitations, restlessness, diaphoresis for 5 days. She had started started amitriptyline in the preceding month for migraine prophylaxis. Exam in emergency room was normal, no triptan use reported. Subacute onset of moderately severe symptoms evaluated in the ED but was not critical. Medications: Sumatriptan Amitriptyline Tramadol Oxycodone with acetaminophen Mirtazapine Hydroxyzine	Sternbach: NO Hunter: NO	NO	NA
3	Female in her 20s with obsessive compulsive disorder and eating disorder, had recently increased fluoxetine dose to 80 mg daily and reported onset of abdominal pain and fever. She subsequently developed facial and finger twitching that progressed over a few days. She was not prescribed triptans at that time, but was taking acetaminophen/ oxycodone more frequently, and had used it with alcohol. On exam in the emergency department lateral irregular jerking movements of the eyes were noted in all positions. Also noted were limb tremor and bilateral knee hyperreflexia.. Follow up: Had recurrent episodes of limb shaking with duration of few hours intermittently in the setting of life stressors, at which time was considered functional disorder. Medications: Fluoxetine Acetaminophen/oxycodone Alprazolam	Sternbach: YES (agitation, myoclonus, tremor, fever) Hunter criteria: YES (tremor, biceps hyperreflexia)	NO	NA

4	Female in her 20s with prior anxiety and abdominal migraine on nortriptyline 10 mg for four months presented to the ED with fatigue, palpitations, feeling "shaky" after concern for drug interaction was raised by a pharmacist who warned her that she should not take cold medicine while taking nortriptyline. She was anxious and tearful, otherwise her exam was normal. Drug screen was normal. Medications: Lorazepam Cepacol Fluconazole Ibuprofen Aluminum/magnesium hydroxide/simethicone Nortriptyline Oxycodone Acetaminophen/doxylamine/dextromethorphan/pseudoephedrine Guaifenesin/pseudoephedrine	Sternbach: NO Hunter: NO	YES	Possible (Rizatriptan, Escitalopram)
5	Woman in her 60s with history of major depression, polysubstance and alcohol abuse was admitted after ingestion of unknown number of pills. After detoxification, multiple medications for insomnia were started. She became agitated, developed tachycardia, mild fever and hypertension, was diaphoretic, and had tremor and elevated reflexes in upper limbs. Symptoms resolved after administration of benzodiazepines. Medications: Trazodone Mirtazapine Quetiapine Sertraline	Sternbach: NO Hunter: YES (tremor and hyperreflexia)	NO	NA

6	Female in her 40s reported that she was worried about serotonin syndrome. She had been admitted for detoxification for opiate and alcohol abuse, at which time she started quetiapine and recently increased citalopram. Her neuro exam was normal. One month later she reported that was admitted to outside hospital for headache, took three tablets of eletriptan and was diagnosed with serotonin syndrome, no records available. She continued taking eletriptan one year later without complications but citalopram was discontinued. Medications: Citalopram Hydrochlorothiazide Gabapentin Eletriptan Quetiapine Trazodone	Sternbach: Not enough information to assess Hunter: Not enough information to assess	YES	Possible (Eletriptan, Citalopram)
7	Female in her 40s with depression, anxiety, prior suicidal attempts reported diarrhea and palpitation within 24 hrs after addition of buspirone. Over subsequent days she also reported auditory and visual hallucinations, facial flushing and headache that she treated with rizatriptan. Later she developed limb tremor and was brought to ER where she had tachycardia, tremor and hyperreflexia. One month later she remained on same medications except rizatriptan and she had intermittent tremor with hyperreflexia. Medications: Buspirone Venlafaxine Rizatriptan Fexofenadine Clonazepam Ziprasidone Lamotrigine Mometasone Esomeprazole Ondansetron Oxycodone Metoclopramide Ursodiol	Sternbach: YES (mental status change, tremor, hyperreflexia) Hunter: YES (tremor and hyperreflexia)	YES	Definite (Sumatriptan, Rizatriptan, Fluoxetine, Venlafaxine) Note: some symptoms started before ingestion of rizatriptan and did not remit after its discontinuation

8	Female in her 40s with migraine reported multiple brief episodes of palpitations, fatigue, hot flashes, and mild diarrhea. Her exam was normal and her symptoms improved with lorazepam and ondansetron injections. Medications: Eletriptan Acetaminophen/aspirin/caffeine Butalbital/acetaminophen/caffeine Nadolol	Sternbach: NO Hunter: NO	YES	Possible (Eletriptan, Sertraline)
9	Female in her 30s with depression, anxiety, irritable bowel syndrome and migraine who had recently begun taking modafinil. She reported abdominal pain and shortness of breath. In the ED she developed brief transient episodes of unresponsiveness with eye twitching and forced eye closure without postictal confusion. Patient reported later that she had serotonin syndrome. Medical records indicated nonepileptic pseudoseizures. Medications: Modafinil Escitalopram Trazodone Divalproex sodium Albuterol Fluticasone propionate/salmeterol Tiotropium Gabapentin Ketorolac Nadolol Omeprazole	Sternbach: NO Hunter: NO	NO	NA
10	Historical report. Female in her 30s with bipolar disorder, migraine, urticaria and chronic fatigue reported recent admission to an outside hospital for worsening of her itching and fatigue. Serotonin syndrome was suggested as a possible diagnosis. Symptoms improved with steroids. No other details available. Medications: Amphetamine/dextroamphetamine Hydroxyzine Ibuprofen Sumatriptan Lithium Prednisone Desvenlafaxine	Sternbach: Not enough information to assess Hunter: Not enough information to assess	NO	NA

	Modafinil Metoclopramide Quetiapine			
11	Diabetic female in her 50s with gastroparesis on tube feedings admitted for fever, abdominal pain, elevated glucose and UTI. She developed transient akathisia soon after starting linezolid and while continuing metoclopramide. Medications: Trazodone Mirtazapine Clonazepam Midodrine Insulin Pravastatin Cholecalciferol Clonazepam Omeprazole	Sternbach: NO Hunter: NO	NO	NA
12	Teenage male with dyslexia, depression, suicidal ideation and migraine was admitted for seizure and mental status change after overdose with OTC cold medicine. Prolonged hospitalization due to aspiration. On exam he had a fever and brisk reflexes. Upon discharge sertraline dose was reduced and he continued taking zolmitriptan as needed without complications. Medications: Zolmitriptan Sertraline Metoclopramide Propranolol	Sternbach: NO Hunter: NO	YES	Possible (Zolmitriptan, Sertraline)

13	Female in her 30s with bipolar disorder, autoimmune thyroiditis and sleep apnea admitted to the hospital after overdose with phenelzine and zolpidem. Within 24 hours she became unresponsive with fever, hypertension, tachycardia, muscle rigidity, tremor and rhabdomyolysis. Diagnosis was MAOI overdose Medications: Phenelzine Trazodone Risperidone Zolpidem Atenolol	Sternbach: YES (mental status change, hyperreflexia, tremor, fever) Hunter: YES (tremor and hyperreflexia)	NO	NA
14	Male in his 40s with long history of regional sympathetic dystrophy, periodic fever, pulmonary embolism, pericardial and pleural effusions; seronegative polyarthritis and myositis of unknown cause admitted for rhabdomyolysis in the setting of polymicrobial bacteremia. He developed a single episode of unresponsiveness with a brief episode of eye and facial twitching with brief postictal confusion. Serotonins syndrome suspected due to administration of Linezolid for polymicrobial sepsis. Of note, serotonin syndrome was noted previously as side effect of meperidine, and seizures as side effect of tramadol. Medications: Hydromorphone Methadone Tylenol Coumadin Cholecalciferol Citalopram Clonazepam Colace Prednsione	Sternbach: YES (mental status change, hyperreflexia, fever) Hunter: NO	YES	Possible (Sumatriptan, Citalopram) Note: fever was attributed to polymictrobial sepsis

15	Female in her 50s with bipolar disorder and anxiety, long history of opiates use with recent withdrawal presented with weight loss. On exam she had a fine tremor (also previously documented), otherwise normal. Multiple complaints of mental status change, agitation, shivering, blurred vision, change in bowel function and tachycardia. In retrospect these symptoms were considered consistent with serotonin syndrome because she had been prescribed triptans and trazodone, although she reports not taking these medications. Medications: Pirbuterol Zolpidem Estradiol transdermal patch Gabapentin Hydroxyzine Lorazepam Pyridostigmine Perphenazine Omeprazole	Sternbach: NO Hunter: NO	NO	NA
16	Female in her 40s with bipolar disorder evaluated for acute onset of anxiety, restlessness and hot flashes. 5 weeks prior she started on escalating dose of nortriptyline (75 mg) in addition to high dose venlafaxine (300 mg/day), also abruptly stopped clonazepam. On exam she had tachycardia and diaphoresis. She was restless with continuous movements in her legs, muscle tone was increased with questionable clonus. She was treated with cyproheptadine with improvement. Medications: Venlafaxine Nortriptyline Clonazepam Albuterol Ibuprofen Calcium carbonate	Sternbach: YES (mental status change, agitation, hyperreflexia, diaphoresis) Hunter: YES (inducible clonus, diaphoresis)	NO	NA

17	Female in her 50s with depression, fibromyalgia and migraine presented to the ED with sweating, abdominal pain and diarrhea for 10 days. She also had headache and took sumatriptan. On exam she was tachycardic, had mild nystagmus, reflexes are elevated. Venlafaxine was gradually tapered off with improvement. Medications: Sumatriptan Venlafaxine Nortriptyline Albuterol Lansoprazole Lorazepam Riboflavin Sumatriptan Verapamil Vitamin D3 Naproxen Excedrin Migraine Tylenol	Sternbach: YES (hyperreflexia, diaphoresis, diarrhea) Hunter: NO	YES	Definite (Sumatriptan, Venlafaxine) Note: clinical chart indicates that sumatriptan was taken after the onset of symptoms