SCHIZOPHRENIA SPECTRUM AND OTHER PSYCHOTIC DISORDERS

Substance/Medication-Induced Psychotic Disorder

SIPD

DSM-5-TR 291.9, 292.9 | ICD-10-CM F1X.159, F1X.259, F1X.959

Delusions or hallucinations arising during intoxication, withdrawal, or medication exposure, beyond what the agent alone would be expected to produce.

FIRST-EPISODE PSYCHOSIS	TYPICAL ONSET	SEX RATIO	COURSE
7-25% of first-episode cases	Any age; peaks late teens-30s	Male predominant	~25% convert to schizophrenia

CLINICAL PICTURE

- Psychosis emerges during intoxication or within a month of withdrawal, with severity clearly exceeding what the agent's usual effects would produce.
- Stimulant psychosis features persecutory delusions, tactile hallucinations of insects on or under the skin, and extreme hypervigilance with clear orientation.
- Cannabis-related psychosis brings paranoia, ideas of reference, and depersonalization, most often in high-potency or synthetic cannabinoid users.
- Alcohol-related hallucinosis produces vivid auditory hallucinations with an intact sensorium, distinguishing it from the clouded state of delirium tremens.
- Medication causes include corticosteroids, anticholinergics, levodopa, interferon, isotretinoin, chloroquine, and high-dose prescription stimulants.
- Agitation, hyperthermia, and violence risk peak in stimulant and synthetic cannabinoid presentations and drive most emergency department contacts.

DIAGNOSTIC CRITERIA AT A GLANCE

- Prominent delusions or hallucinations that developed during or soon after substance intoxication, withdrawal, or exposure to a medication.
- The implicated substance or medication must be capable of producing the symptoms, established by history, physical examination, or laboratory findings.
- Not better explained by an independent psychotic disorder, which is suggested by symptoms preceding use or persisting well beyond acute withdrawal.
- The symptoms do not occur exclusively during delirium and cause clinically significant distress or functional impairment.
- Specify the substance, whether onset occurred during intoxication or withdrawal, and code with or without a comorbid substance use disorder.

NEUROBIOLOGY & PHYSIOLOGY

- Stimulants flood striatal synapses with dopamine through transporter reversal, producing the closest available pharmacologic model of positive symptoms.
- Repeated stimulant exposure sensitizes mesolimbic dopamine release, so psychosis recurs faster and at progressively lower doses with each episode.
- THC acts at CB1 receptors on GABAergic interneurons and disrupts cortical synchrony; potency and synthetic full agonists drive the greatest risk.
- NMDA antagonists such as ketamine and phencyclidine reproduce positive, negative, and cognitive symptoms, supporting the glutamatergic model of psychosis.
- Alcohol withdrawal psychosis reflects glutamate rebound after chronic GABAergic suppression, with thiamine deficiency compounding the vulnerability.
- Polygenic risk for schizophrenia is elevated among those whose substance-induced psychosis later converts, indicating an unmasked underlying liability.

PSYCHOLOGICAL MECHANISMS

- Users often continue the substance to relieve the distress the psychosis creates, closing a self-reinforcing loop that blocks any spontaneous recovery.
- Sleep deprivation during stimulant binges is an independent psychotogenic factor, and restoring sleep alone resolves many milder presentations.
- Attribution matters clinically: patients who see the drug as the cause engage with abstinence, while those who do not relapse into psychosis quickly.
- Childhood adversity and trauma exposure raise both substance use and psychosis proneness, so the two conditions share upstream risk.
- Denial is reinforced by long stretches of use without psychosis, which undermines the credibility of abstinence advice at exactly the wrong moment.

DIFFERENTIAL & COMORBIDITY

- A primary psychotic disorder is suggested by symptoms preceding substance use, persistence beyond a month of abstinence, or a strong family history.
- Delirium is separated by fluctuating attention and disorientation, whereas substance-induced psychosis characteristically leaves the sensorium clear.
- Consider medical causes uncovered by heavy use: head injury, HIV, hepatic encephalopathy, thiamine deficiency, and endocarditis in injection drug users.
- Roughly a quarter of cases convert to schizophrenia, with cannabis-induced episodes carrying the highest rate, so follow these patients for years.
- Substance use disorder, PTSD, mood disorders, and antisocial or borderline traits are frequent comorbidities and set the intensity of aftercare.

Treatment EVIDENCE-BASED MANAGEMENT

PHARMACOLOGIC

- Manage acute agitation with **lorazepam 1-2 mg** first in stimulant and withdrawal states, since benzodiazepines are preferred over antipsychotics here.
- Short-course antipsychotics such as **olanzapine 5-10 mg** or **haloperidol 2-5 mg** control persistent psychosis; watch QTc and seizure threshold.
- Alcohol withdrawal requires symptom-triggered benzodiazepine dosing guided by **CIWA-Ar**, plus **thiamine 500 mg IV** given before any glucose load.
- Taper the antipsychotic within weeks to a few months once psychosis clears, since indefinite maintenance implies a primary psychotic disorder instead.
- Treat the underlying use disorder directly with **naltrexone**, **buprenorphine**, or contingency management, which has the strongest stimulant evidence.

PSYCHOTHERAPY

- **Motivational interviewing** builds commitment to abstinence during the window when the psychotic episode itself has made consequences vivid.
- **Contingency management** with escalating incentives remains the most effective psychosocial treatment for stimulant use disorder.
- Integrated dual-diagnosis treatment outperforms parallel or sequential care by addressing psychosis and substance use within one team.
- **CBT for substance use** identifies high-risk situations, builds refusal skills, and installs a written relapse prevention plan.
- Family involvement and community reinforcement approaches improve retention and supply collateral information about ongoing use.

ADJUNCT & SUPPORTIVE

- Obtain expanded urine toxicology, since standard panels miss synthetic cannabinoids, cathinones, and many designer stimulants entirely.
- Observe for at least 24 to 48 hours before committing to a diagnosis, because most substance-induced psychosis improves substantially in that window.
- Re-evaluate at 1 month and 6 months of abstinence, since persistent symptoms reclassify the case as a primary psychotic disorder.
- Use **ASAM criteria** to set residential versus outpatient level of care, and provide harm reduction including take-home naloxone.
- Document the specific agent and its temporal relationship to symptoms, because this diagnosis is frequently revised by later clinicians.

CLINICAL PEARLS

- Symptoms preceding use, or persisting a month past abstinence, mean a primary psychosis.
- About one in four substance-induced psychoses converts to schizophrenia.
- In stimulant toxicity reach for benzodiazepines before antipsychotics.

References

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NOTE

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