Case 1: Schizophrenia

They told me so

Ryan is a 21-year-old male brought to the clinic by his parents after his teachers expressed concerns that he was failing his university examinations and had poor attendance. Over the past six months, Ryan had accused his classmate of inserting thoughts into his head and controlling his actions. He reported this as true because he heard 'the voices' warning him. His friends noticed that Ryan was more withdrawn, and he was seen talking to himself. Ryan denied taking recreational drugs, and a routine drug screen performed last month revealed no abnormalities.

- **Question 1: What are the diagnosis and differential diagnoses?**

Ryan accused his classmate of working for a sinister network of aliens called 'The Organisation.' They reference him on the radio whenever the radio uses a word that starts with 'R'. When these ideas were challenged, he rebuffed your assertions that perhaps he might be mistaken.

- **Question 2: What type of delusion is being demonstrated?**

You ask Ryan about the voices that he hears. He describes a male voice coming from outside his head, which talks to him throughout the day. The voices occasionally comment on his actions, for example 'Ryan is drinking the cup of coffee now' and at other times suggest that his classmate is going to hurt him 'They are coming to get you'. There had been times when he heard his thoughts spoken out loud, which bothered him greatly.

- **Question 3: How would you describe his hallucinations?**

With the constellation of symptoms presented, you diagnose Ryan with schizophrenia. Ryan's cousin (Jake) was also diagnosed with schizophrenia, but had a very different presentation. Jake was found to be increasingly quiet, and when he did speak, he was often incoherent. He refused to leave

his room and did not appear to be excited over anything, often giving a blank stare with little emotion shown.

- **Question 4: How will you explain Jake's seemingly different presentation of schizophrenia?**

Ryan's parents suspect that he might have used recreational drugs in the past and wonder if that might have contributed to the development of his psychotic episode.

- **Question 5: Which illicit substance has a known association with the development of schizophrenia?**

Now that he has been diagnosed with psychosis, Ryan's parents want to know what investigations will be done.

- **Question 6: How will you investigate Ryan's first presentation of psychosis?**

Having heard his conspiracy theories, you ask Ryan if he feels safe currently. Ryan replies that he is worried "The Organisation" is plotting to abduct him and states that he would rather die than be abducted. He intends to hurt himself and shows you a kitchen knife he has hidden in his bag.

- **Question 7: What is the next step of management?**

Ryan is admitted, and investigations return as unremarkable. You explain to Ryan's parents that early intervention may improve cognition and will be in his best interest. His parents cautiously accept the treatment plan. However, his parents mention that Ryan was previously bullied for his heavy weight, and are worried about the side effects.

- **Question 8: Which antipsychotic medications would you avoid for Ryan?**

Ryan was started on haloperidol. Unfortunately, despite treatment with haloperidol and subsequently risperidone for six weeks each at a therapeutic dose, he remains symptomatic. He is diagnosed with treatment-resistant schizophrenia (TRS).

- **Question 9: What is the definition of TRS?**

Having diagnosed Ryan with TRS, clozapine is commenced.

- **Question 10: What are the potentially life-threatening side effects of clozapine ?**

Ryan's condition stabilises on clozapine and he reports compliance with his medications. While the risk of extrapyramidal side effects (EPSEs) with clozapine is low, he remains concerned about the side effects of antipsychotics.

- **Question 11: What are EPSEs and what are the different types?**

Answers to Case 1

Question 1
What are the diagnosis and differential diagnoses?

Answer
Schizophrenia

Apart from organic causes, the main differentials to consider for symptoms of psychosis without prominent affective symptoms would be:

- Acute and transient psychotic disorder
- Delusional disorder
- Schizotypal disorder

Explanation

Diagnosis of schizophrenia

At least two of the following symptoms must be present (by the individual's report or through observation by the clinician or other informants) most of the time for a period of 1 month or more. At least one of the qualifying symptoms should be from items (1) to (4) below:

1. Delusions
2. Hallucinations
3. Disorganised thinking
4. Passivity phenomenon
5. Negative symptoms
6. Grossly disorganised behaviour
7. Psychomotor disturbances (e.g., catatonia)

Specify if the first episode or multiple episodes, are continuous or in remission.

The onset of schizophrenia generally occurs in late adolescence or early adulthood. Auditory hallucinations are the most common form of hallucination, with an estimated prevalence of 40–80% [1, 2].

A diagnosis of delusional disorder is less likely as there is impairment in functioning with odd behaviour and prominent hallucinations. The history given in the vignette suggests an acute deterioration, which is not typically seen in personality disorders. Acute and transient psychotic disorder often lasts for a few days up to a month and does not exceed three months. Schizotypal disorder persists for at least two years and the individual must not have fulfilled the criteria for schizophrenia.

First-rank symptoms are commonly seen in schizophrenia:

First-rank symptoms in schizophrenia

- Hearing thoughts spoken aloud
- Third-person hallucinations
- Auditory hallucinations in the form of a 'running commentary'
- Somatic (bodily, tactile) hallucinations
- Thought withdrawal or insertion
- Thought broadcasting
- Delusional perception
- Passivity (feelings or actions felt as influenced by external forces)

Exam Essentials

- Schneider's **first-rank symptoms** of schizophrenia – **ABCD**
  - **A**uditory hallucinations
  - **B**roadcasting, insertion, withdrawal
  - **C**ontrol, passivity
  - **D**elusional perception
- There are **two age peaks** of schizophrenia: early 20s and 40s
- **Late-onset schizophrenia**: aged 40 to 60 years

- **Very late-onset schizophrenia**: > 60 years
- Although first-rank symptoms are highly prevalent in patients with schizophrenia, they **should not be used as a sole diagnostic tool** due to their higher specificity but lower sensitivity

Clinical Pearls

- While auditory hallucinations are more common, visual hallucinations are also present in schizophrenia. The **visual hallucinations** experienced are **often unformed**, such as glowing orbs or flashes of colour
- If the patient presents with **predominant non-auditory hallucinations** (e.g., visual, olfactory, gustatory), it is important **to rule out organic causes** (e.g., epilepsy, encephalitis, brain tumours)

Question 2
What type of delusion is being demonstrated?

Answer
Delusions of reference

Explanation
A delusion is defined as a firmly maintained false belief contradicted by reality; idiosyncratic, incorrigible and preoccupying. Delusion of reference is characterised by the erroneous belief that innocuous events have strong personal significance, with complete conviction. Approximately 80% [2] of people with schizophrenia have delusions.

Impairment of insight is common and a delusional explanation for their hallucinations is often elicited. Bizarre delusions are implausible and absurd to same-culture peers and do not derive from ordinary life experiences (e.g., the belief that one's organ has been replaced entirely with another's, although there are no scars or evidence of such). A non-bizarre delusion is one that, while not true, can be derived from ordinary life experience with the possibility of it being true (e.g., believing that valuables have been stolen).

Exam Essentials

- Features of delusion can be remembered as three 'U's:
  - **U**ntrue
  - **U**nshared
  - **U**nshakeable

Clinical Pearls

- The differences between a delusion and an overvalued idea lie in the **degree of conviction and how it is being derived**

Question 3
How would you describe his hallucinations?

Answer
Second- and third-person auditory hallucinations in the form of a 'running commentary' with the presence of a thought echo.

Explanation
Perception is the organisation, identification and interpretation of sensory information to represent and understand the presented information or environment. Hallucinations are false perceptions that are not in any way distortions of a real perception but spring up on their own as something quite new and occur simultaneously with and alongside real perception. They may take the form of noises, music, single words, brief phrases, or whole conversations.

Approach to hallucinations should include:

1. Where?

   The first distinction is between hallucinations and pseudohallucinations. Ask where the voices are from and assess the degree of insight lost.

	Hallucination	Pseudohallucination
Space	External space	Inner subjective (not seeming to the patient to represent external reality, being located within the mind)
Insight	Impaired	Intact
Control	Cannot be willfully modified	Can be modified by will (initiated or interrupted) [3]

2. Who?
   Assess who the voice(s) have been identified as.
3. How?
   If it is an auditory hallucination, distinguish between the second person (voice speaking to the person addressing him as 'you') and the third person (voice talking about the person as 'he' or 'she'). Third-person auditory hallucinations are part of the first-rank symptoms in schizophrenia.
4. What?
   Examine the content of the hallucinations and determine if they are mood congruent or incongruent. Auditory hallucination may come in the form of a running commentary or voices arguing etc.

A thought echo refers to a form of auditory hallucination where the person hears his or her thoughts aloud after thinking them.

Clinical Pearls

- **Check for the presence of command hallucinations and passivity** as part of the risk assessment – higher risk if the patient has both

Question 4
How will you explain Jake's seemingly different presentation of schizophrenia?

Answer
Jake has predominantly negative symptoms of schizophrenia, whereas Ryan presents with predominantly positive symptoms of schizophrenia.

Explanation
Positive symptoms are characterised by delusions and hallucinations.

Negative symptoms are characterised by deficit symptoms leading to the absence or diminution of normal processes and functioning. They are often listed as the six 'A's: anhedonia (inability to feel pleasure), apathy (disinterest in daily activities), avolition (decreased motivation), alogia (decreased spontaneous speech), affective flattening (lack of emotional expressivity, but not depressed) and asociality (social withdrawal).

Patients may present in a varied manner, with features consisting of both positive and negative symptoms.

Exam Essentials

- **6 'A's** of negative symptoms:
  - **A**nhedonia
  - **A**pathy
  - **A**volition
  - **A**logia
  - **A**ffect flattening
  - **A**sociality

Clinical Pearls

- Differentials for apathy include:
  - Schizophrenia (negative symptoms)
  - Depression
  - Parkinsonism
  - Behavioural-variant frontotemporal neurocognitive disorder
  - Drug-induced (e.g., amotivation syndrome from chronic cannabis use)
  - Drug withdrawal (e.g., 'crash' from cocaine or stimulant use)

Question 5
Which illicit substance has a known association with the development of schizophrenia?

Answer
Cannabis

Explanation
Cannabis use has been associated with a two- to threefold increased prevalence of schizophrenia and schizophrenia spectrum disorders [4]. The reverse causation hypothesis also postulates that schizophrenia risk itself predicts the likelihood of cannabis initiation and a genetic predisposition for schizophrenia was associated with increased use of cannabis [5, 6].

While other drugs do not have as clear an association with the development of schizophrenia, their use can still precipitate an acute psychotic episode:

Recreational drugs	Alcohol Stimulants (e.g., amphetamine, cocaine, cannabis) Hallucinogens (e.g., phencyclidine, MDMA, LSD, ketamine) Inhalants
Medications	Steroids Anticholinergics Anti-Parkinson's disease drugs

Exam Essentials

- Cannabis users who have **homozygous VAL/VAL alleles in the COMT genotype** have a higher risk of more severe psychosis [7]

Clinical Pearls

- The lifetime prevalence of co-morbid substance use disorder in patients with schizophrenia is 74% [8]
- The risk of schizophrenia increases with the younger onset of cannabis use [9]

Question 6
How will you investigate Ryan's first presentation of psychosis?

Answer

Category	Investigations
Point-of-care test	Electrocardiogram
Biochemical	Electrolytes Liver panel Calcium Full blood count (FBC) Glucose Urine drug screen Urine microscopy and culture* HIV and syphilis screening* Thyroid function test* Parathyroid hormone* Cortisol* Urine and blood toxicology screen* Autoimmune workup including ANA, SLE panels, serum autoimmune encephalitis screens* Lumbar puncture*
Imaging	CT or MRI brain (in the presence of suggested neurological abnormality or persistent cognitive impairment)* Electroencephalogram (if there is a history of seizure or symptoms suggestive of temporal lobe epilepsy)*

* When suggested by history/examination.

Explanation

Psychosis can be a symptom of an underlying acute medical illness or chronic condition. Hence it would be prudent to rule out medical causes and medication and substance-related causes before considering primary psychiatric causes of the psychosis.

Exam Essentials

Symptoms suggestive of organic causes:

- Sudden onset
- Predominant non-auditory hallucinations (visual, gustatory, olfactory)
- Fluctuating altered mental status