PSYCHOSIS

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PSYCHOSIS

- Psychosis is a break from reality involving delusions, perceptual disturbances, and/or disordered thinking.

- Schizophrenia and substance-induced psychosis are examples of commonly diagnosed psychotic disorders.

DISORDERED THOUGHT

- Includes disorders of thought *content and thought process (see chapter on Examination* and Diagnosis for further clarification):

- Disorders of thought *content reflect the patient's beliefs, ideas, and interpretations* of his or her surroundings. (*Examples: Paranoid delusions*, ideas of reference, and loss of ego boundaries)

- Disorders of thought *process involve the manner in which the patient* links ideas and words together. (*Examples: Tangentiality, circumstantiality,* loosening of associations, thought blocking, perseveration, etc.)

DELUSIONS

- Fixed, false beliefs that cannot be altered by rational arguments and cannot be accounted for by the cultural background of the individual

- **Types**
  - **Paranoid delusion—irrational belief that one is being persecuted** ("**The** CIA is after me and taps my phone.")
  - **Ideas of reference—belief that some event is uniquely related to the** individual ("Jesus is speaking to me through TV characters.")
  - **Thought broadcasting—belief that one's thoughts can be heard by others**
  - **Delusions of grandeur—belief that one has special powers beyond** those of a normal person ("I am the all-powerful son of God and I shall bring down my wrath on you if I cannot have a smoke.")
  - **Delusions of guilt—false belief that one is guilty or responsible for** something ("I caused the flood in Mozambique.")

PERCEPTUAL DISTURBANCES *(HALLUCINATIONS VERSUS ILLUSIONS)*

- **Hallucination**
  - Sensory perception without an actual external stimulus

- **Types**
  - **Auditory hallucination—most commonly exhibited by schizophrenic** patients
  - **Visual hallucination—commonly seen with drug intoxication**
  - **Olfactory hallucination—usually an aura associated with epilepsy**
  - **Tactile hallucination—usually secondary to drug abuse or alcohol withdrawal**

- **Illusion**
  - Misinterpretation of an existing sensory stimulus (such as mistaking a shadow for a cat)

DI FFERENTIAL DIAGNOSIS OF PSYCHOSIS

- Psychosis secondary to general medical condition
- Substance-induced psychotic disorder
- Delirium/Dementia
- Bipolar disorder
- Major depression with psychotic features
- Brief psychotic disorder
- Schizophrenia
- Schizophreniform disorder
- Schizoaffective disorder
- Delusional disorder

PSYCHOSIS SECONDARY TO GENERAL MEDICAL CONDITION

- Medical causes of psychosis include:

1. ***CNS disease (cerebrovascular disease, multiple sclerosis, neoplasm***, Parkinson's disease, Huntington's chorea, temporal lobe epilepsy, encephalitis, prion disease)

2. ***Endocrinopathies (Addison's/Cushing's disease, hyper/hypothyroidism***, hyper/hypocalcemia, hypopituitarism)

3. ***Nutritional/Vitamin deficiency states (B12, folate, niacin)***

4. ***Other (connective tissue disease [systemic lupus erythematosus, temporal*** arteritis], porphyria)

- **DSM-IV criteria for psychotic disorder secondary to a general medical condition** include:
  - Prominent hallucinations or delusions
  - Symptoms do not occur only during episode of delirium
  - Evidence to support medical cause from lab data, history, or physical

PSYCHOSIS SECONDARY TO MEDICATION OR SUBSTANCE USE

- Causes of medication/substance-induced psychosis include antidepressants, antiparkinsonian agents, antihypertensives, antihistamines, anticonvulsants, digitalis, beta blockers, antituberculosis agents, corticosteroids, hallucinogens, amphetamines, opiates, bromide, heavy metal toxicity, and alcohol.

- **DSM-IV Criteria**
  - Prominent hallucinations or delusions
  - Symptoms do not occur only during episode of delirium
  - Evidence to support medication or substance-related cause from lab data, history, or physical
  - Disturbance is not better accounted for by a psychotic disorder that is not substance-induced.

SCHIZOPHRENIA

- Schizophrenia is a psychiatric disorder characterized by a constellation of abnormalities in thinking, emotion, and behavior.
- There is no single symptom that is pathognomonic, and the disease can produce a wide spectrum of clinical pictures.
- It is usually chronic and debilitating.

- **Positive and Negative Symptoms**
  - In general, the symptoms of schizophrenia are broken up into two categories:
  - **Positive symptoms—hallucinations, delusions, bizarre behavior, or** thought disorder
  - **Negative symptoms—blunted affect, anhedonia, apathy, and inattentiveness.**
    - Although negative symptoms are the less dramatic of the two types, they are considered by some to be at the "core" of the disorder.

THREE PHASES

- Symptoms of schizophrenia usually present in three phases:

1. **Prodromal—decline in functioning that precedes the first psychotic** episode. The patient may become socially withdrawn and irritable. He or she may have physical complaints and/or newfound interest in religion or the occult.

2. **Psychotic—perceptual disturbances, delusions, and disordered thought** process/content

3. **Residual—occurs between episodes of psychosis. It is marked by flat affect,** social withdrawal, and odd thinking or behavior (negative symptoms). Patients can continue to have hallucinations even with treatment.

DIAGNOSIS OF SCHIZOPHRENIA

- **DSM-IV Criteria**
  - *Two or more of the following must be present for at least 1 month:*
    1. **Delusions**
    2. **Hallucinations**
    3. **Disorganized speech**
    4. **Grossly disorganized or catatonic behavior**
    5. **Negative symptoms (such as flattened affect)**

- Must cause significant social or occupational functional deterioration
- Duration of illness for at least 6 months (including prodromal or residual periods in which above criteria may not be met)
- Symptoms not due to medical, neurological, or substance-induced disorder

SUBTYPES OF SCHIZOPHRENIA

- Patients are further subdivided into the following five subtypes:

1. **Paranoid type—highest functioning type, older age of onset. Must** meet the following criteria:
   - Preoccupation with one or more delusions or frequent auditory hallucinations
   - No predominance of disorganized speech, disorganized or catatonic behavior, or inappropriate affect

2. **Disorganized type—poor functioning type, early onset. Must meet the** following criteria:
   - Disorganized speech
   - Disorganized behavior
   - Flat or inappropriate affect

3. Catatonic type—rare. Must meet at least two of the following criteria:

- Motor immobility
- Excessive purposeless motor activity
- Extreme negativism or mutism
- Peculiar voluntary movements or posturing
- **Echolalia or echopraxia**

4. Undifferentiated type—characteristic of more than one subtype or none of the subtypes

5. Residual type—prominent *negative symptoms (such as flattened affect* or social withdrawal) with only minimal evidence of positive symptoms (such as hallucinations or delusions)

PSYCHIATRIC EXAM OF SCHIZOPHRENICS

- The typical findings in schizophrenic patients on exam include:
  - Disheveled appearance
  - Flattened affect
  - Disorganized thought process
  - Intact memory and orientation
  - Auditory hallucinations
  - Paranoid delusions
  - Ideas of reference (feel references are being made to them by the television or newspaper, etc.)
  - Concrete understanding of similarities/proverbs
  - Lack insight into their disease

EPIDEMIOLOGY

- Schizophrenia affects approximately 1% of people over their lifetime.
- Men and women are equally affected but have different presentations and outcomes:
- Men tend to present around 20 years of age.
- Women present closer to 30 years of age.

- The course of the disease is generally more severe in men, as men tend to have more negative symptoms and are less able to function in society.
- Schizophrenia rarely presents before age 15 or after age 45.
- There is a strong genetic predisposition:
  - 50% concordance rate among monozygotic twins
  - 40% risk of inheritance if both parents have schizophrenia
  - 12% risk if one first-degree relative is affected

- There is a strong association with substance use which may be a form of self medication and depression.
- Postpsychotic depression occurs in 50% of patients.

DOWNWARD DRIFT

- Lower socioeconomic groups have higher rates of schizophrenia.
- This may be due to the **downward drift hypothesis, which postulates that people suffering** from schizophrenia are unable to function well in society and hence enter lower socioeconomic groups.
- Many homeless people in urban areas suffer from schizophrenia.

PATHOPHYSIOLOGY OF SCHIZOPHRENIA: THE DOPAMINE HYPOTHESIS

- Though the exact cause of schizophrenia is not known, it appears to be partly related to increased dopamine activity in certain neuronal tracts.

- Evidence to support this hypothesis is that most antipsychotics that are successful in treating schizophrenia are dopamine receptor antagonists.

- In addition, cocaine and amphetamines increase dopamine activity and can lead to schizophrenic-like symptoms.

- **Theorized Dopamine Pathways Affected in Schizophrenia**
  - *Prefrontal cortical—responsible for negative symptoms*
  - *Mesolimbic—responsible for positive symptoms*
  - **Other Important Dopamine Pathways Affected by Neuroleptics**
    - *Tuberoinfundibular—blocked by neuroleptics, causing hyperprolactinemia*
    - *Nigrostriatal—blocked by neuroleptics, causing extrapyramidal side effects*

OTHER NEUROTRANSMITER ABNORMALITIES IMPLICATED IN SCHIZOPHRENIA

- **Elevated serotonin—some of the atypical antipsychotics (such as risperidone** and clozapine) antagonize serotonin (in addition to their effects on dopamine).

- **Elevated norepinephrine—long-term use of antipsychotics has been** shown to decrease activity of noradrenergic neurons.

- **Decreased gamma-aminobutyric acid (GABA)—recent data support the**hypothesis that schizophrenic patients have a loss of GABAergic neurons in the hippocampus; this loss might indirectly activate dopaminergic and noradrenergic pathways.

PROGNOSTIC FACTORS

- Schizophrenia is usually chronic and debilitating.
- Forty to 50% of patients remain significantly impaired after their diagnosis, while only 20 to 30% function fairly well in society with medication.
- Several factors are associated with a better or worse prognosis:

- **Associated with Better Prognosis**
  - Later onset
  - Good social support
  - Positive symptoms
  - Mood symptoms
  - Acute onset
  - Female sex
  - Few relapses
  - Good premorbid functioning

- **Associated with Worse Prognosis**
  - Early onset
  - Poor social support
  - Negative symptoms
  - Family history
  - Gradual onset
  - Male sex
  - Many relapses
  - Poor premorbid functioning (social isolation, etc.)

TREATMENT

- A multimodality approach is the most effective, and therapy must be tailored to the needs of the specific patient. **Pharmacologic treatment consists primarily** of antipsychotic medications, otherwise known as neuroleptics. (For more detail, see Psychopharmacology chapter.)

- **Typical neuroleptics: *Chlorpromazine*, *thioridazine*, *trifluoperazine*,** *haloperidol*. *These are dopamine (mostly D2) antagonists. They are classically* better at treating positive symptoms than negative. They have important side effects and sequelae such as extrapyramidal symptoms, neuroleptic malignant syndrome, and tardive dyskinesia (see below).

- **Atypical neuroleptics: *Risperidone*, *clozapine*, *olanzapine*, *quetiapine*,** *aripiprazole, ziprosidone. These antagonize serotonin receptors (5-HT2)* as well as dopamine receptors. Atypical neuroleptics are classically better at treating negative symptoms than traditional neuroleptics. They have a much lower incidence of extrapyramidal side effects.

- medications should be taken for at least 4 weeks before efficacy is determined.

- If the medication fails, it is appropriate to switch to another medication in a different class.

- **Behavioral therapy attempts to improve patients' ability to function in society.**
- Patients are helped through a variety of methods to improve their social skills, become self-sufficient, and act appropriately in public.
- **Family therapy** and **group therapy are also useful adjuncts.**

IMPORTANT SIDE EFFECTS AND SEQUELAE OF ANTIPSYCHOTIC MEDICATIONS

- Side effects of antipsychotic medications include:

1. Extrapyramidal symptoms (especially with the use of high-potency traditional antipsychotics):

- Dystonia (spasms) of face, neck, and tongue
- Parkinsonism (resting tremor, rigidity, bradykinesia)
- Akathisia (feeling of restlessness)
- *Treatment: Antiparkinsonian agents (benztropine, amantadine, etc.),* benzodiazepines

2. Anticholinergic symptoms (especially low-potency traditional antipsychotics

- and atypical antipsychotics):
- Dry mouth, constipation, blurred vision
- *Treatment: As per symptom (eyedrops, stool softeners, etc.)*

3. Tardive dyskinesia (high-potency antipsychotics):

- Darting or writhing movements of face, tongue, and head
- *Treatment: Discontinue offending agent and substitute atypical neuroleptic.*
- Benzodiazepines, beta blockers, and cholinomimetics may be
- used short term. The movements often persist despite withdrawal of
- the offending drug.

4. **Neuroleptic malignant syndrome (high-potency antipsychotics):**
   - Confusion, high fever, elevated blood pressure, tachycardia, “lead pipe” rigidity, sweating, and greatly elevated creatine phosphokinase (CPK) levels
   - Can be life-threatening. Is not an “allergic” reaction to a drug.

5. **Weight gain, sedation, orthostatic hypotension, electrocardiogram** changes, hyperprolactinemia (leading to gynecomastia, galactorrhea, amenorrhea, diminished libido, and impotence), hematologic effects (agranulocytosis may occur with *clozapine, necessitating weekly blood* draws when this medication is used), ophthalmologic conditions (*thioridazine* may cause irreversible retinal pigmentation at high doses; deposits in lens and cornea may occur with *chlorpromazine)*, *dermatologic* conditions (such as rashes and photosensitivity), hyperlipemia, and glucose intolerance.

SCHIZOPHRENIFORM DISORDER

- DIAGNOSIS AND DSM-IV CRITERIA
  - The diagnosis of schizophreniform disorder is made using the same DSM-IV criteria as schizophrenia.
  - The only difference between the two is that in schizophreniform disorder the symptoms have lasted between 1 and 6 months, whereas in schizophrenia the symptoms must be present for more than 6 months.
- PROGNOSIS
  - One third of patients recover completely; two thirds progress to schizoaffective disorder or schizophrenia.
- TREATMENT
  - Hospitalization, 3- to 6-month course of antipsychotics, and supportive psychotherapy

SCHIZOAFFECTIVE DISORDER

- DIAGNOSIS AND DSM-IV CRITERIA
  - The diagnosis of schizoaffective disorder is made in patients who:
    - Meet criteria for either major depressive episode, manic episode, or mixed episode (during which criteria for schizophrenia are also met)
    - Have had delusions or hallucinations for 2 weeks in the absence of mood disorder symptoms (this condition is necessary to differentiate schizoaffective disorder from mood disorder with psychotic features)
    - Have mood symptoms present for substantial portion of psychotic illness
    - Symptoms not due to general medical condition or drugs

- PROGNOSIS
  - Better than schizophrenia but worse than mood disorder

- TREATMENT
  - Hospitalization and supportive psychotherapy
  - Medical therapy: Antipsychotics as needed for short-term control of psychosis; mood stabilizers, antidepressants, or electroconvulsive therapy
  - (ECT) as needed for mania or depression

BRIEF PSYCHOTIC DISORDER

- DIAGNOSIS AND DSM-IV CRITERIA
  - Patient with psychotic symptoms as defined for schizophrenia; however, the symptoms last from 1 day to 1 month.
  - Symptoms must not be due to general medical condition or drugs.
  - This is a rare diagnosis, much less common than schizophrenia.
- PROGNOSIS
  - Fifty to 80% recovery rate; 20 to 50% may eventually be diagnosed with schizophrenia or mood disorder.
- TREATMENT
  - Brief hospitalization, supportive psychotherapy, course of antipsychotics for psychosis itself and/or benzodiazepines for agitation

Comparing Time Courses and Prognoses of Psychotic Disorders

- **Time Course**
  - < 1 month—brief psychotic disorder
  - 1–6 months—schizophreniform disorder
  - > 6 months—schizophrenia

- **Prognosis from Best to Worst**
  - Mood disorder > brief psychotic disorder > schizoaffective disorder > schizophreniform disorder > schizophrenia

DELUSIONAL DISORDER

- Delusional disorder occurs more often in older patients (after age 40), immigrants, and the hearing impaired.

- DIAGNOSIS AND DSM-IV CRITERIA
  - To be diagnosed with delusional disorder, the following criteria must be met (see Table 3-1):
    - Nonbizarre, fixed delusions for at least 1 month
    - Does not meet criteria for schizophrenia
    - Functioning in life not significantly impaired

TABLE 3-1. Schizophrenia vs. Delusional Disorder

Schizophrenia	Delusional Disorder
▪ Bizarre delusions (or nonbizarre)	▪ Nonbizarre delusions (never bizarre)
▪ Daily functioning significantly impaired	▪ Daily functioning not significantly impaired

▪ Must have two or more of the following:
  ▪ Delusions
  ▪ Hallucinations
  ▪ Disorganized speech
  ▪ Disorganized behavior
  ▪ Negative symptoms
	▪ Does not meet the criteria for schizophrenia as described in left column

TYPES OF DELUSIONS

- Patients are further categorized based on the types of delusions they experience:
  - Erotomanic type—delusion revolves around love (Eros is the goddess of love)
  - Grandiose type—inflated self-worth
  - Somatic type—physical delusions
  - Persecutory type—delusions of being persecuted
  - Jealous type—delusions of unfaithfulness
  - Mixed type—more than one of the above

- PROGNOSIS
  - 50% full recovery, 20% decreased symptoms, and 30% no change

- TREATMENT
  - Psychotherapy may be helpful. Antipsychotic medications are often ineffective, but a course of them should be tried (usually a high-potency traditional antipsychotic or one of the newer atypical antipsychotics is used).

SHARED PSYCHOTIC DISORDER

- DIAGNOSIS AND DSM-IV CRITERIA
  - Also known as *folie à deux*, *shared psychotic disorder is diagnosed when a patient* develops the same delusional symptoms as someone he or she is in a close relationship with.
  - Most people suffering from shared psychotic disorder are family members.

- PROGNOSIS
  - Twenty to 40% will recover upon removal from the inducing person.

- TREATMENT
  - The first step is to separate the patient from the person who is the source of shared delusions (usually a family member with an underlying psychotic disorder).
  - Psychotherapy should be undertaken, and antipsychotic medications should be used if symptoms have not improved in 1 to 2 weeks after separation.

CULTURE-SPECI FIC PSYCHOSES

These are psychoses seen only within certain cultures:

	Psychotic Manifestation	Culture
Koro	Patient believes that his penis is shrinking and will disappear, causing his death.	Asia
Amok	Sudden unprovoked outbursts of violence of which the person has no recollection. Person often commits suicide afterwards.	Malaysia, Southeast Asia
Brain fag	Headache, fatigue, and visual disturbances in male students	Africa

QUICK AND EASY DISTINGUISHING FEATURES

- **Schizophrenia—lifelong psychotic disorder**
- **Schizophreniform—schizophrenia for < 6 months**
- **Schizoaffective—schizophrenia + mood disorder**
- **Schizotypal (personality disorder)—paranoid, odd or magical beliefs,** eccentric, lack of friends, social anxiety. Criteria for true psychosis are not met.
- **Schizoid (personality disorder)—withdrawn, lack of enjoyment from social** interactions, emotionally restricted

ANTIPSYCHOTICS

- Antipsychotics are used to treat psychotic disorders and psychotic symptoms associated with other psychiatric and medical illnesses.

- *Traditional antipsychotics* are classified according to potency and work by blocking dopamine receptors.

- *Atypical (newer) antipsychotics block both dopamine and serotonin* receptors; however, their effect on dopamine is weaker, so they are associated with fewer side effects.

TRADITIONAL ANTIPSYCHOTICS

- **Low potency: Have a lower affinity for dopamine receptors and therefore a** higher dose is required. Remember, *potency refers to the action on dopamine* receptors, not the level of efficacy.
  - **Chlorpromazine (Thorazine)**
  - **Thioridazine (Mellaril)**

- These antipsychotics have a higher incidence of anticholinergic and antihistaminic side effects than high-potency traditional antipsychotics.
- They have a lower incidence of extrapyramidal side effects (EPSEs) and neuroleptic malignant syndrome. (See below for detailed description of side effects.)

- **High potency: Have greater affinity for dopamine receptors, and therefore a** relatively low dose is needed to achieve effect.
  - **Haloperidol (Haldol)**
  - **Fluphenazine (Prolixin)**
  - **Trifluoperazine (Stelazine)**
  - **Perphenazine (Trilafon)**
  - **Pimozide (Orap)**

- These antipsychotics have a higher incidence of **EPSEs and neuroleptic malignant** syndrome than low-potency traditional antipsychotics (see below).
- They have a lower incidence of anticholinergic and antihistaminic side effects.
- Both traditional and atypical neuroleptics have similar efficacies in treating the presence of *positive psychotic symptoms, such as hallucinations and delusions;* atypical antipsychotics have been shown to be more effective in treating *negative symptoms (such as flattened affect and social withdrawal)*.

- Side effects and sequelae of traditional antipsychotics include:

1. Antidopaminergic effects:

- **Extrapyramidal side effects**
  - *Parkinsonism—masklike face, cogwheel rigidity, pill-rolling tremor.*
  - *Akathisia—subjective anxiety and restlessness, objective fidgetiness*
  - *Dystonia—sustained contraction of muscles of neck, tongue, eyes* (painful)
  - *Hyperprolactinemia—leading to decreased libido, galactorrhea,*
  - gynecomastia, impotence, amenorrhea, osteoporosis

- Treatment of EPSEs includes reducing dose of antipsychotic and administering antiparkinsonian, anticholinergic, or antihistaminic medications, such as amantadine (Symmetrel), Benadryl, or benztropine (Cogentin).

2. **Anti-HAM effects: Caused by actions on histaminic, adrenergic, and muscarinic receptors:**
   - *Antihistaminic—results in sedation*
   - *Anti-alpha adrenergic—results in orthostatic hypotension, cardiac abnormalities,* and sexual dysfunction
   - *Antimuscarinic—anticholinergic effects: Dry mouth, tachycardia, urinary* retention, blurry vision, constipation

3. **Weight gain**
4. **Elevated liver enzymes, jaundice**
5. **Ophthalmologic problems (irreversible retinal pigmentation with high** doses of Mellaril, deposits in lens and cornea with chlorpromazine)
6. **Dermatologic problems, including rashes and photosensitivity (bluegray** skin discoloration with chlorpromazine)
7. **Seizures: Antipsychotics lower seizure thresholds. Low-potency antipsychotics** are more likely to cause seizures than high potency.

8. **Tardive dyskinesia: Choreoathetoid (writhing) movements of mouth** and tongue that may occur in patients who have used neuroleptics for more than 6 months. It most often occurs in older women. Though 50% of cases will spontaneously remit, untreated cases may be *permanent*.
   - **Treatment involves discontinuation of current antipsychotic if clinically possible** (and sometimes administration of anxiolytics or cholinomimetics).

9. **Neuroleptic malignant syndrome: Though rare, occurs most often in** males early in treatment with neuroleptics. It is a **medical emergency** and has a 20% mortality rate if left untreated. It is often preceded by a catatonic state. It is characterized by:
    - **Fever (most common presenting symptom)**
    - **Autonomic instability (tachycardia, labile hypertension, diaphoresis)**
    - **Leukocytosis**
    - **Tremor**
    - **Elevated creatine phosphokinase (CPK)**
    - **Rigidity (*lead pipe rigidity is considered almost universal)***

- **Treatment involves discontinuation of current medications and administration** of supportive medical care (hydration, cooling, etc.). Sodium dantrolene, bromocriptine, and amantadine are also useful but are infrequently used because of their own side effects. This is *not an allergic reaction*.
- *Patient is not* prevented from restarting the same neuroleptic at a later time.

ATYPICAL ANTIPSYCHOTICS

- Atypical antipsychotics block both dopamine and serotonin receptors and are associated with **fewer side effects than traditional antipsychotics; in particular,** they rarely cause EPSEs, tardive dyskinesia, or neuroleptic malignant syndrome.

- They are more effective in treating **negative symptoms of schizophrenia** than traditional antipsychotics.

- Because they have fewer side effects and increased effectiveness in treating negative symptoms, these drugs are now first line in the treatment of schizophrenia.

- Atypical antipsychotics include:
  - **Clozapine (Clozaril)**
  - **Risperidone (Risperdal)**
  - **Quetiapine (Seroquel)**
  - **Olanzapine (Zyprexa)**
  - **Ziprasidone (Geodon)**

- SIDE EFFECTS
  - Some anti-HAM effects (antihistaminic, antiadrenergic, and antimuscarinic)
  - 1% incidence of agranulocytosis and 2 to 5% incidence of seizures with
  - clozapine
  - Olanzapine can cause hyperlipidemia, glucose intolerance, weight gain, and liver toxicity; monitor liver function tests (LFTs).
  - Quetiapine has less propensity for weight gain but has been shown to cause cataracts in beagle dogs, so periodic (every 6 months) slit lamp examination is recommended.