APPROACH TO PSYCHOSIS IN PRIMARY CARE

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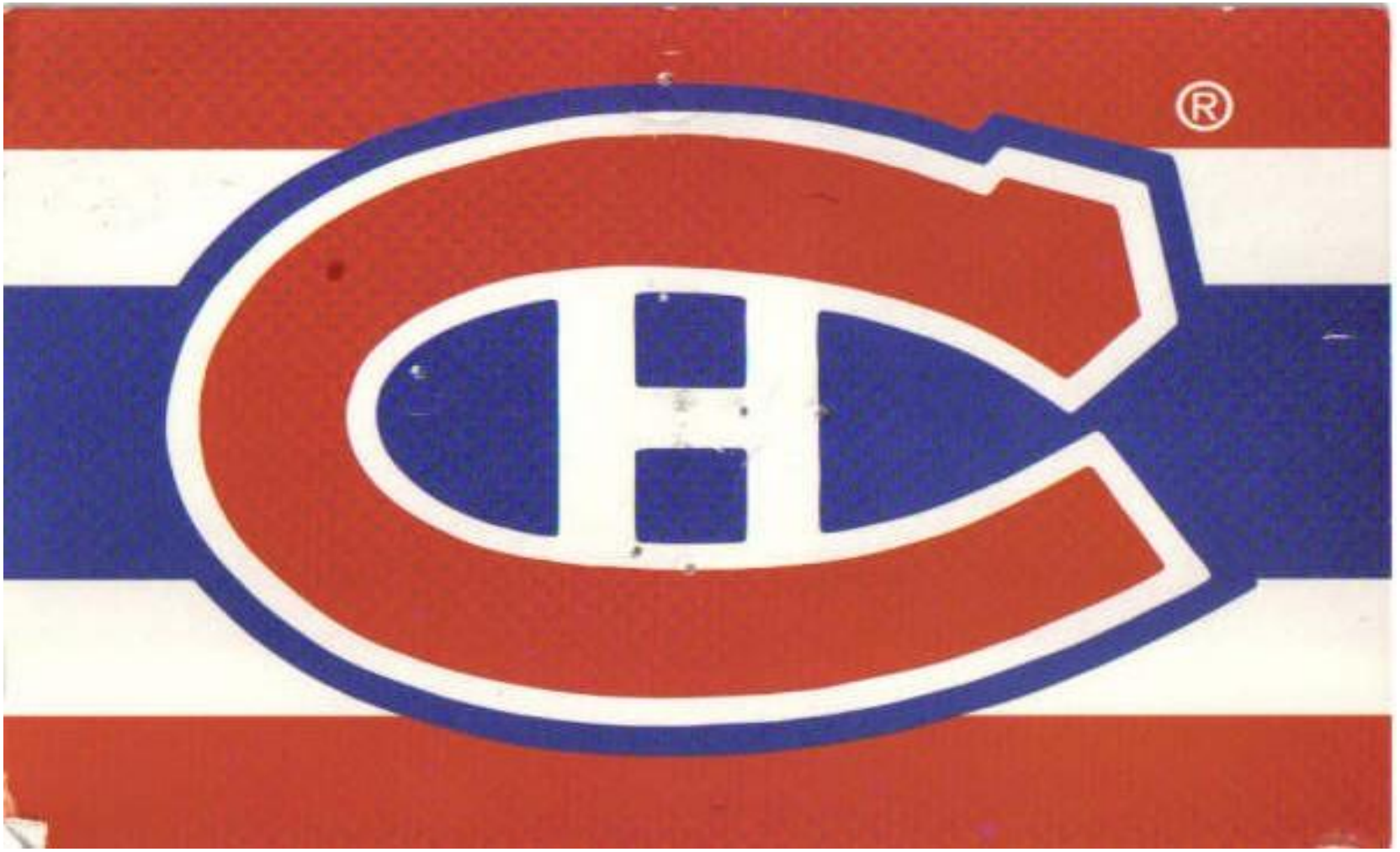


Objectives

- Learn effective questioning to evaluate psychosis.
- Be familiar with the complete differential diagnosis of psychotic disorders.
- Learn about current psychopharmacologic treatments of psychotic disorders.

PSYCHOSIS

- Delusion: Fixed, false idea; not consistent with one's culture
- Hallucination: Perceptual experiences without any external stimuli

- N.B. Illusions: Misinterpretation of stimulus

- Disorganized thinking, or behaviour

ASKING ABOUT PSYCHOSIS

- Do you have unusual experiences, such as hearing voices other people cannot; or seeing things other people cannot?
- Do you have unusual thoughts; such as feeling you have special powers no one else on earth has; or do you feel there is a plot out there, by people you don't even know, who want to harm you?

ASKING ABOUT PSYCHOSIS

- Do you ever feel the radio or TV has special messages just for you?(ideas of reference)
- Do you feel your thoughts are “broadcast” so that anyone around you can know what you’re thinking. Do you feel thoughts can be inserted or taken out of your head?

ASKING ABOUT PSYCHOSIS

- Do you feel your thoughts, actions, or feelings are controlled by some external power?
- Do you feel there is something very unusually wrong with your body(somatic delusion)?

GENTLE QUESTIONING:

- “I think you may be misinterpreting things,”
- “I think your thoughts may be getting away from you.”
  “What do you think?”

N.B. Delusion is a fixed false idea not consistent with one’s cultural beliefs. Therefore, see if thought is fixed.

DELUSIONS

- Predicting the future, reading people's minds, may not be delusional.
- May be schizotypal personality
- Religious thought often gets tricky. Compare to what was happening in the past

STRATEGY:

- Try to ally with patient's complaints:
  - e.g. "This will help you sleep."
  - "Feel less agitated" etc.

When trying to persuade them to take antipsychotic medication.

STRATEGY

- You can reality test for the patient:
  - “I know this is real for you, but I see things somewhat differently...”

ENSURE SAFETY

- Command hallucinations
- Suicidal ideation
- Homicidal ideation
- Caring for self - food, shelter

Note: Can make a contract with a psychotic person, but trickier

R/O ORGANIC

1. Non-auditory, e.g., Visual Hallucinations

2. Clouded Sensorium

3. Older age at first onset

D	Drugs
I	Infection
M	Metabolic
E	Endocrine
V	Vascular
E	Epilepsy
T	Tumour/trauma
S	Syphilis

DIFFERENTIAL:

- Time Course

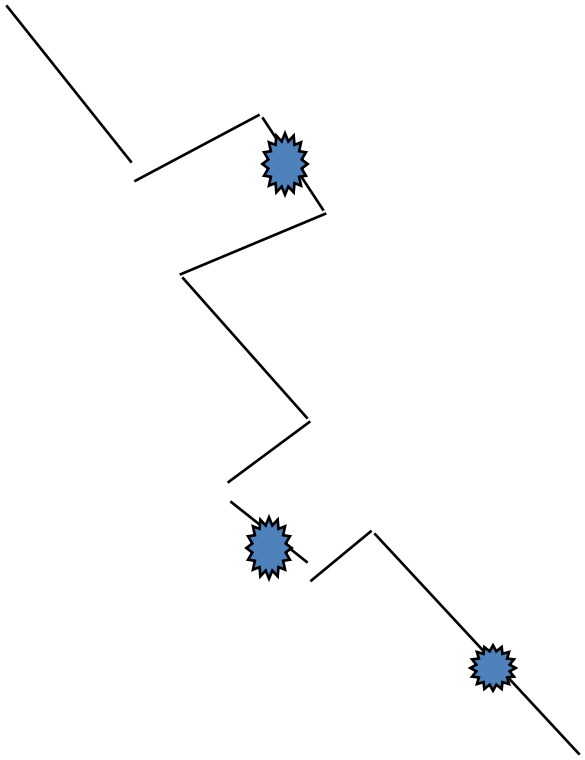
Brief Psychotic Reaction: less than 1 month

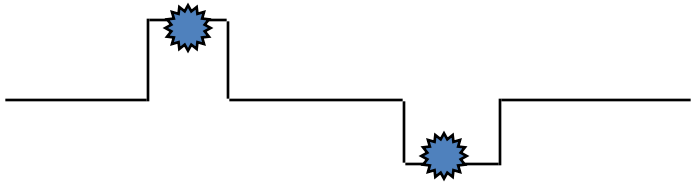
Schizophreniform Psychosis: 1 – 6 months

DIFFERENTIAL OF PSYCHOSIS

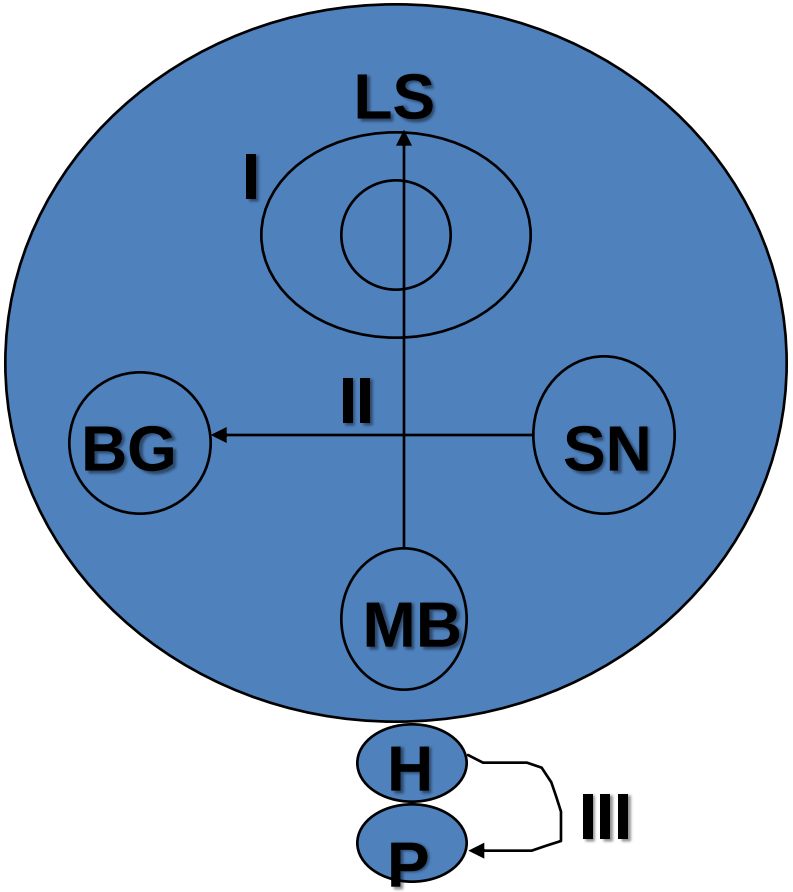
	Hallucination	Bizarre vs Non Bizarre	Downward Drift	Affect at time of Psychosis
Schizophrenia	+/-	NB/B	+	-
Schizoaffective	+/-	NB/B	+	+
Affective Disorder	+/-	NB/B	-	+
Delusional Disorder	-	NB	-	-

SCHIZOAFFECTIVE VS. BIPOLAR





POSITIVE SYMPTOMS:



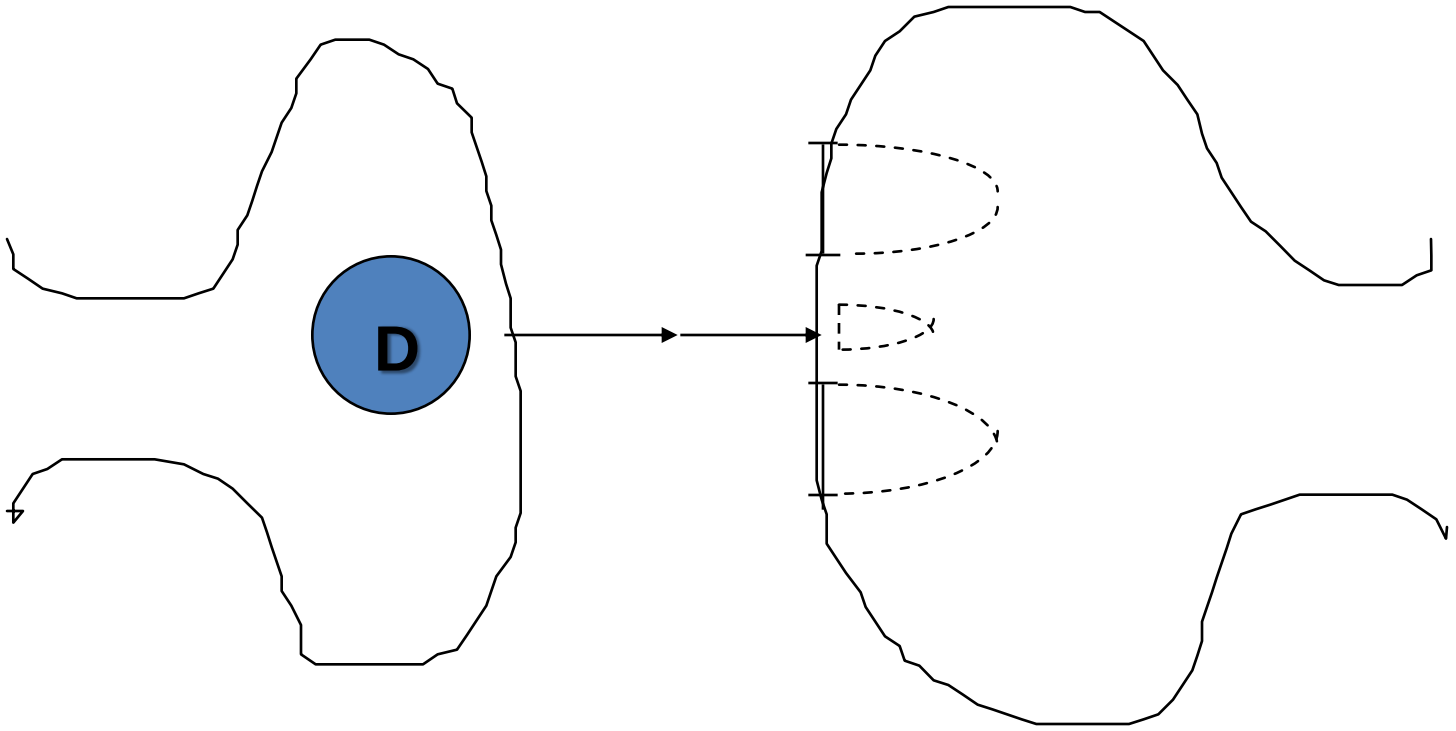
Dopaminergic Tracts

I. Mesolimbic

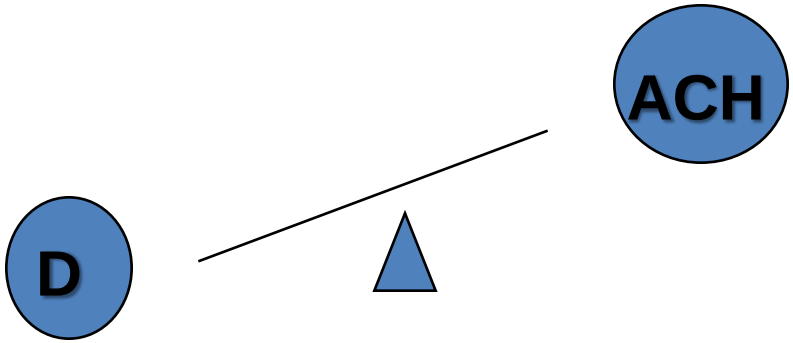
II. Nigro-Striatal

III. Hypothalamic-Pituitary

TARDIVE DYSKINESIA



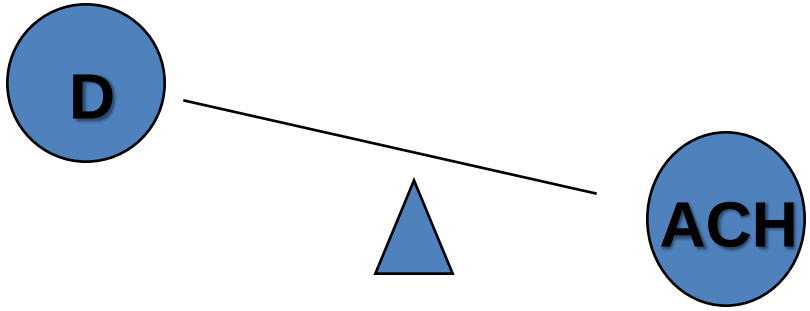
EPS



“IATROGENIC PARKINSON’S”

1. Parkinsonism
2. Akathesia
3. Dystonias

TD



"IATROGENIC HUNTINGTON'S"

- 15-20% of people on neuroleptics
- Cumulative dosage
- Older, women, on large dose, x years
- Sometimes idiosyncratic. Can be just a brief number of months.

DRUG TREATMENT

ATYPICAL NEUROLEPTICS

- Considered treatment of choice:
  - Olanzapine
  - Risperidone
  - Quetiapine
  - Clozapine
- No psychosis is considered treatment resistant until Clozapine is tried.

ATYPICAL NEUROLEPTICS

ADVANTAGES:

- Better s/e profile
  - less EPS
  - less TD
- Possible better response with respect to negative symptoms.
- CUTLASS1 study argues against this.
  - Jones, Peter, et al. Archives of General Psychiatry, Vol.63, October, 2006, pp. 1079-1987
- Equal efficacy with respect to positive symptoms
- Liver cleared - do LFT's prior. If history of liver problems, do LFT's q 6-12 months

RISPERIDONE (RISPERDAL)

- Blocks D_2/$5HT_2$
  also alpha adrenergic
- Peak Plasma: 1-2 hours
- Half life: 20-24 hours
- Liver metabolized

RISPERIDONE - (RISPERDAL)

EPS increased

May increase prolactin – can cause amenorrhea, galactorrhea, sexual problems

RISPERIDONE

Dosage:

Start 0.5 mg. BID

Range:

2-4 mg OD

Few studies, re pregnancy

OLANZAPINE (ZYPREXA)

BLOCKS: D_2/$5HT_2$
Also D_1, D_3, D_4
Muscarinic
Alpha adrenergic
Histamine

Peak plasma 5-8 hrs after intake
1/2 life 21-54 hours
metabolized by liver - P450-2D6
Little P450 interactions

OLANZAPINE - (ZYPREXA)

- somnolence
- orthostatic hypotension, dizziness
- ⇧ hepatic transaminase (ALT, AST, GGT)
- weight gain
- no increase in prolactin
- few studies re: pregnancy/lactation

OLANZAPINE

Dosage:

Start: 5 mg PO OD

Range:10-20 mg OD

Geriatric/hepatic impairment:

Start 2.5 mg PO OD

QUETIAPINE (SEROQUEL)

- Blocks: $5HT_2/D_2$ Receptors
  also D_1
  H_1
  Alpha Adrenergic
- Peak plasma: 2 hours after dosage
- Half life: 6-7 hours
- Metabolized by the liver - CYP 3A4

QUETIAPINE - (SEROQUEL)

Somnolence

Cataracts - in animals

slit lamp examination recommended

hypothyroid

weight gain less

no increased prolactin

few studies safety in pregnancy

QUETIAPINE

DOSAGE:		DAY
Start:	50 mg OD	1-2
	100 mg OD	3-4
	200 mg OD	5-6
	300 mg OD	7 & beyond

Treatment range: 300-600 mg/day

sometimes needs 600-800 mg/day

New Form: Quetiapine XR 300 mg. Tabs-- Can start 300 mg. OD on day 1. Can increase to 300 mg. BID on Day 2.

CLOZAPINE (CLOZARIL)

- Blocks D_1 and D_4 and $5HT_2$. Less D_2
- Peak levels 2-5 hours (1-6 hours)
- 1/2 life 12 hours (6-30 hours)

- Liver metabolized - mainly P450 1A2,
  somewhat P450 2D6

CLOZAPINE

Agranulocytosis - Follow WBC, Neutrophils

- Weekly x 26 weeks, then biweekly indefinitely / idiosyncratic effect

Seizures - dosage linked esp >600 mg/day

- Drowsiness
- Hypotension, dizziness, tachycardia
- Hypersalivation
- Weight gain
- Fever

Little tardive dyskinesia

No increase in prolactin

CLOZAPINE

- Do not use with Carbamazepine/depot Neuroleptics
- Pregnancy/Lactation not established
- Due to agranulocytosis and blood work, less used as first line in primary care

CLOZAPINE

Dosage:

12.5 mg OD	Day 1
25 mg OD	Day 2
25 BID	Day 3

- then ⇧ by 25-50 mg increments daily
- target dose 300-450 mg/day by 2 weeks
- dosage range 300-600 mg/day in divided doses
- maximum 900 mg/day

Ziprasidone

- Equal Eficacy
- Less EPS and TD
- Less Metabolic
- BUT……
- Prolonged QT. To be avoided with hx of prolonged QT, hx of cardiac arrhythmias, post MI, CHF, avoid with other drugs that prolong QT
- Dosage: 20 or 40 mg. PO BID up to 80 mg. PO BID

Aripiprazole

- Equal Efficacy
- Less EPS and TD
- Less Metabolic Effects
- No QT Prolongation
- If this all holds true, we will all be using this a lot!!
- Dosage: 10-15 mg. Po OD. Maximum is 30 mg. PO OD

Metabolic Syndrome

- Increased glucose: Diabetes Type II
- Increased cholesterol
- Increased tryglycerides
- It is possible that rate of Diabetes Type II may be linked to weight gain but not clear.
- Check fasting blood sugar every four months, along with cholesterol and triglycerides.

Weight Gain

Olanzapine and Clozapine more than Risperidone and Seroquel

TRADITIONAL NEUROLEPTICS

		Alpha Blocking	Antihistamine	Anticholinergic	EPS inducing
CPZ	100	H	H	H	L
Mellaril	100				
Perphenazine	8	M	M	M	M
Stelazine	5				
Loxapine	10-15				
Haldol	2	L	L	L	H

Usual daily antipsychotic dosage: CPZ 300-500 mg

TRADITIONAL NEUROLEPTICS

- Haldol/Stelazine safer re: pregnancy
- May increase prolactin

Use of Neuroleptics I

- Anti-psychotic
  - Organic
  - Psychiatric
- Anti-manic (After Mood Stabilizer, Benzos)
- For Prophylaxis in schizophrenia and schizoaffective
- Olanzapine approved for Bipolar prophylaxis

Use of Neuroleptics II

- For treatment resistant OCD patients
- For agitation in demented patients (low dose)
- For nausea: often in cancer patients ?after Gravol
- Tourette’s Syndrome
- Sometimes in Borderline Personality
- Possibly in bipolar depression
- For augmentation in depression

Use of Neuroleptics III

- Do not use in general for nighttime sedation, or as anxiolytic.
- Benzos/hypnotics preferred, because no risk of T.D.

Three Pronged Effect of Neuroleptics

1. Motor Agitation - minutes to hours
2. Perceptual - three to seven days
3. Disordered Thoughts - three to six weeks

NMS

- can happen in 1-2% of people on neuroleptics
- has 15% mortality

NMS - Neuroleptic Malignant Syndrome

- ⇧ Temperature

Sympathetic lability (BP, Pulse)

Confusion

Rigidity

NMS

- Usually associated with:
  - Starting Neuroleptic
  - Increasing Neuroleptic
  - Changing Neuroleptic

But can be anytime

No neuroleptic better than another

NMS

1. ↑ CPK
2. Myoglobinuria
3. ↑ WBC, ↓ FE

NMS

Treatment:

D/C Neuroleptic

Bromocriptine - no advantage

Dantrolene - no advantage

Use Benzos for agitation, sedation

NMS

As per P. Rosebush Studies

- After two weeks symptom free, can rechallenge with another neuroleptic. Switch to a different class.

- If you don’t wait two weeks, NMS may reappear

NMS

- NB:

  If FUO and on neuroleptic:

  d/c Neuroleptic

  use Benzos for agitation

I.M. NEUROLEPTIC

- e.g.

		Given
Modecate	(Fluphenazine Decanoate)	q 2-4 wks
Moditen	(Fluphenazine Enanthate)	
Haldol LA	(Haloperidol Decanoate)	
Risperidal Consta	(Risperidone)	25 mg q 2 wks

Close if compliance an issue e.g. paranoid states

But - stuck if problems with side effects.

- For EPS, use Anticholinergics

Benzotropine	(Cogentin)	2-6 mg OD
Procyclidine	(Kemadrin)	2.5 mg -5 mg BID - TID

NB: I.M. Benztropine 2 mg for acute dystonic reaction e.g. oculogyric crisis

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