ANTIPSYCHOTICS

WHEN AND WHAT TO PRESCRIBE

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ANTI = AGAINST

ANTIPSYCHOTIC

AGAINST PSYCHOSIS

PSYCHOSIS

- DEFN : IMPAIRMENT IN REALITY

- DSM 1V : SYMPTOM DEFINITION

1. HALLUCINATIONS
2. DELUSIONS
3. DISORGANIZED SPEECH
4. DISORGANIZED BEHAVIOUR

INDICATIONS

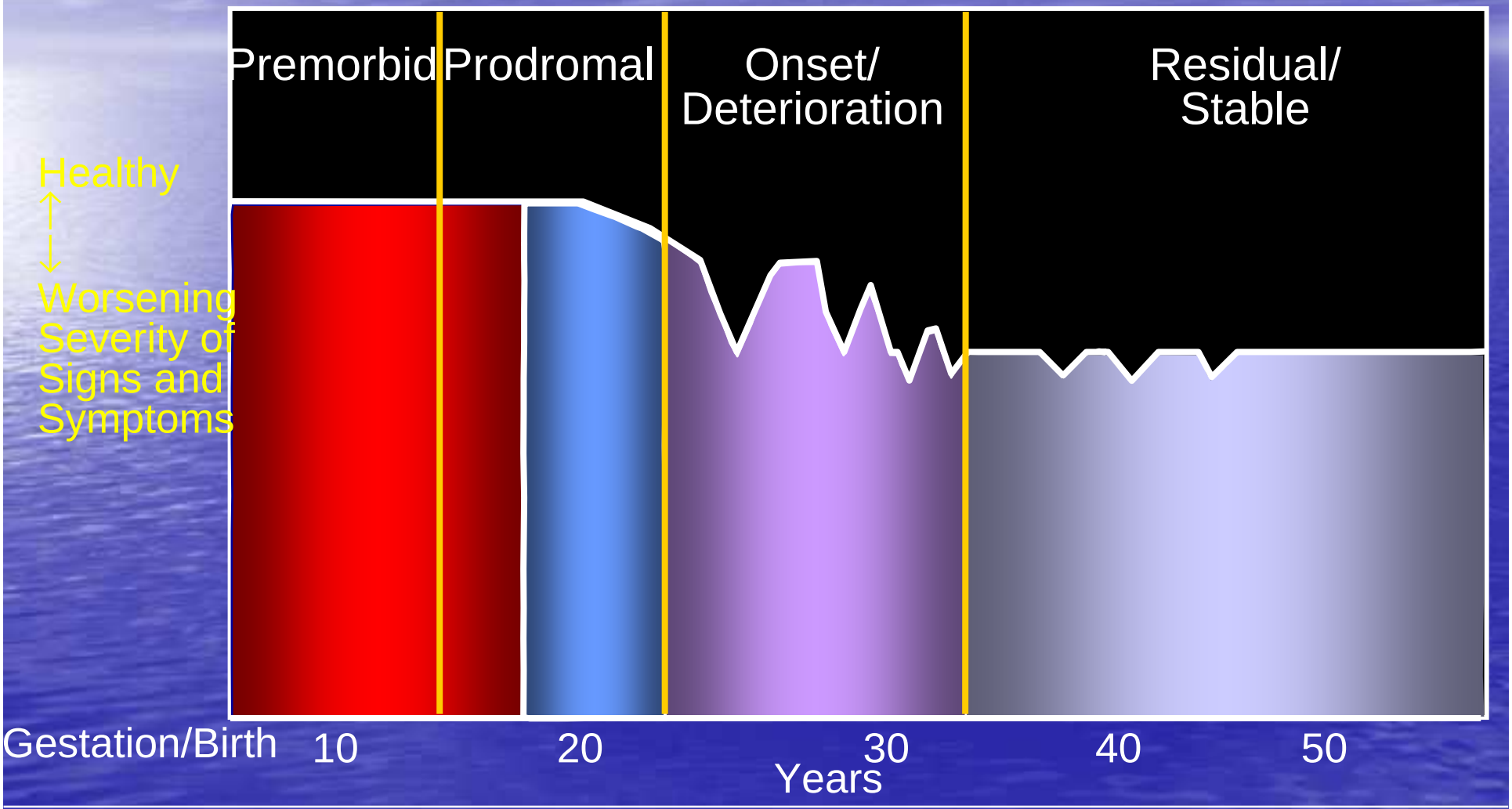
- **ANY** CONDITION WHERE THESE SYMPTOMS OCCUR

PSYCHOTIC DISORDERS

1. Schizophrenia
2. Schizophreniform disorder
3. Brief psychotic disorder
4. Delusional disorder
5. Psychotic disorder due to GMC

Natural History of Schizophrenia

Stages of Illness



Lieberman J. Presented at: 154th APA Annual Meeting; May 5-10, 2001; New Orleans, La.

MOOD DISORDERS

- DEPRESSION WITH PSYCHOTIC FEATURES

Combine with an Antidepressant

- MANIA WITH PSYCHOTIC FEATURES

Combine with a mood stabiliser

. AUGMENT ANTIDEPRESANT

Treatment resistant depression

Cognitive Disorders

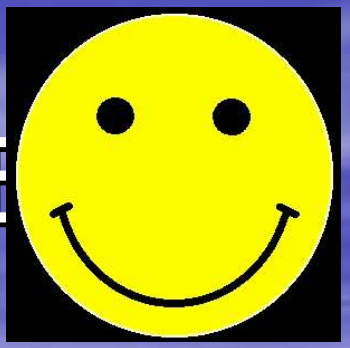
1. DELIRIUM

2. DEMENTIA

FOR THE SIDE EFFECT OF THE DRUG

1. SEDATION ----Behaviour Disturbance
2. ANTI EMETIC
3. HICCUPS

Dawn of the Antipsychotic E



- Revolutionised treatment
- Held great promise
- Extract from *Mental Hospitals* February 1956

Many hospital psychiatrists are being pressured by relatives to use Chlopromazine where it did not seem to be indicated. To hold off relatives he would say "If you buy it, we will give it" being sure they would not do so.But they always obtained the money somehow

Antipsychotics broadly classified into two major classes :-

a) Typical antipsychotics
b) Atypical (novel) antipsychotics

other names : Neuroleptics
Major tranquilisers

What makes an antipsychotic Typical ?

A) Its mechanism of action
D2 receptor blockers

b) Its site of action
Block Dopamine pathways non –
selectively

DOPAMINE PATHWAYS

1) Mesolimbic

2) Mesocortical

3) Nigrostriatal

4) Tuberoinfundibular

Mesolimbic ☞ **reduction in positive symptoms**

blockade

Mesocortical ☞ **worsening of negative symptoms. Cognitive deficit**

blockade

Nigrostriatal ☞ **Movement disorders**

blockade

Tuberoinfundibular ☞ **hyperprolactinaemia**

blocade

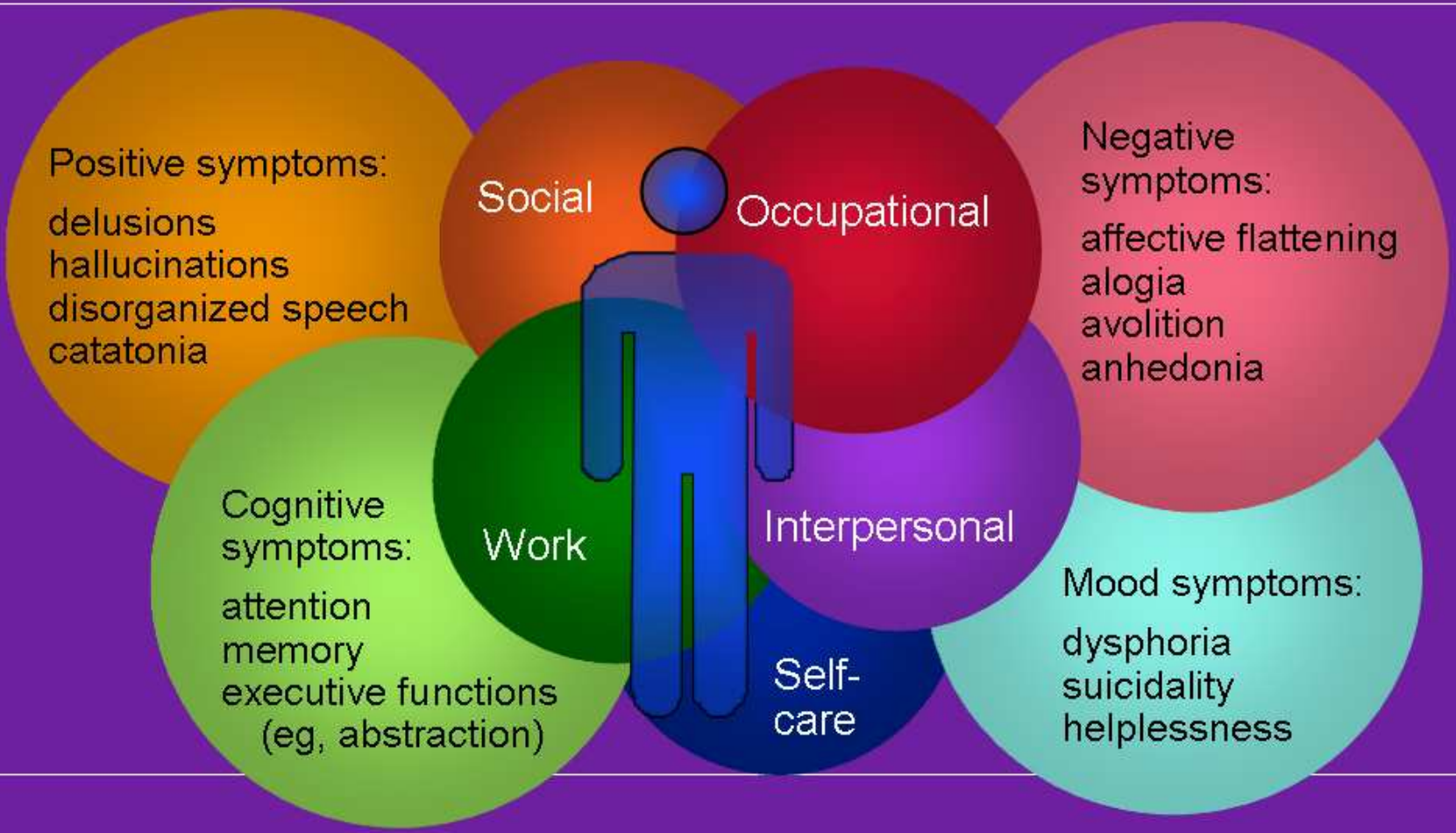
IDEAL

a) Block Dopamine receptors in mesolimbic but not in other pathways.

This has been partly achieved by novel antipsychotics.

B) No effects / minimal effects on other receptors

GOALS


Positive symptoms:
delusions
hallucinations
disorganized speech
catatonia
Social
Occupational
Negative symptoms:
affective flattening
alogia
avolition
anhedonia
Cognitive symptoms:
attention
memory
executive functions
(eg, abstraction)
Work
Interpersonal
Mood symptoms:
dysphoria
suicidality
helplessness
Self-care

ON CODE

1. Haloperidol----Serenace

2. Chlorpromazine---Largactil

3. Some clinics---Clozapine---Leponex

CHLORPROMAZINE

- Largactil
- Typical Antipsychotic
- Discovered in 1952
- Price—R20 –R25 per month
- Formula---tablets,syrup and injections
- D 2 Receptor blocker

PROPERTIES

- Sedating
- High incidence of anticholinergic side effects—constipation,blurred vision,urinary retention,cognitive effects
- Less EPS than Haloperidol
- Cardiotoxic
- Hepatotoxic—induces liver enzymes

DOSE

- Do not use injections---can cause precipitous drop in blood pressure and severe tissue necrosis
- Tablets---START LOW
- Max—600 mg daily
- Monitor side effects

HALOPERIDOL

- High incidence of EPS
- Less sedating than Largactil
- Less incidence of anticholinergic side effects
- Less cardiotoxic
- Lesser propensity to cause seizures
- Drug of choice in children,elderly and those with medical co morbidity

Largactil vs Serenace

- YOUNG
- FIT
- HEALTHY
- AGGRESSIVE
- PROMINENT BEHAVIOUR DISTURBANCE

USE LARGACTIL

PROBLEMS WITH TYPICALS

- Not always effective---25-30% of patients show no improvement
- Lots of side effects
- Not effective for negative symptoms
- No effect on cognition
- Poor compliance
- Affects work

SIDE EFFECTS

Typical antipsychotics also block :

1) **Muscarinic receptors**

2) **Histaminic receptors**

3) **∝1 (alpha one) receptors**

Muscarinic blockade causes

urinary retention, constipation, blurred vision, memory deficit

Histaminic blockade causes

weight gain, sedation

∝ 1 blockade causes

Postural hypotension, reflex tachycardia

EXTRAPYRAMIDAL SIDE EFFECTS

- ACUTE DYSTONIA
- PARKINSONISM
- AKATHISIA
- TARDIVE DYSKINESIA
- NMS

ACUTE DYSTONIA

- YOUNG MALES PRONE TO IT
- DEVELOPS WITHIN HOURS OR DAYS
- SPASM OF NECK .BACK ,EYE MUSCLES
- POTENTIALLY FATAL
- GIVE AKINETON 1 AMP. IMI OR IVI
- CHANGE TYPICAL OR SWITCH TO ATYPICAL

PARKINSONISM

- Most common side effect—50-75%
- Onset within days
- Triad of tremor ,bradykinesia and rigidity
- Treated with anticholinergic meds i.e Disipal or oral akineton
- NEVER give prophylactic anticholinergics

AKATHISIA

- Prevalence 10%
- Onset usually within days
- Treated with beta blockers or benzodiazepines

TARDIVE DYSKINESIA

- Involuntary movements
- Classically oro-bucco-facio-lingual movements
- Develops late
- Receptors supersensitive
- Largely irreversible
- Switch to clozapine

NEUROLEPTIC MALIGNANT SYNDROME

- IDIOSYNCRATIC
- ANY TIME
- ANY DOSE
- TETRAD OF FEVER,RIGIDITY,AUTONOMIC HYPERAVTIVITY AND CONFUSION
- MEDICAL EMERGENCY
- SWITCH TO ATYPICALS

So it stayed for……40 years!

YOU CAN REFER

WHEN TO REFER

- NON RESPONDERS
- SENSITIVE TO EPS
- PROMINENT NEGATIVE SYMPTOMS
- SEVERE DEPRESSION

Early warning signs

- Worried
- Restless
- Irritable
- Insomnia
- Paranoia
- Social withdrawal
- Substance abuse pattern change

What to do

- Ensure compliance
- Exclude substances
- Exclude GMC
- Increase dose
- Switch to another typical
- Refer for atypical

- 1970’s – Leponex
- 1994 – Risperdal
- 1996 – Olanzapine
- 2000 – Seroquel
- 2002 – Geodon
- 2003 – Solian
- 2006 – Abilify

Definition of Atypical

- Clinical distinction – Minimal risk of EPS

  ? Dose related phenomenon
- Chemical Distinction – Transient increase in prolactin levels
- Serotonin antagonism
- Mesolimbic / Mesocortical specificity
- A measure of dissociation at the receptor

CLOZAPINE

- PROBLEMS
- AGRANULOCYTOSIS
- EXCESSIVE SALIVATION
- SEDATION
- SEIZURES AT HIGH DOSES
- WEIGHT GAIN
- METABOLIC SYNDROME

- Evidence of atypical antipsychotics superior efficacy to conventional antipsychotics has been neither consistent nor robust
- Need information from unbiased sources to guide clinicians and policy makers
- Precedents from other fields in addressing critical questions
- Lack of longer term head-to-head comparisons of atypical and conventional antipsychotics

CATIE=Clinical Antipsychotic Trials of Intervention Effectiveness.
Stroup TS, et al. *Schizophr Bull.* 2003;29(1):15-31.

AT THE END OF THIS LECTURE YOU SHOULD BE ABLE TO :

1) Define a Typical antipsychotic
2) Name the Dopamine pathways and know what effects Dopamine blockade there produces
3) Describe the presentation and management of the extrapyramidal syndromes
4) Discuss the side effects of Typical antipsychotics
5) Name and know the core properties of the Typical Antipsychotics on the EDL

WE SPEND MORE BUT WE HAVE LESS

WE HAVE MORE DEGREES BUT WE HAVE LESS SENSE

WE HAVE MORE MEDICATIONS BUT LESS WELLNESS