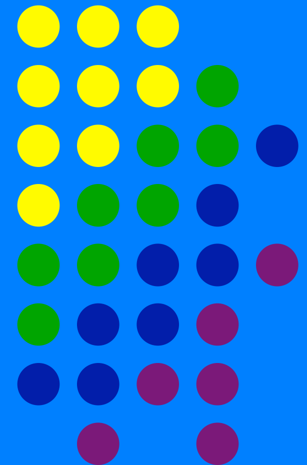
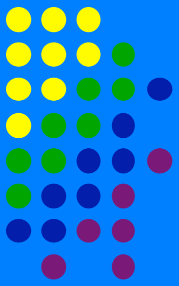
HOW TO THINK ABOUT MEDICATIONS IN THE TREATMENT OF BPD

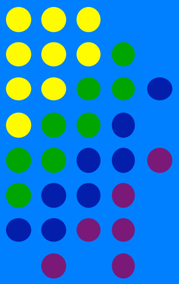


Kenneth R Silk, MD
Professor Emeritus of Psychiatry
University of Michigan Health System
Ann Arbor, MI 48109-2700
ksilk@umich.edu



DISCLOSURES

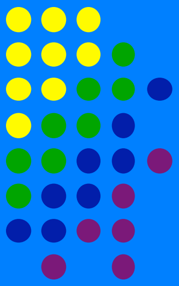
- **I receive royalties from the American Psychiatric Press, Cambridge University Press, Up-to-Date**
- **I am one of 3 Co-editors-in chief of *Personality and Mental Health*, a journal owned by Wiley-Blackwell**
- **I will talk about the off-label use of psychiatric medication**



BPD PSYCHOPHARM: IMMEDIATE PROBLEMS

- **No medications carry a specific indication for use in treatment of personality disorders**
- **Thus all medications must be used "off label" though not uncommon (in U.S.) to use medications off-label**
- ***Medications for BPD are less effective for symptom or symptom complex than when used in other disorders (primarily Axis I)***
- ***BPD patients seem exquisitely sensitive to side effects***

NEVERTHELESS WE TREAT PERSONALITY DISORDERS PHARMACOLOGICALLY



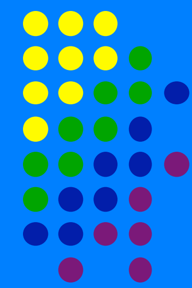
- **CLPS* – 81 % (of patients w/ personality disorders)**
- **Zanarini et al**:**
  - **78% BPD on meds >75% over 6 years**
  - **68% OPD on meds > 75% over 6 years**

  - **71% BPD still on meds at 6 years**
  - **54% OPD still on meds at 6 years**

  - **BPD 51%, OPD 22% on 2 or more meds at 6 years**
  - **BPD 37%, OPD 8% on 3 or more meds at 6 years**

*** Bender at al: Am J Psychiatry, 2001; 158: 295-302**

**** Zanarini et al, J Clin Psychiatry, 2004; 65:26-36.**



Patient exhibits mood lability, rejection sensitivity, inappropriate intense anger, depressive "mood crashes," or outbursts of temper

Initial Treatment: SSRI or Related Antidepressant

Efficacy → Maintenance | Partial Efficacy | No Efficacy

Switch

Second SSRI or Related Antidepressant

Efficacy → Maintenance | Partial Efficacy | No Efficacy

Add

Add:
Low-Dose Neuroleptic (for symptoms of anger),
Clonazepam (for symptoms of anxiety)

(If ineffective) Switch to MAOI

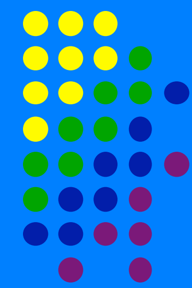
Efficacy → Maintenance | Partial Efficacy | No Efficacy

Add | Switch

Lithium, Carbamazepine, or Valproate

"EMOTION DYSREGULATION"

American Psychiatric Association. Practice Guideline for the Treatment of Patients with Borderline Personality Disorder. Am J Psychiatry 2001, 158(Suppl)1-52



“IMPULSE AGGRESSION”

Patient exhibits impulsive aggression, self-mutilation, or self-damaging binge behavior (e.g., promiscuous sex, substance abuse, reckless spending)

Initial Treatment: SSRI
(e.g., fluoxetine, 20–80 mg/day
sertraline, 100–200 mg/day)

Efficacy → Maintenance

Partial Efficacy → Add

No Efficacy → Switch

Low-Dose Neuroleptic

Efficacy → Maintenance

Partial Efficacy → Add

No Efficacy → Switch

Lithium Carbonate → (If ineffective) Switch to Carbamazepine or Valproate

OR

MAOI[b] → (If ineffective) Add Lithium; Switch to Carbamazepine or Valproate if Lithium is Ineffective

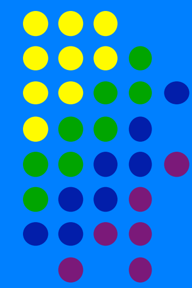
Efficacy → Maintenance

No Efficacy → Add

Efficacy → Maintenance

Atypical Neuroleptic

American Psychiatric Association. Practice Guideline for the Treatment of Patients with Borderline Personality Disorder. Am J Psychiatry 2001, 158(Suppl)1-52



Patient exhibits suspiciousness, referential thinking, paranoid ideation, illusions, derealization, depersonalization, or hallucination-like symptoms

Initial Treatment: Low-Dose Neuroleptic
(e.g., perphenazine, 4–12 mg/day
trifluoperazine, 2–6 mg/day
haloperidol, 1–4 mg/day
olanzapine, 2.5–10 mg/day[b]
risperidone, 1–4 mg/day[b])

Efficacy → Continue

Partial Efficacy

No Efficacy

Increase Dose
(e.g., perphenazine, 12–16 mg/day
trifluoperazine, 5–15 mg/day
haloperidol, 4–6 mg/day)

Efficacy → Continue

Partial Efficacy

No Efficacy

Prominent Affective Symptoms

Few Affective Symptoms

Add

SSRI (or MAOI)

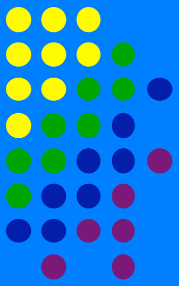
Switch

Atypical Neuroleptic or Clozapine

"COGNITIVE PERCEPTUAL"

American Psychiatric Association. Practice Guideline for the Treatment of Patients with Borderline Personality Disorder. Am J Psychiatry 2001, 158(Suppl)1-52

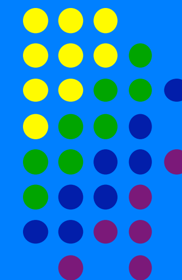
APA GUIDELINE RECOMMENDATION (2001)



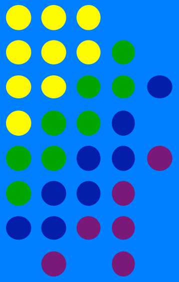
- **“Pharmacotherapy often has an important adjunctive role, especially for diminution of targeted symptoms such as affective instability, impulsivity, psychotic-like symptoms, and self-destructive behavior. However, pharmacotherapy is unlikely to have substantial effects on some interpersonal problems and some other features of the disorder…..Clinical experience indicates that many patients will benefit most from a combination of psychotherapy and psychopharmacology.”**
- -APA Guidelines, 2001, p. 10

COMMON STUDIES - BPD

AD, MS, AP, vs PLACEBO, (NO OMEGA-3)



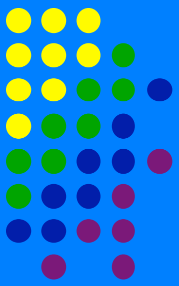
Study									
Bogenschutz , Nurnbg, 2004	Dug	WF	ING	NOSE		COCHL	TOR	NICE	VITA
Coccaro, Kavoussi, 1997	Dug	WF	ING	NOSE			TOR		VITA
Cowdry , Gardner 1998		WF	ING				TOR	NICE	VITA
De la Fuente , 1994	Dug	WF	ING	NOSE	COCH	COCHL		NICE	
Frankenburg , Zanarini 2002	Dug	WF	ING			COCHL	TOR	NICE	VITA
Goldberg 1986	Dug	WF	ING	NOSE	COCH	COCHL		NICE	
Hollander 2001	Dug	WF	ING	NOSE	COCH	COCHL	TOR	NICE	VITA
Hollander 2003/2005	Dug	WF	ING	NOSE			TOR	NICE	VITA
Leone 1982	Dug				COCH	COCHL			
Loew 2006	Dug	WF	ING				TOR	NICE	
Montgomery 1983	Dug	WF	ING		COCH	COCHL			
Nickel 2004	Dug	WF	ING	NOSE		COCHL	TOR	NICE	VITA
Nickel 2005	Dug	WF	ING	NOSE		COCHL	TOR	NICE	VITA
Nickel 2006	Dug	WF	ING	NOSE		COCHL	TOR	NICE	VITA
Pascual 2008						COCHL	TOR	NICE	VITA
Rinne 2002	Dug	WF	ING	NOSE		COCHL	TOR	NICE	VITA



- Salzman 1995 Dug WF ING NOSE COCH COCHL TOR NICE VITA
- Simpson 2004 Dug WF ING NOSE COCHL TOR VITA
- Soler 2005 Dug WF ING NOSE COCHL TOR VITA
- Soloff 1993 Dug WF ING NOSE COCH COCHL TOR NICE VITA
- Soloff 1989 Dug WF ING NOSE COCH COCHL TOR NICE VITA
- Tritt 2005 Dug WF ING NOSE COCHL TOR NICE VITA
- Zanarini , Frankenburg 2001 Dug WF ING NOSE COCH COCHL TOR NICE

- 23 COMMON STUDIES
- Ingenhoven – 21 <1998 9
- Cochrane-Lieb -25 = 2 Omega-3s 1998-2005 11
- Cochrane – Binks – 10 >2005 3
- Mercer – 18
- Nose – 22
- WFSBP - 21
- Duggan – 22
- Saunders – 20
- Vita 17

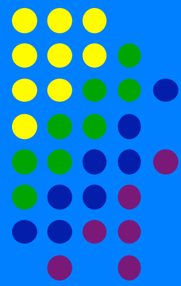
DIMENSIONS OF PSYCHOPATHOLOGY



- **Affective Instability:** abandonment, affective instability, capacity for pleasure, depression, emptiness, euphoria/ mania, identify disturbance, interpersonal sensitivity, irritability, rejection sensitivity, suicidality
- **Anxiety inhibition:** general anxiety, anxiety – intropunitiveness, obsessive-compulsive score, phobic anxiety, somatization
- **Cognitive perceptual:** paranoid ideation, perceptual distortion, psychoticism-schizotypy
- **Impulsivity/Aggression:** aggression, anger, hostility, impulsiveness

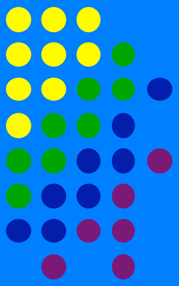
Siever & Davis (1991). "A psychobiological perspective on the personality disorders." Am J Psychiatry 148(12): 1647-58

CONVERGENT (OR CONTRADICTORY) EVIDENCE



	Afft/Instb	Aggrs/Impul	CogPer	Anx/In	Glob
Binks (Coch)	(AD)	(AD)	AP	NA	(AP)
Lieb (Coch)	MS (AP)	MS (AP)	AP	NA	
Nosè	AD/MS	AP	NA	NA	(AP)
WFSBP	AD**	AP/MS	AP	AD	
Duggan	NA	MS	AP	NA	
Mercer	AP/MS	MS	---	----	
Ingenhoven	MS	MS/AP	AP	MS	MS
Vita	MS (AD)	MS (AP)	AP		
SUMMARY	MS (AD**)	MS/AP	AP	(AD/MS)	AP

Silk & Fuerino III: Psychopharmacology of personality disorders. In Widiger, T. (Ed.). The Oxford Handbook of Personality Disorder. Oxford University Press, Oxford, UK, 2012, pp. 713-724.



WHERE DOES THIS LEAVE US?

- **Probably consider a revision**
- **Greater role for MS and AP with diminished role for AD (Abraham & Calabrese, 2008)**
- **The role of psychopharmacology is still adjunctive to psychotherapy**
- **Need to consider the algorithm, whatever its current decision tree, as iterative**
- **Many contradictions remain**

Abraham and Calabrese: Evidenced-based pharmacologic treatment of borderline personality disorder: a shift from SSRIs to anticonvulsants and atypical antipsychotics? J Affect Disord J 2008 ;111:21-30

Patient exhibits mood lability, rejection sensitivity, inappropriate intense anger, depressive "mood crashes," or outbursts of temper

Initial Treatment: SSRI or Related Antidepressant

- Efficacy → Maintenance
- Partial Efficacy
- No Efficacy

Switch

Second SSRI or Related Antidepressant

- Efficacy → Maintenance
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- No Efficacy

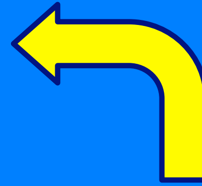
Add

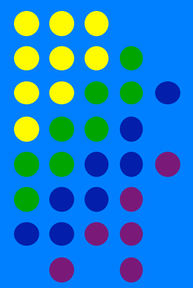
Add:
Low-Dose Neuroleptic (for symptoms of anger),
Clonazepam (for symptoms of anxiety)

(If ineffective) Switch to MAOI

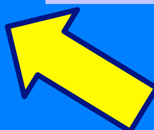
- Efficacy → Maintenance
- Partial Efficacy — Add
- No Efficacy — Switch

Lithium, Carbamazepine, or Valproate





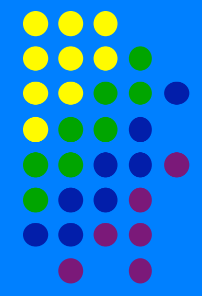
Angry/Labile – MS/AP
Depressed – SSRI, AP

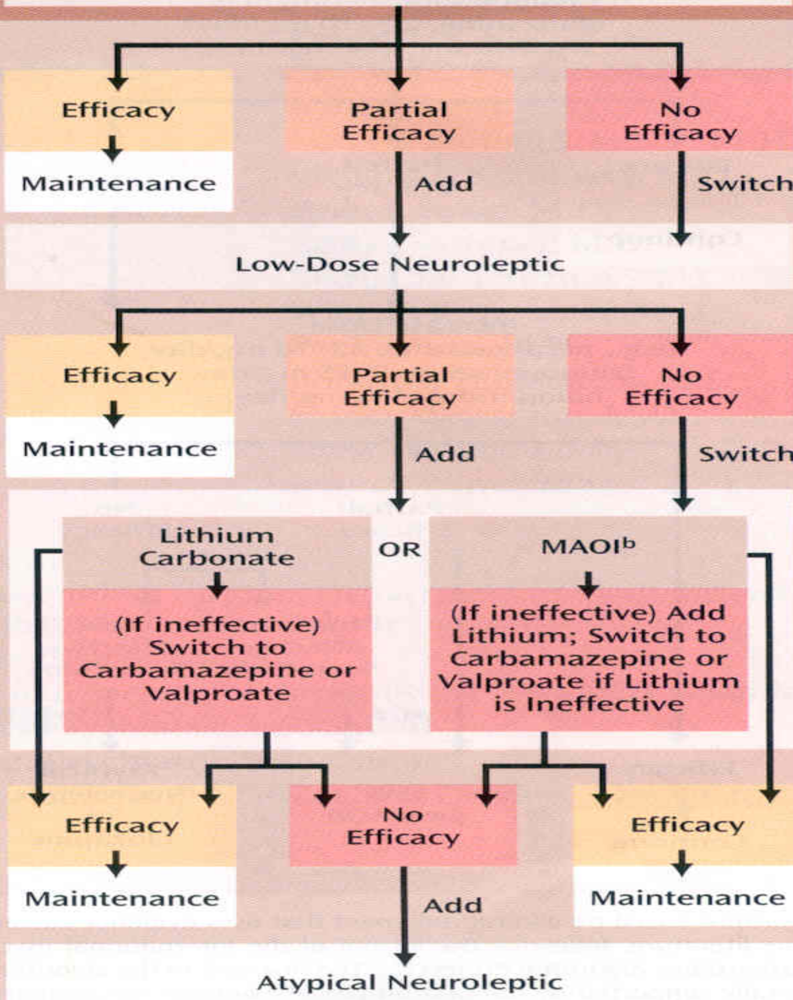


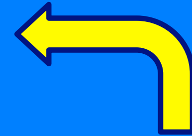
Augment* – AP w/ MS
Augment* – AC w/ AP
Depression--????

*** Caution should be used when augmenting to minimize polypharmacy**

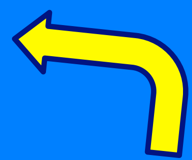
"EMOTION DYSREGULATION"







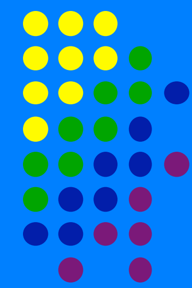
MS or AP (low dose)
AP-w/ AD qualities
MS-Topiramate?



Augment * w/ other (AD or MS)

* Caution should be used when augmenting to minimize polypharmacy

"IMPULSE AGGRESSION"



Patient exhibits suspiciousness, referential thinking, paranoid ideation, illusions, derealization, depersonalization, or hallucination-like symptoms

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(e.g., perphenazine, 4–12 mg/day
trifluoperazine, 2–6 mg/day
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olanzapine, 2.5–10 mg/day[b]
risperidone, 1–4 mg/day[b])

- Efficacy → Continue
- Partial Efficacy → Increase Dose
- No Efficacy → Increase Dose

Increase Dose
(e.g., perphenazine, 12–16 mg/day
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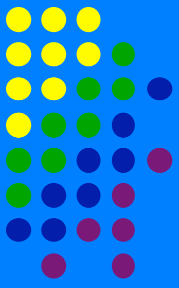
haloperidol, 4–6 mg/day)

- Efficacy → Continue
- Partial Efficacy → SSRI (or MAOI)
- No Efficacy
  - Prominent Affective Symptoms → Add → SSRI (or MAOI)
  - Few Affective Symptoms → Switch → Atypical Neuroleptic or Clozapine

"COGNITIVE PERCEPTUAL"

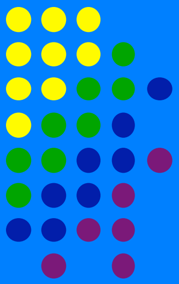
OUR REVIEW
(Saunders & Silk, 2009)



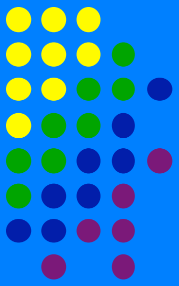
- Out of 20 studies, only 3 had more than 100 subjects and most (13) had less than 50
- 73 % of the subjects are women
- 16 different instruments for affective instability
  - 6 for Anxiety-Inhibition
  - 7 for Cognitive-Perceptual disturbances
  - 16 for Impulse, Impulsive-Aggression

Saunders & Silk: Personality trait dimensions and the pharmacologic treatment of borderline personality disorder. J Clin Psychopharm 2009, 29: 461-267.

THEN
DO MEDICATIONS WORK HERE?



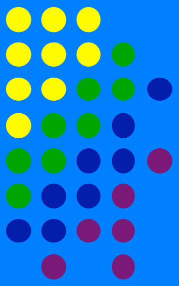
- The best we can say is that they remain non-specific in their response
- There is a high placebo response rate in clinical trials
- Some times we can’t appreciate that the medications are working until we experience the patient in the absence of the medication
- No long-term studies
- No continuation studies



POLYPHARMACY DANGER

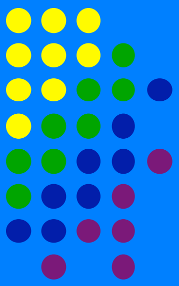
- Potential for polypharmacy exists
  - Especially when the psychopharmacologist is over-enthusiastic
    - Believes that medications can and will cure if only the right combination can be found
      - "The less than completely responsive patient meets increasing forms of sadism disguised as treatment" – T.F. Main, 1957
- What polypharmacy can guarantee are drug-drug interactions and weight gain

TRANSFERENCE-COUNTERTRANSFERENCE REACTIONS



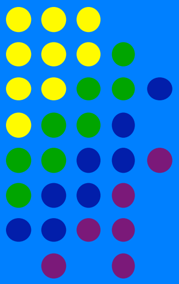
- These people are in real pain
- Their ability to express that pain verbally and behaviorally can at times be profound
- These people can have serious problems with impulsivity, self-destructive behavior, and suicidality
- This is America and more is always better
- We live in an age where augmentation of one medication with another is *de rigueur*
- Often we are trying to rid the patient of "depression" or at least to reduce it "even more"

DECIDING ON A MEDICATION



- What's happening in patient's life at that moment
- Is there a symptom or symptom complex reminiscent of an Axis I disorder?
- Is there evidence for positive medication effect for that symptom/symptom complex in Axis II?
  - e.g. depression, panic
- Try to distinguish true Axis I episode from emotion dysregulation
- Try to distinguish a true major depressive episode from chronic dysphoria, loneliness, emptiness
- Always consider co-morbid substance misuse

DECIDING ON A MEDICATION



"If there were two medications, one for depression and one for moods bouncing around, and if you could only take one, which one would you choose?"

- **No evidence that two medications work better than one for any symptom**
- **No evidence that two medications within the same class of medications work better than one**

THANK YOU FOR YOUR ATTENTION!!