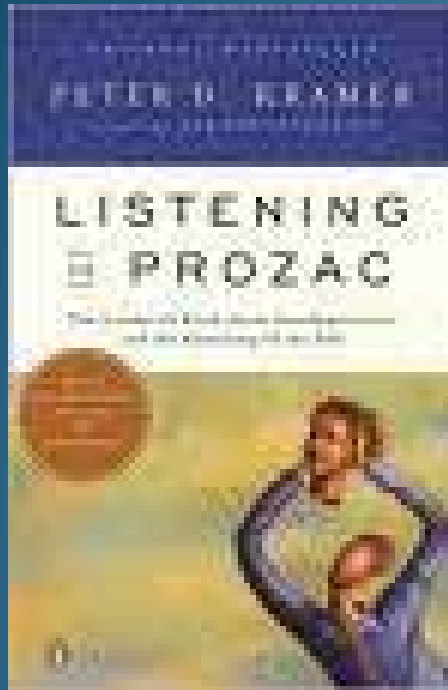


# MDD: Primary Care Challenges

Henry Fischer

Denver Health Medical Center

October 2009

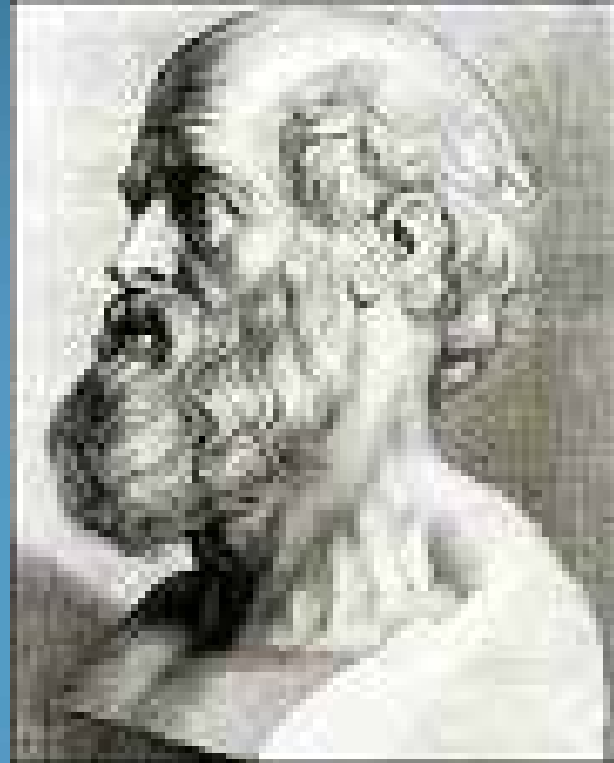


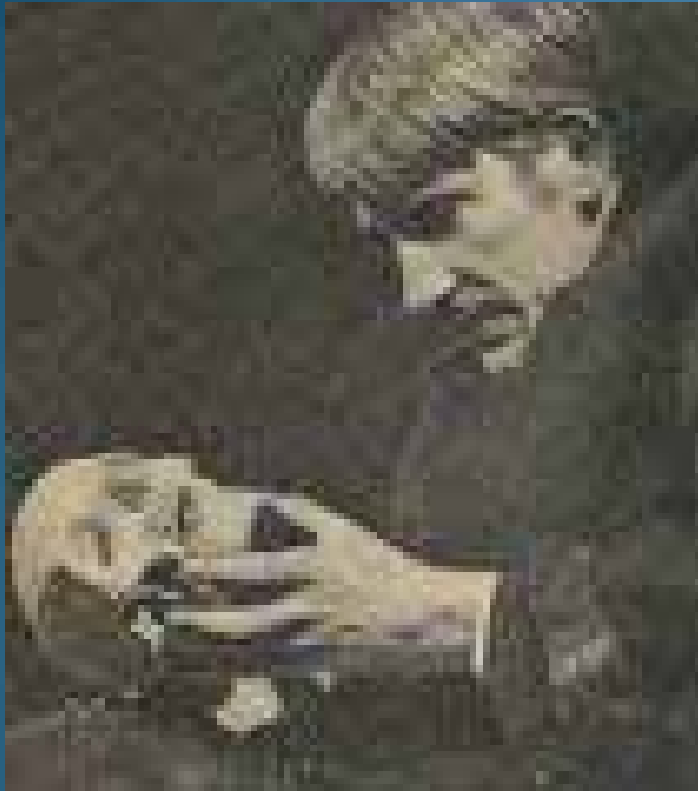
A book about the potential of medications to modify personality traits.....

.....that invigorated public discussion of depression

Hippocrates responds to  
claims of mental  
Illness as inspiration....

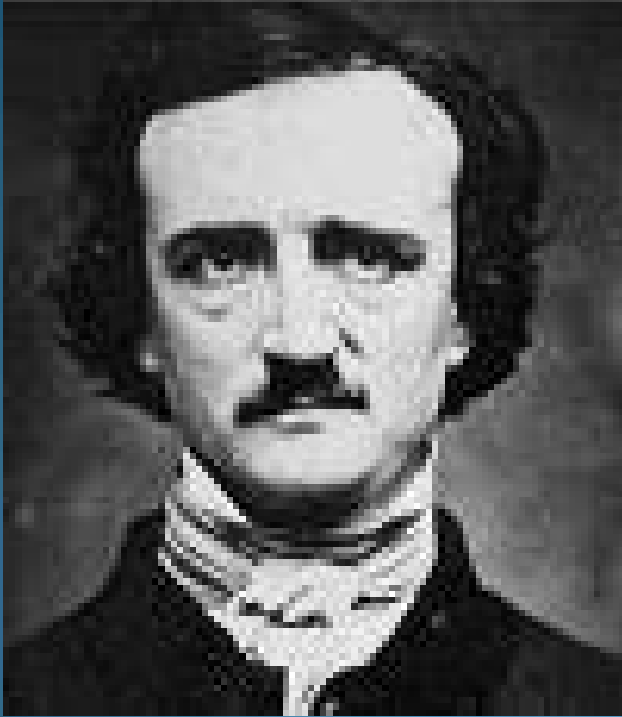
....by designating  
melancholy as a *disease* of  
excess bile, leading to  
dejection, ulcers,  
rashes, lung diseases





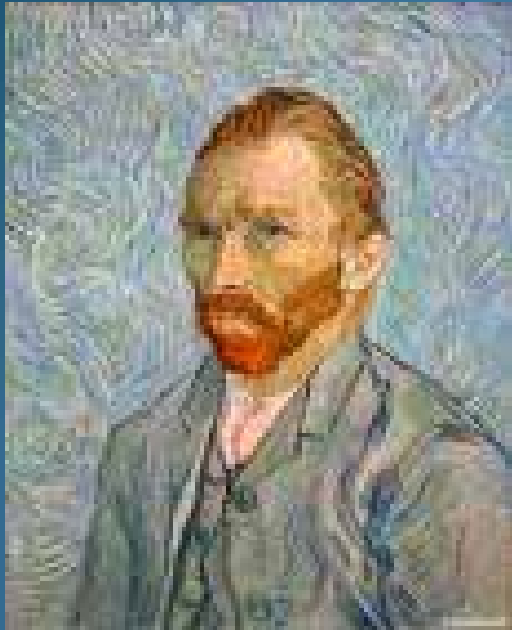
Does heroic melancholy lend  
a nobleness....

....and make depression less  
than a disease?



“An utter depression  
of soul....

...the hideous dropping  
off of the veil.”



Is depression a heavy dose of artistic temperament?.....

...and anti-depressants a means of remolding personality into a more acceptable form?

# YOU CAN CHANGE

God's transforming power  
for our sinful behaviour  
and negative emotions

Tim Chester

Are the depressed paying for their  
sins....

# Depression as Disease

- The fourth leading cause of temporary and permanent disability in 1990
- Molecular and imaging technologies show abnormalities in:
  - Cell signaling
  - Neuronal and glial survival
  - Brain region connectivity
  - Genetic predisposition
  - Include ref

Rubinow DR. Treatment strategies after SSRI failure—the good and bad news.  
NEJM March 2006

# Outline of Talk

- Diagnosis
  - Under-diagnosis or mis-diagnosis of depression in primary care?
  - Screening Tools
- Treatment: a focus on medications
  - Psychotherapy versus Medication
  - Monitoring and duration
  - Disease management programs
  - Comparison of classes of anti-depressants
  - Comparison of SSRI's: efficacy, side effects, half-life
  - Suicide and SSRI's
  - Bereavement and depression
  - Pregnancy and SSRI's
  - Resistant depression
  - Somatization and depression treatment

## 3-Year Incidence and Probable Etiology of 14 Common Symptoms in 1000 Internal Medicine Outpatients

Symptom	Number with Symptoms	Organic Etiology (%)	Psychogenic Etiology (%)	Unknown (%)
<b>Chest pain</b>	96	11	6	83
<b>Fatigue</b>	82	13	21	66
<b>Dizziness</b>	55	18	2	80
<b>Headache</b>	52	10	15	75
<b>Edema</b>	45	36	0	54
<b>Back pain</b>	41	10	0	90
<b>Dyspnea</b>	37	24	3	73

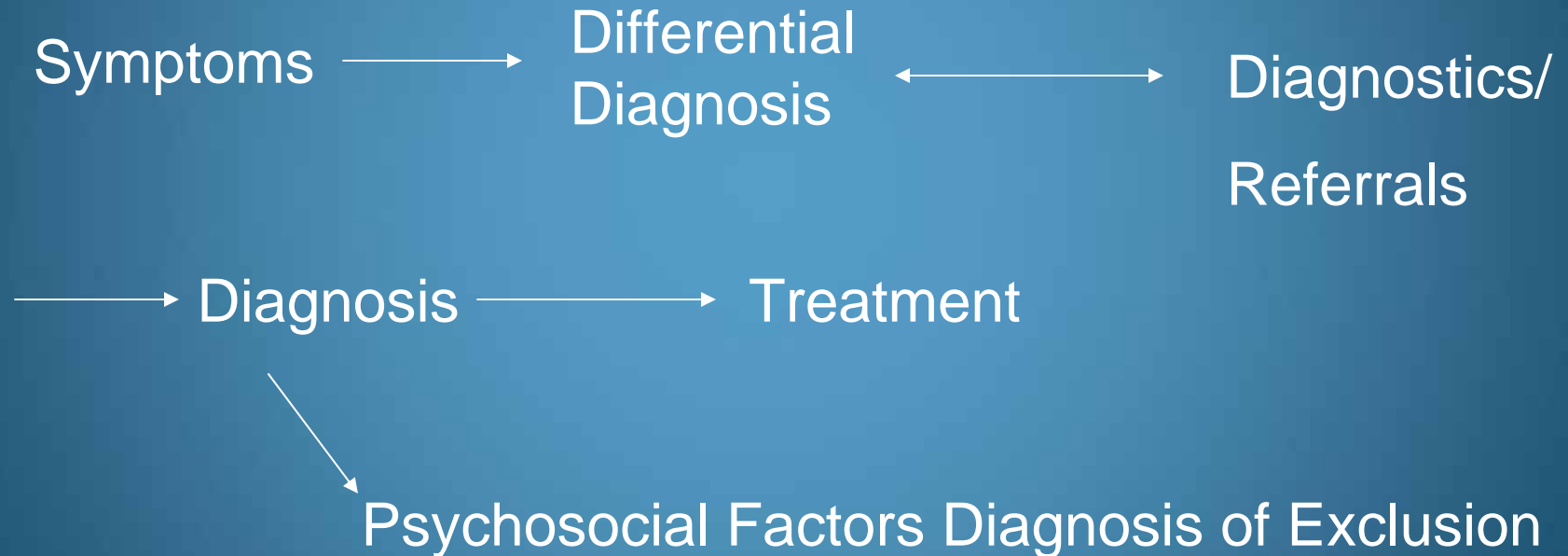
Kroenke, *American Journal of Medicine*, March 1989

## Prevalence of Major Depression in Patients with Medically Unexplained Symptoms versus Controls

Symptom		Lifetime Incidence of Depression
Chest Pain	CAD -	64%
	CAD+	16%
Gastrointestinal	Irritable Bowel Syndrome	61%
	Inflammatory Bowel Disease	17%
Musculoskeletal Pain	Fibromyalgia	86%
	Rheumatoid Arthritis	31%

Katon, *Psych Med*, 1991

# Traditional Biomedical Model vs Biopsychosocial Model



# Primary Care: Mis-diagnosis of Mental Disorders

- Only 33% of patients with a DSM-IV mental disorder receive treatment
- Medical treatment provided to patients who do not meet DSM-IV criteria (about ½ of treated patients)
- Treatment monitoring and duration not optimal

Kessler RC et al. Prevalence and Treatment of Mental Disorders: 1990-2003.  
NEJM June 2005.

# DSM-IV Diagnosis

- Major Depressive Disorder
  - At least 2 weeks of depressed mood and anhedonia and at least 5 associated sx: depressed mood, anhedonia, appetite, guilt, concentration, Suicidality, motor, sleep, ? libido
- Dysthymia
  - Depressed mood most days for at least 2 years. Does not meet criteria for MDD
- Subsyndromal Depression (Or “Minor” or “Subthreshold”)
  - Depressed mood at least 2 weeks, with fewer symptoms than MDD
- Melancholia
  - Severe MDD with anhedonia as major feature.
  - Includes early awakening, motor effects, and anorexia or weight loss

# Screening Tools

- **Patient Centered Interviewing** techniques superior?
- **PHQ-9**: valid in primary care and reliable—does not require follow-up confirmation of diagnosis
  - Score > 10 likely MDD, > 20 Severe MDD
  - Can be used to follow response to treatment
- **PHQ-2** (anhedonia or depressed mood in past 2 weeks)
  - Sensitivity is 0.83 and specificity 0.92 for score  $\geq 3$
- **Widespread Screening** of depression in primary care
  - has not been shown to improve management or outcome of depression
- **Bipolar Screen** (family hx, mania, sleep, racing thoughts, Mood Disorder Questionnaire—MDQ or BSDS)

# Therapy and public perception

From the extreme.....



# Discussion with patient

- **WHAT IS THE PATIENT'S PERCEPTION OF DEPRESSION AND ITS TREATMENT?**
- Depression is common (15 to 20% life incidence)
- Associated with emotional and physical sx
- Due to chemical changes in the brain
- Medication and/or psychotherapy shortens the course and diminishes sx

# Psychotherapy versus pharmacotherapy

- 69% of 203 pharmacotherapy trials sponsored by pharmaceuticals
  - “Real-World” study showed 28% remission in mean time of 6.7 weeks; 47% response rate ( $\geq 50\%$  reduction in symptom scores)
- Depression-specific psychotherapy with equivalent outcomes to well-monitored pharmacotherapy
- Combined psychotherapy and pharmacotherapy with better response than either alone
  - ? Cost effective; ? a viable option

Schulberg HC et al. The effectiveness of pharmacotherapy at treating depressive disorders in primary care practice. Gen Hosp Psych July 2002.

# Medication Choice

- Similar efficacy but less side effects for 2<sup>nd</sup> generation versus 1<sup>st</sup> generation anti-depressants
  - 1<sup>st</sup> generation: tricyclics, MAO inhibitors
  - 2<sup>nd</sup> generation: SSRI, SSNRI (duloxetine), SNRI (venlafaxine, mirtazapine), and other (bupropion)

# Impact on Associated Symptoms

- No clear evidence of improved superiority of any 2<sup>nd</sup> generation agent impact on:
  - Anxiety
    - (10 head to head trials)
  - Sleep
    - (some mixed results over 8 head-to-head trials)
  - Pain
    - (Duloxetine versus paroxetine in 4 head-to-head trials)

# Rates of Adverse Events

- GI side effects/Headaches/anxiety
  - similar side effect profiles
- Sexual Dysfunction
  - Rates are likely under-reported
  - Bupropion lower rate than fluoxetine
  - Paroxetine higher rate than multiple other SSRI's
- Weight Gain
  - Paroxetine and Mirtazapine more weight gain than sertraline, trazodone, or venlafaxine

# Therapy: Monitoring and Duration

- Assess for response and side effects 1-2 weeks after initiation of therapy
- Modify therapy at 6-8 weeks if insufficient response
- 4 to 9 months after a satisfactory response for first time episode
- Longer duration may be beneficial for patients with 2 or more episodes of depression

# Disease Management Programs

- Studies of primary care nurses or telephone-based health coaches showed similar benefit
- 10% gain in depression recovery and appropriate treatment over 1 year
- Between 2 to 4 weeks of more work days in a year
- DH managed care: health coaches after SSRI initiation

# Treatment of depression in selected populations

- No convincing difference in efficacy between agents for age, race, and sex
- Based on subgroup analyses in numerous studies: need RCT's for these subgroups

# Treatment-Resistant Depression

- Definition: failure to produce significant clinical improvement with trials of 2 different pharmacological classes of anti-depressant
  - Reassess dx, adherence, and barriers
- Augmentation with psychotherapy effectiveness is reasonable although evidence limited (1 high quality RCT)
- No good evidence for superior medication treatment strategy (Star\*D Trial)—initial therapy citalopram
  - Level 2 (remission 25% response rate 25%)
    - Switch agents: sertraline, bupropion, or venlafaxine
    - augment with buspirone or bupropion or CBT
  - Level 3 (remission rate 8-20%; response rate (13-23%))
    - Switch agents mirtazapine or nortriptyline
    - Augmentation of citalopram with tri-iodothyronine, lithium, CBT



SSRI discontinuation and withdrawal

# Discontinuation of SSRI's

- Withdrawal sx: HA, GI, anxiety, insomnia
- $\frac{1}{2}$  lives of SSRI's after multiple doses: Fluoxetine > Citalopram > Sertraline > Fluvoxamine > Paroxetine
- Withdrawal sx observed with venlafaxine (not well studied), but infrequent with bupropion
- Small trial (N=28) comparing taper over 3 days versus 2 weeks showed no difference in withdrawal
- Common recommendation: taper over 2 to 4 weeks; dose reduction of 25% per week

Tint A et al. The effect of rate of anti-depressant tapering on the incidence of discontinuation symptoms. J. of Psychopharm 2008 May; 22(3): 330-2.

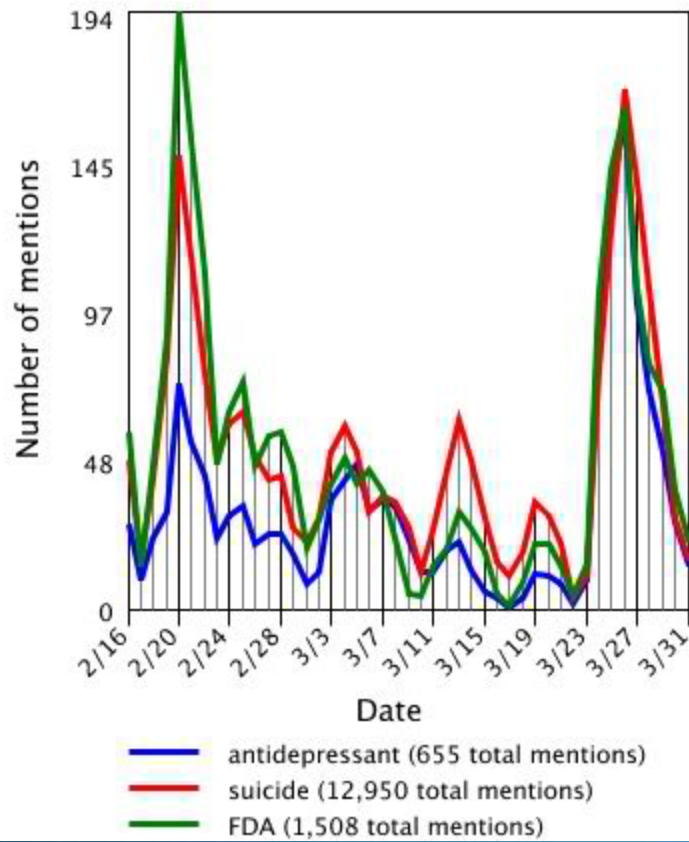


Bereavement or depression?

# Depression in Bereavement

- Part of the normal grieving process or a harbinger for prolonged, substantial morbidity?
- Expert opinion: treat for depression if meet criteria for MDD 6-8 weeks after a major loss
  - Studies (few and small) show decreased depressive symptoms but unchanged grief symptoms
- Risk factors for poor bereavement outcomes
  - Poor social support
  - h/o depression or psychiatric illness
  - Major concurrent stressors
  - h/o abuse or neglect

The Waypath Weblog Buzz-o-meter  
For the 45 days preceding March 31, 2004  
<http://www.waypath.com>



# SSRI's and Suicide

# SSRI's and Suicide in Adults

## Two Contrasting Hypotheses

- **RCT's:** No evidence of increased Risk
  - Small studies of short duration
  - Often exclude at-risk patients
- **Meta-analyses:** Increased SI
  - SI sometimes used as surrogate for suicide risk
- **Ecological Studies:** decreased suicides or no change in suicides with increased SSRI prescriptions
- **Observational Studies:** no difference in risk in SSRI's and TCA's
  - Confounding by indication
  - Small numbers of suicides
- **Conclusions**
  - If risk is increased, it is likely small
  - Benefits, at least in adults, outweigh risks
  - Prudent to monitor SI in first weeks of treatment (dz management programs)

Hall DW. Anti-depressants and Suicide Risk. Lancet, June 2006.

# Risk of teratogenicity from SSRI's?

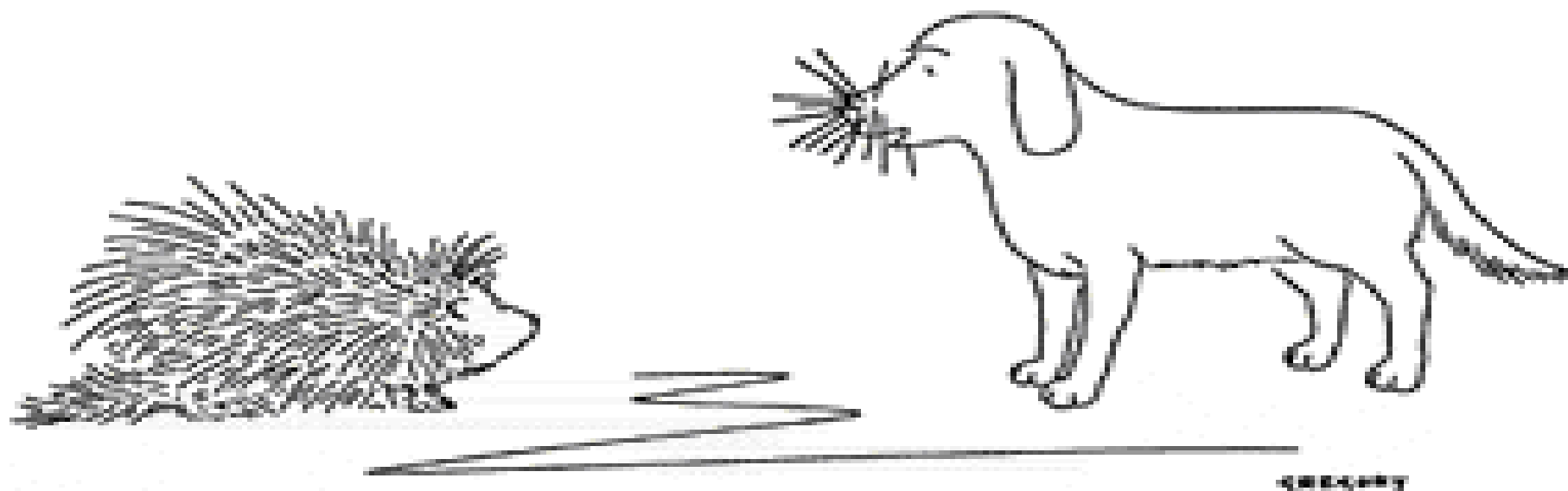


# SSRI's and teratogenicity

- Based on pharmaceutical safety data and 3 large studies
- Retrospective case-control methods
- Mixed results regarding risk of: cardiac malformations and CNS/neural tube defects
- Data suggests a small increased absolute risk of teratogenicity, unlikely to exceed absolute 1%
  - Risk may be higher with paroxetine

# Somatization and Depression

- Kroenke: over 2/3 of somatic symptoms have no identifiable organic etiology
  - Hypothesis: psychosocial factors often precipitate symptoms
- Somatoform Disorder and concomitant MDD
  - Somatic Sx diminish with pharmacotherapy/CBT
- Somatization and failure to meet DSM criteria of MDD
  - Limited study of SSRI's/psychotherapy



*“On the plus side, you’ve cured my back pain.”*