Scope of the Problem: Epidemiology of Sexual Dysfunction: Men

Common problem worldwide

- 30 million in US; 152 million worldwide
- 31% incidence of any dysfunction in men 18-59 years old
- Erectile dysfunction (ED) most commonly reported, but effects on libido also occur

ED may be age related

- US: Complete impotence increased from 5% in men 40 years old to 15% in 70 years old
- Netherlands: ED 22% men 50-54, increased to 54% in 70-78 year old

Feldman et al J. Urol 1994;151:54-
Laumann et al JAMA 1999;281:537-544
Blanker et al Urology 2001;57:763-
## Hormonal Changes in the Aging Male

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone</td>
<td>decreased</td>
</tr>
<tr>
<td>Bioactive testosterone</td>
<td>decreased</td>
</tr>
<tr>
<td>Dihydroepiandrosterone</td>
<td>decreased</td>
</tr>
<tr>
<td>Sex hormone binding globulin (SHBG)</td>
<td>increased</td>
</tr>
<tr>
<td>Lutenizing hormone (LH)</td>
<td>increased</td>
</tr>
</tbody>
</table>

*Steftel J Urol 2003;169:1999-2007*
Scope of the Problem:
Epidemiology of Sexual Dysfunction:
Women

• Female dysfunction can be subdivided into disorders of desire, arousal, orgasmic, pain
• Incidence varies depending upon ascertainment methodology
  • 40% women 18-59 years
    • Low desire 22%, arousal problems 14%, pain 7%

Laumann et al. JAMA 1999;281:537-544
### Spectrum of Potential Sexual Dysfunction in Women

<table>
<thead>
<tr>
<th>Alterations in Desire</th>
<th>Dyspareunia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyposexuality</td>
<td>Pain during intercourse</td>
</tr>
<tr>
<td>Inhibition of desire</td>
<td>Pain after intercourse</td>
</tr>
<tr>
<td>Aversion</td>
<td>Painful orgasm</td>
</tr>
<tr>
<td>Hypersexuality</td>
<td></td>
</tr>
<tr>
<td>Panic/phobia</td>
<td></td>
</tr>
<tr>
<td>Obsessive-compulsive</td>
<td></td>
</tr>
<tr>
<td><strong>Lubrication Disorders</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Orgasmic Disorders</strong></td>
<td><strong>Menstrual Disorders</strong></td>
</tr>
<tr>
<td>Orgasmic inhibition</td>
<td>Dysmenorrhea</td>
</tr>
<tr>
<td>Anorgasmia</td>
<td>Menorrhagia</td>
</tr>
<tr>
<td><strong>Diminished number of orgasms</strong></td>
<td>Amenorrhea</td>
</tr>
<tr>
<td>Altered perception</td>
<td></td>
</tr>
<tr>
<td>Anesthetic orgasm</td>
<td></td>
</tr>
<tr>
<td>Spontaneous orgasm</td>
<td></td>
</tr>
<tr>
<td>Infertility</td>
<td>Clitoral Hypertrophy</td>
</tr>
<tr>
<td>Decreased frequency of ovulation</td>
<td></td>
</tr>
<tr>
<td>Decreased quality of egg</td>
<td></td>
</tr>
<tr>
<td>Hypofertility</td>
<td></td>
</tr>
<tr>
<td>Breast Disorders</td>
<td></td>
</tr>
<tr>
<td>Galactorrhea</td>
<td></td>
</tr>
<tr>
<td>Gynecomastia</td>
<td></td>
</tr>
<tr>
<td>Pain/tenderness</td>
<td></td>
</tr>
<tr>
<td>Paraphilia</td>
<td></td>
</tr>
</tbody>
</table>

# Spectrum of Potential Sexual Dysfunction in Men

<table>
<thead>
<tr>
<th>Alterations in Desire</th>
<th>Orgasm/Ejaculation Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypossexualty</td>
<td>Ejaculatory incompetence (inability)</td>
</tr>
<tr>
<td>Inhibition of desire</td>
<td>Ejaculatory inhibition (delay)</td>
</tr>
<tr>
<td>Aversion</td>
<td>Ejaculation without orgasm</td>
</tr>
<tr>
<td>Hypersexuality</td>
<td>Orgasm without ejaculation</td>
</tr>
<tr>
<td>Panic/phobia</td>
<td>Retrograde ejaculation</td>
</tr>
<tr>
<td>Obsessive-compulsive</td>
<td>Decreased ejaculatory volume</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Erection Abnormalities</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability/difficulty obtaining erection</td>
<td>Anesthetic ejaculation</td>
</tr>
<tr>
<td>Inability/difficulty maintaining erection</td>
<td>Spontaneous orgasm</td>
</tr>
<tr>
<td>Decreased firmness of erection</td>
<td>Painful ejaculation</td>
</tr>
<tr>
<td>Ejaculation through flaccid or semi-erect penis</td>
<td>Premature ejaculation</td>
</tr>
<tr>
<td>Painful erection</td>
<td>Dyspareunia</td>
</tr>
<tr>
<td>Peyronie’s disease</td>
<td>Pain during intercourse</td>
</tr>
<tr>
<td>Priapism</td>
<td>Pain after intercourse</td>
</tr>
<tr>
<td>Decreased or absent nocturnal/morning erections</td>
<td>Painful ejaculation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infertility</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased or malformed spermatogenesis</td>
<td>Breasts</td>
</tr>
<tr>
<td>Decreased sperm motility</td>
<td>Galactorrhea</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td>Gynecomastia</td>
</tr>
<tr>
<td>Testicular atrophy</td>
<td>Breast pain/tenderness</td>
</tr>
</tbody>
</table>

| Paraphilia             |
|------------------------|-----------------------------|
Assessment of Sexual Adverse Effects: How good is the data?

- Many studies retrospective in nature
- Many studies lack controls
- Imprecise classification/description of medical and/or psychiatric comorbidities
- Insufficient data on drug exposure (how many, how long, previous exposure, doses, etc…)
- Patient self report vs clinician interview
Assessment of Sexual Dysfunction

• Early clinical studies rarely detect sexual dysfunction
  • Few studies systematically evaluate for this adverse effect

• Post-marketing surveillance studies also historically report low incidence

• Relatively few physicians (~50%) routinely obtain sexual history from their patients
  • Direct inquiry yields higher reporting rates as compared with spontaneous reports (58% vs 14%)

Bull et al Sex Tram Dis 1999;26:584-589
Montejo-Gonzalez et al J Sex Marital Ther 1999;23:176-194
Neurophysiology of Sexual Response
The Sexual Response

- Sexual response is a complex, multifactorial process

- Sexual dysfunction may result from a disturbance in 1 or more domains including
  - Cognitive
  - Psychosocial
  - Neurological
  - Vascular
Neurophysiology of Sexual Response

• Requires intact libido and arousal response
  • Libido (desire) involves both affective and cognitive processes
  • Arousal (capacity to respond to stimuli) depends on neural, muscular and vascular response
• Sexual response is under control of both central & peripheral neural systems

Limbic system & Hypothalmus

Adapted: Marieb. Human Anatomy 4th Ed.
Positive Modulators of Sexual Response: Neurotransmitters & Neuropeptides

NATURALLY OCCURRING ENDOGENOUS SUBSTANCES WITH GENERALLY EXCITATORY SEXUAL ACTIONS
(Increase in dose or activity favorable to sex; decrease in dose or activity unfavorable to sex.)

- Adrenergic (Alpha₁) Activity
- Adrenergic (Beta₂) Activity
- Calcitonin-Gene-Related-Peptide (CGRP)
- Cholinergic Activity
- Dehydroepiandrosterone (DHEA/DHEAS)
- Dopamine (DA)
- Endothelium-derived Relaxing Factor (EDRF)
- Estrogen (female only)
- Excitatory Peptides
- Growth Hormone (GH)
- Histamine
- Luteinizing Hormone Releasing Hormone (LHRH)
- Nitric Oxide (NO)
- Oxytocin
- Prostaglandins
- Substance P (SP)
- Testosterone
- Vasoactive Intestinal Peptide (VIP)
- Vasopressin
- Zinc (replacement value only)
Neurophysiology of Sexual Response: Facilitatory Effects

- Activation of oxytocinergic neurons projecting to limbic structures and spinal cord by dopamine, norepinephrine and excitatory amino acids facilitates erectile function.
  - Activation of these neurons secondary to activation of nitric-oxide synthase → nitric oxide.
Inhibitory Modulators of Sexual Response: Neurotransmitters & Neuropeptides

NATURALLY OCCURRING ENDogenous SUBSTANCES WITH GENERALLY INHIBITING SEXUAL ACTIONS
(Increase in dose or activity unfavorable to sex; decrease in dose or activity favorable to sex.)

Adrenergic (Alpha₂) Activity
Angiotensin II (Ang II)
Cortisol
Estrogen (male only)
Melatonin
Monoamine Oxidase (MAO)
Neuropeptide Y (NPY)
Opioids
Progesterone
Prolactin
Serotonin (5-HT) (5HT 1B, 2C, 2A, 3)
Thyroid Hormone*
Vasoconstrictive Peptides (Ang II and NPY)
Neurophysiology of Sexual Response: Inhibitory Effects

- GABA, opioid peptides reduces activation of nitric oxide synthase, and impairs erection
- Increased serotonin neurotransmission in lateral hypothalamus can result in decreased libido and impaired orgasm, ejaculation
  - Variable effects depending on 5-HT receptor subtype being stimulated
  - Postulated mechanisms include modulation of CNS dopamine, inhibition of NO synthase
Control of Sexual Response: Sex Steroids

Estrogen
- Effect on sexual desire relatively small in both men and women
- Does appear important in maintaining arousal in women
- Hypothalamic aromatase suggests some central conversion of testosterone to estradiol

Androgens
- Male sexual behavior largely modulated by testosterone and DHT
- Androgens important in maintaining arousal in women
- Very low levels of testosterone consistently associated with decreased desire and occasionally ED
- Supra-physiologic concentrations of testosterone do not modify desire or behavior

Local Control of Sexual Response: Modulation of Cavernosal Smooth Muscle

Involvement of adrenergic & cholinergic systems

• Alpha Adrenergic stimulation $\rightarrow$ contraction of cavernosal tissue $\rightarrow$ flaccid
  • $B_2$ activation $\rightarrow$ positive
  • $B_2$ blockade $\rightarrow$ inhibitory

Cholinergic inhibitory control $\rightarrow$ relaxation of cavernosal tissue $\rightarrow$ erection

• Neuronal & endothelial derived nitric oxide $\rightarrow$ activation of guanylate cyclase $\rightarrow$ $\uparrow$ cyclic GMP $\rightarrow$ relaxation of smooth muscle $\rightarrow$ erection

• VIP, NPY prostaglandins also involved in control of erection
Summary

• Sexual dysfunction is a common problem
• Not limited to men
• Prevalence likely increased with advancing age
• Understanding drug/disease interactions a necessary 1st step in assessment
• Knowledge of drug pharmacological properties valuable in predicting potential adverse effects
Sexual Dysfunction

Looking at the whole patient:
The role of co-morbid disorders
Sexual Dysfunction In PWE: A Biopsychosocial Model

John J. Barry, MD
Associate Professor of Psychiatry
Stanford University Medical Center
Biological Issues In Sexual Dysfunction – Part 2

- Overall medical issues need to be assessed
- Specific issues related to PWE
- Medication side-effects
  - Related to epilepsy
  - Other common co-morbid disorders seen in PWE, i.e. psychiatric disorders
Causes of Sexual Dysfunction

- **Drugs****!
- **Medical** – vascular; endocrine (hyperprolactinemia, thyroid dysfunction and specifically low testosterone); systemic illness – renal, hepatic, cardiac, pulmonary and cancer; urogenital – infections and injury.
- **Neurological** – spinal cord, neuropathy and cortical lesions
- **Psychogenic** – psychiatric (psychosis, affective illness); intrapsychiatric (religious, social, family taboos, sexual experiences and low self-esteem); extrapsychic (dysfunctional relationship)

## Causes of Sexual Dysfunction: Effect of Co-morbid Disorders

<table>
<thead>
<tr>
<th>Endocrine</th>
<th>Gastrointestinal</th>
<th>Gynecological</th>
<th>Immunological</th>
<th>Neurological</th>
<th>Urological</th>
<th>Vascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acromegaly</td>
<td>Constipation</td>
<td>Dysfunctional bleeding</td>
<td>AIDS/HIV</td>
<td>Alzheimer’s disease</td>
<td>Chronic kidney disease</td>
<td>Arteriosclerosis</td>
</tr>
<tr>
<td>Adrenal dysfunction</td>
<td>Diarrhea</td>
<td>Dyspareunia</td>
<td>Arthritis &amp; other bone/joint disorders</td>
<td>Brain lesions</td>
<td>Cystitis (acute, chronic &amp; postcoital)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Irritable bowel syndrome</td>
<td>Endometriosis</td>
<td>Cancer</td>
<td>Dementia</td>
<td>Epididymitis</td>
<td>Fistula</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>Ulcerative colitis</td>
<td>Genital warts</td>
<td>Chronic fatigue syndrome</td>
<td>Diabetic neuropathy</td>
<td>Peyronie’s disease</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Hypogonadism</td>
<td></td>
<td>Infertility / pregnancy</td>
<td>Respiratory diseases</td>
<td>Epilepsy</td>
<td>Parkinson’s disease</td>
<td>Ischemia</td>
</tr>
<tr>
<td>Thyroid dysfunction</td>
<td>Menopause</td>
<td>Infertility / pregnancy</td>
<td>Respiratory diseases</td>
<td>Multiple sclerosis</td>
<td>Renal failure</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td></td>
<td>Menstrual cycle disorders</td>
<td></td>
<td></td>
<td></td>
<td>Parkinson’s disease</td>
<td>Stroke</td>
</tr>
<tr>
<td></td>
<td>PMS</td>
<td></td>
<td></td>
<td></td>
<td>Renal failure</td>
<td>Transient ischemic attacks (TIAs)</td>
</tr>
<tr>
<td></td>
<td>Vaginismus</td>
<td></td>
<td></td>
<td></td>
<td>Parkinson’s disease</td>
<td>Venous insufficiency</td>
</tr>
<tr>
<td></td>
<td>Vaginitis</td>
<td></td>
<td></td>
<td></td>
<td>Renal failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(bacterial, fungal, trichomonal, viral)</td>
<td></td>
<td></td>
<td></td>
<td>Parkinson’s disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Spinal injury or tumors</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stroke</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Urinary incontinence</td>
<td></td>
</tr>
</tbody>
</table>
Comorbid Disorders in Elderly Patients with Epilepsy

- Dyslipidemia 80%
- Hypertension 53.8%
- Stroke 52.7%
- Cardiac disease 48.1%
- Diabetes 28.3%
- Cancer 23.8%
- Psychiatric disease 21.6%
- Renal disease 12.3%
- Liver disease 2.7%
- Parkinson’s disease 2.7%

Ramsay et al, Epilepsia 2002;35(Suppl 8):91
The Role of Co-Morbid Disorders: Epilepsy

Sexual dysfunction described in 33-66% of men and women with epilepsy

- Men report less sexual experience, anorgasmia and high incidence of ED (self-reported data)
- Low testosterone concentrations, and impaired nocturnal penile tumescence reported
- Both men and women with temporal lobe epilepsy demonstrate diminished physiologic arousal (genital blood flow) in response to visual erotic stimuli
- Likelihood of sexual dysfunction may increase in patients with continued seizures, and those with a longer history of seizures

Morrell Epilepsia 1991;32(Suppl 6):38-45
Morrell et al Neurology 1994;44:243-247
Herzog et al Arch Neurol 1986;43:347-350
The Role of Co-Morbid Disorders: Epilepsy-Possible Etiologies

Epilepsy as a cause:

- Higher frequencies in partial epilepsies (60% Vs 10%)
- Noted in PWE naïve to AED
- Laterality – right > left
- Improvement with Anterior Temporal Lobectomy
- Influence of interictal discharges on gonadotropins and prolactin and altered hypothalamic-pituitary activity
Biology – Sexual Dysfunction in PWE

• Morrell et al: (1994)¹ studies of genital blood flow (GBF) in both men (N=8) and women (N=9) showed significant decreases in response to viewing erotic material compared to control (12 women and 7 men). Women with epilepsy reported less arousal and more anxiety perhaps associated with seizure activity. Fewer sexual experiences were reported by both men and women with epilepsy.

• Morrell et al: (1996)² Nocturnal penile tumescence in 5 of 6 men with TLE epilepsy were abnormal

• Morrell et al: (1996)³ 116 women were evaluated (99 with LRE and 17 with PGE) – reported no dysfunction in sexual desire but rather one third had dysfunction in sexual arousal which included (in those with LRE) dyspareunia, vaginismus, arousal insufficiency and (in those with PGE) anorgasmia with both groups c/o sexual dissatisfaction. Conclusion – treatable conditions warranting GYN referral

Biology – Sexual Dysfunction in PWE

- Herzog et al: (1991)¹ Reported androgen deficiency in men with epilepsy. Noted the importance of free testosterone levels and the development of hypogonadism and functional hyperprolactinemia. Role of increased conversion of testosterone to estradiol in men with epilepsy and the use of aromatase inhibitor or the antiestrogen clomiphene.

  - Sexual dysfunction scores significantly higher in women with temporal lobe epilepsy vs control (right > left)
  - Inverse relationship between bioactive testosterone sexual dysfunction
  - Serum estradiol lower in women with epilepsy vs controls

- Herzog et al. (2004)³ Reviewed the effects of AED on sexual functioning and hormone levels in 63 men with epilepsy. Noted the superiority of lamotrigine in contrast to the enzyme inducing AEDs.

Biological Issues In Sexual Dysfunction

Drugs
Medications & Sexual Function

Psychotropic agents
• SSRI’s
• MAOI’s
• Lithium
• -typical & atypical antipsychotics

Antiepileptic drugs
• phenytoin
• carbamazepine
• phenobarbital
• primidone

# Medications & Sexual Function

<table>
<thead>
<tr>
<th><strong>Antihypertensives</strong></th>
<th><strong>Misc</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Beta blockers</td>
<td>• Opiods</td>
</tr>
<tr>
<td>• Thiazides</td>
<td>• Metoclopramide</td>
</tr>
<tr>
<td>• Clonidine, methyldopa</td>
<td>• Cimetidine</td>
</tr>
<tr>
<td>• Spironolactone</td>
<td>• Statins</td>
</tr>
<tr>
<td>• Alpha antagonists</td>
<td>• Alcohol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Hormones</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Estrogen</td>
</tr>
<tr>
<td>• Antiandrogens</td>
</tr>
</tbody>
</table>

AED Effects on Sexual Function: Potential Mechanisms

• Older AEDs (phenytoin, carbamazepine, phenobarbital & primidone) induce hepatic drug metabolism

• Cytochrome P450 isozymes participate in metabolism of estradiol and testosterone

• Increased hepatic synthesis of sex hormone binding globulin (SHBG) → ↓ concentrations of bioactive androgen
Differential Effects of AEDs on Sexual Function and Reproductive Hormones in Men with Epilepsy

<table>
<thead>
<tr>
<th>Group</th>
<th>S-score (/20)</th>
<th>SHBG (μg/dl)</th>
<th>BAT (ng/dl)</th>
<th>BAE (pg/ml)</th>
<th>BAT/BAE</th>
<th>BAT/LH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 18)</td>
<td>18.8</td>
<td>0.83</td>
<td>307</td>
<td>25.1</td>
<td>129</td>
<td>70.9</td>
</tr>
<tr>
<td>(n = 9)</td>
<td>[18.2–19.4]</td>
<td>[0.65–1.05]</td>
<td>[265–350]</td>
<td>[21.7–28.5]</td>
<td>[107–147]</td>
<td>[54.6–87.2]</td>
</tr>
<tr>
<td>LRE/No AED</td>
<td>17.3</td>
<td>0.85</td>
<td>236&lt;sup&gt;a&lt;/sup&gt;</td>
<td>26.6</td>
<td>93&lt;sup&gt;a&lt;/sup&gt;</td>
<td>64.3</td>
</tr>
<tr>
<td>(n = 9)</td>
<td>[14.6–20.0]</td>
<td>[0.55–1.10]</td>
<td>[152–320]</td>
<td>[20.3–32.9]</td>
<td>[63–123]</td>
<td>[48.1–90.5]</td>
</tr>
<tr>
<td>LRE/LTG (n = 18)</td>
<td>18.3</td>
<td>0.85</td>
<td>262</td>
<td>21.7</td>
<td>128</td>
<td>58.1</td>
</tr>
<tr>
<td>(n = 18)</td>
<td>[17.5–19.1]</td>
<td>[0.66–1.04]</td>
<td>[215–309]</td>
<td>[18.4–25.0]</td>
<td>[105–151]</td>
<td>[48.4–67.8]</td>
</tr>
<tr>
<td>LRE/EIAED (n = 36)</td>
<td>16.2&lt;sup&gt;be&lt;/sup&gt;</td>
<td>1.47&lt;sup&gt;bde&lt;/sup&gt;</td>
<td>211&lt;sup&gt;be&lt;/sup&gt;</td>
<td>23.5</td>
<td>98&lt;sup&gt;ee&lt;/sup&gt;</td>
<td>44.7&lt;sup&gt;bde&lt;/sup&gt;</td>
</tr>
<tr>
<td>(n = 36)</td>
<td>[15.0–17.4]</td>
<td>[1.21–1.73]</td>
<td>[180–242]</td>
<td>[21.2–25.8]</td>
<td>[83–113]</td>
<td>[36.8–52.6]</td>
</tr>
</tbody>
</table>
Differential AED Effects on Sexual Dysfunction in Women

Morrell et al 2004

- Women with epilepsy (31.5.6 years) more likely to report sexual dysfunction than were healthy controls
- Women receiving enzyme inducing drugs, particularly phenytoin or phenobarbital had significantly lower sexual arousal scores as compared to controls
- As compared to controls, depression was more common in women with partial seizures
- Effects were modestly correlated with reduced androgen (DHEAS) concentrations

Morrell M et al, Submitted Epilepsy & Behavior 2004
Strategies for the Management of Sexual Dysfunction Related to AEDs¹

- Need baseline sexual functioning
- Eliminate other causes of sexual dysfunction
- Choose an AED with a low frequency of sexual dysfunction and one with few effects of SHBG
- Use alternative strategies for sexual dysfunction, ie psychotherapy
- Use monotherapy and consider a switch in anticonvulsants if necessary and possible

Biological Issues In Sexual Dysfunction

Psychiatric disorders - Depression
The Role of Co-morbid Disorders: Depression

- Sexual dysfunction is correlated with depression. Changes in sexual function (particularly libido) can be symptoms of depression. It has been estimated that between 30-70% of patients with a Depressive Disorder suffer from a primary sexual dysfunction.

- In addition - treatment emergent sexual dysfunction noted in 50-60% of men and women

- Sexual side effects can have a negative impact on medication adherence.

Fava J Clin Psych 2002;63(Suppl 5):13-16
Laumann et al. JAMA 1999;281:537-544
Shabsigh et al Urology 1998;52:848-852
Incidence of Psychiatric Disorders in PWE – Depression and Anxiety

- **Lifetime-to-date major depression**
  - Chronic epilepsy: 29% mean of 7 studies\(^1\)
  - Kessler et al in 1994 found a rate of 17.1% in the general population\(^2\)

- **Evaluation of 174 patients with epilepsy**
  - 48.9% had a current Axis I disorder; 24.1% had a mood disorder (n = 42) and 52.3% had an anxiety disorder (n = 91); 72.9% of patients with a depressive disorder also had an anxiety disorder\(^3\)

- **Community sample**
  - 24.9% of those with epilepsy had a significant depression (nearly 10× higher than the no-disease group). People with epilepsy and depression had an increased seizure frequency, poorer compliance, greater unemployment, and higher medical usage than people with epilepsy and no depression.\(^4\)

---


Medication Effects on Sexual Function: Antidepressant Agents

- Erectile dysfunction (10-30%)
- Loss of libido (40-60%)
- Delayed orgasm (46-59%)
- Anorgasmia (31-48%)

Incidence of Sexual Side-Effects of Antidepressants

< 10%:
  • bupropion, mirtazepine, moclobemide

10%-30%:
  • citalopram, duloxetine, venlafaxine

>30%:
  • fluoxetine, fluvoxamine, paroxetine and sertraline

Incidence of TCA’s and MAOI are similar to SSRIs and dual action antidepressants
Potential Treatment Options for Sexual Dysfunction Associated with Antidepressants¹

- Avoidance of potentially offending drug
- Switching/dose reduction/drug holiday
- Herbals (Ginkgo)
- Yohimbine
- Cyproheptadine
- Testosterone replacement
- Dopaminergic agents
- Type 5 phosphodiesterase inhibitors

Addition of Sildenafil

• Reportedly safe for restoring sexual performance in PWE with a usual dosage of 50 mg/day¹

• Gilad et al. reported two cases of new onset seizure activity seemingly associated with sildenafil, i.e. caution is needed²

From Pharmacology to Psychology – Bridging the Gap!!

Annie Hall:

D Keaton – (to her psychiatrist)
• “He wants sex all the time”

W Allen – (to his psychiatrist)
• “She never wants sex”

• The psychiatrist in both sessions asks the insightful question – “how many times is that”

• Both answer separately – “Oh! about three times a week”
The transition from abstinence to intimacy:

- The Sexual Equilibrium – each partner is simultaneously responding to the other partner. A destabilization can result in sexual avoidance

- Chronic dysfunction → sexual apathy (as a result of “erections and intercourse are necessary”, male embarrassment, hypoactive sexual desire in one or both partners, lack of satisfaction in past sexual relationship, preexisting psychopathology and relationship discord)
Sexual Assessment and Psychosocial Management

Mimi Callanan, RN, MSN
Epilepsy Clinical Nurse Specialist
Stanford Comprehensive Epilepsy Center
Epidemiology of Sexual Dysfunction

- General population
- Chronic illness
- Epilepsy
Sexual Assessment

- Formulating the question
- Using sexual assessment tools
Sexual Assessment

• Past sexual experiences
• Family and cultural values
• Religious beliefs
• Psychosocial factors
Assessment of Sexual Function

• Direct interviews
• Questionnaires
  • Specific questionnaires
  • Quality of Life questionnaires
• Diagnostic testing
Development of tools

- Brief
- Specific
- Gender specific
- Perceived as non-intrusive
- Able to separate illness from medication effect
- Monitor change over time
- Assess pre-morbid and lifelong sexual functioning before illness or treatment and over time
Advantages of Specific Sexual Assessment Questionnaires

• Inexpensive
• Easy to use
• Specific to problem
• Specific to gender
• Research
Disadvantages of Specific Sexual Assessment Questionnaires

• Lengthy
• May not cover full scope of problem
• May not answer the question
• May not differentiate between psychological and organic etiologies
• Few have been validated against physiologic measurements
Sexual Assessment Tools

- Arizona Sexual Experience Scale (ASEX)
- International Index of Erectile Function (IIEF)
- Swedish health-related quality of life survey (SWED-QUAL)
- Florida Sexual History Questionnaire
The Arizona Sexual Experience Scale (ASEX)

- Five item rating scale
- 6 point Likert scale
- Responses from the last week
- Male and female version
The Arizona Sexual Experience Scale (ASEX)-Male

- How strong is your sex drive?
- How easily are you sexually aroused (turned on)?
- Can you easily get and keep an erection?
- How easily can you reach an orgasm?
- Are your orgasms satisfying?
The Arizona Sexual Experience Scale (ASEX)-Female

- How strong is your sex drive?
- How easily are you sexually aroused (turned on)?
- How easily does your vagina become moist or wet during sex?
- How easily can you reach an orgasm?
- Are your orgasms satisfying?
International Index of Erectile Dysfunction

- 15-item self administered questionnaire
- Assesses male sexual function
- Validated in several languages
- 5 response domains
International Index of Erectile Function

- Erectile function
- Orgasmic function
- Sexual desire
- Intercourse satisfaction
- Overall satisfaction
Swedish Quality of Life Questionnaire (Swed-Qual)

- Sexual functioning scale
  - I am not interested in sex
  - I have difficulties in relaxing and enjoying sex
  - I have difficulties in becoming sexually aroused
  - I am afraid of the physical effort involved in sexual intercourse
  - I have difficulties in getting and/or keeping an erection (Men)
  - I have difficulties in having an orgasm (Women)
Florida Sexual History Questionnaire

- 20 item questionnaire
- Assesses male sexual dysfunction
Florida Sexual History Questionnaire

- Interest and desire
- Sexual development
- Current sexual behaviors
- Satisfaction with current sexual functioning
Psychosocial Interventions

• Education
  • Awareness of issues
  • Normal sexual response
  • Partner

• Counseling
  • Individual
  • Couple
Sexual Counseling

- Pre illness sexual activity
- Correct misinformation
- Defuse anxiety
- Psychosocial needs of partner
- Function of the couple
PLISSIT Model for sexual counseling

- Permission
- Limited information
- Specific suggestions
- Intensive therapy
Interventions

• Impact psychological and physiological sexual response
• Impact quality of life
Taking a Sexual History

Alan B. Ettinger, M.D.

Director, Long Island Jewish Comprehensive Epilepsy Center, New Hyde Park, NY
Associate Professor, Department of Clinical Neurology, Albert Einstein College of Medicine
www.epilepsylongisland.com
THE FOLLOWING PREVIEW HAS BEEN APPROVED FOR ALL AUDIENCES BY THE MOTION PICTURE ASSOCIATION OF AMERICA

THIS FILM HAS BEEN RATED

<table>
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<th>R</th>
<th>RESTRICTED</th>
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<tr>
<td></td>
<td>UNDER 17 REQUIRES ACCOMPANYING PARENT OR GUARDIAN</td>
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“You’ll find that what the Doctor lacks in technique, he makes up in warmth and sincerity.”
Janet became extremely depressed when, six months after her second marriage, she found herself unable to have an orgasm during sex. She didn’t think of this response as a medical problem, but even if she had, she would have been too embarrassed to mention it to her doctor.

It was only by accident that she began to suspect that the cause of her sexual difficulty was her blood pressure medicine, methyldopa (Aldomet). By a stroke of luck, she developed a stomach virus and temporarily stopped taking her Aldomet. As she recovered from the virus, her libido and ability to have orgasms returned. But then, when she went back on the Aldomet, her sexual problems returned.

A few experiments of not taking her medicine a couple of days and then having sex increased her growing suspicions, and her doctor confirmed the link between the drug and her sex life when she finally asked him.

The doctor inquired, perhaps rather naively, “Why didn’t you tell me about this when your sexual problems first started?”

She was too nice to respond, “Why didn’t you inform me about the possible side effects?”

Challenges on the Clinician Side

- Lack of training
- Embarrassment
- Fear of offending pt (yet most pts say it is appropriate for MD to ask)
- Provider’s discomfort w/ own sexuality
- Clinician’s moral tenets re: homosexuality, abortion, extramarital sex, contraception, prostitution
Challenges on Patient Side

• Harboring:
  • Misinformation
  • Guilt or Shame
  • Rigid attitudes
• Denial of a problem
• GETTING BOTH PARTNERS INVOLVED
Rapport w/ Patient

- Sexual hx when done w/ sensitivity, strengthens clinician-pt rapport
- Strive for open communication, active listening, honesty
- Convey neutral, non-judgmental attitude
- See beyond somatic complaints
- Intuition and nonverbal cues. Be sensitive to signs of anxiety: sudden overactivity, rapid talking, sudden shift to abstract or intellectualized terms
- Use humor w/ discretion
Dangers of Direct Questions

• Avoid questions that require direct yes/no responses

• Direct question: “Do you masturbate?” may cause defensiveness vs. open-ended “How often do you masturbate?”

• Direct: “Have you ever had intercourse?” vs. Open-ended: “How old were you when you first had intercourse?”
Open-ended questions

• “Sexual health is important to overall health, therefore I always ask pts about it. If it’s OK with you, I’d like to ask a few questions about this?”

• “I would like to ask you some questions about your sexual history just like I have about your medical history. This is an important part of a complete health assessment.”

• “How do you feel about your sexual life?”

• “Is sex a problem for you?”

• “Are you sexually active?”

• “Tell me about a sexual experience that was troubling for you.”
Addressing Sexual Orientation

• “Are you sexually active?”
• If +, “With men, women or both?”
• If -, “Have you ever been sexually active?”
Deferring Sexual Hx

- For sensitive subjects that pt is not ready to discuss: “I think it is an important matter- we should discuss it sometime.”
- Discussion of sexuality may need to wait till subsequent visit. Trust may need to be established over time for more detailed inquiries
- Distinguish screening questions from complete sexual history
Who Takes the Sexual History?

• Is the pt uncomfortable w/ MD or staff members?
Questionnaires

• Benefits: For some, may be easier to provide info rather than discuss openly
• Deficits: Some feel uncomfortable writing down such info
Screening for Sexual Problems & Concerns-1

• Are you sexually active?
• Have you noticed any changes or problems in your sexual functioning (lately)?
• If yes to 1 or 2

• For men:
  • Do you have any problems developing or maintaining an erection?
  • Do you have any trouble having an orgasm (ejaculating or coming too soon, not soon enough, or in the wrong direction)?
Screening-2 (For Women Only)

- Do you have pain during intercourse?
- Do you have problems with lubrication or becoming excited?
- Have you had an orgasm?
Screening-3 (For Women and Men)

- Do you think your epilepsy (and/or other illnesses) has affected your sexual functioning?
- Do you have sex with men, women, or both?
- What is your pattern of sexual activity (one partner, multiple or casual partners, etc.)?
- Do you have sex with people who are (or might be) in high-risk groups (IV drug users, homosexual or bisexual men, prostitutes, unknown partners, etc.)?
- Are you using birth control? What type?
- Are you using condoms to prevent disease?
- Do you have any concerns about getting a sexual disease or AIDS?
- Do you have any other questions or concerns about sex?
Be Careful w/ Terms

- Don’t make assumptions about sexual behavior or orientation (e.g. “partner” vs. “wife”)
- Use straight-forward anatomical terms
- Accept from pt but don’t use slang
- Avoid technical medical terms
- Constantly monitor if pt understands terms being used
Other Tips

• Assure confidentiality
• Avoid religious or moral judgments
• Use of 3rd person “Many people find …”
Link to Current Health

- e.g. “It's known that epilepsy can be associated with some difficulties in sexual health, I would like to ask some questions about this.”
- Women: Reproductive hx \(\rightarrow\) contraceptive needs \(\rightarrow\) sexual activity \(\rightarrow\) complete sexual hx
- Men: Prostate sx (e.g. hesitancy, weak urinary stream) \(\rightarrow\) sexual hx or concerns.
Role of Relationship in Sexual Dysfunction

- Self-esteem
- Quality of relationship between sexual partners
- Communication between partners
- Personality patterns
Not to worry, Mr. Salem, all medications can produce mild side effects. The question is, have they affected your quality-of-life?
Sexual Dysfunction w/ Med Problems

- Impotence common w/ many med disorders
- Anxiety about sexual capability as sequelae to acute med event
- Decreased libido w/ depression accompanying med disorder
- Ask about temporal relationship w/ med use and onset of difficulties. Ask about ETOH, tobacco, and illicit drugs
- Alternatively, beginning by discussion of above can lead to discussion of sexuality
- “Sometimes sexual experiences or incidents in your past can cause the type of difficulties you are reporting today. Is there any such incident in your past that you can identify?”
Sexual Response Cycle

Desire Phase:
- Fantasies or thoughts about sexual activity and/or desire to have sexual activity

Excitement Phase:
- A subjective sense of sexual pleasure with accompanying physiological changes related to pelvic vasoconstriction: erection in men and the lubrication-swelling response in women

Orgasm Phase:
- A peaking of sexual pleasure associated with rhythmic contractions of the perineal muscles and pelvic organs and with ejaculation in men

Resolution Phase:
- A sense of physical relaxation and emotional well-being following orgasm; men are refractory to further orgasms for a variable period of time; women are not
Desire Phase

• Does the pt experience fantasies and/or desires?
• Are they directed toward the available partner(s) or activities, or elsewhere?
• Is there a lack of interest in sex, or aversion?
• Under what conditions or situations does sexual activity occur?
• Who initiates sex, and how is it decided when to have sex?
Excitement Phase

- What is the nature and duration of foreplay?
- Is it of sufficient intensity, focus, and duration to produce the sensations and physiological changes of this phase?
- Is intercourse of adequate duration and nature to produce orgasm?
Orgasm Phase

• Does orgasm occur?
• Does it occur always, sometimes, or only under certain conditions?
• If it does not occur, is this because of lack of sufficient excitement, or “shut off” prior to orgasm?
• For men: Does orgasm occur too soon, too late (too soon to satisfy partner, or later than patient wishes), or in the wrong direction?
Resolution Phase

• Does feeling of relaxation occur?
• If not, what seems to interfere?
"Well now, Mr. Fenderson, what seems to be the problem?"
Sexual Dysfunctions

Sexual desire disorders:
- Hypoactive sexual desire
- Sexual aversion disorder
- Hypersexuality

Sexual arousal (excitement phase disorders):
- Female: impairment of the lubrication-swelling response
- Male erectile disorder

Orgasm disorders:
- Anorgasmia
- Inhibited female orgasm
- Inhibited male orgasm
- Premature ejaculation

Sexual pain disorders:
- Dyspareunia (genital pain in a man or woman before, during, or after sexual intercourse)
- Vaginismus (spasm of the vagina preventing intercourse)
- Priapism
<table>
<thead>
<tr>
<th></th>
<th>Psychogenic</th>
<th>“Organic”</th>
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<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Usually abrupt</td>
<td>Usually gradual</td>
</tr>
<tr>
<td><strong>Course</strong></td>
<td>Selective, intermittent, episodic, or transient</td>
<td>Usually persistent, often progressive</td>
</tr>
<tr>
<td><strong>Degree of impairment</strong></td>
<td>Partial: may respond to strong erotic stimulation or change of partner or situation</td>
<td>Partial in earlier stages: absolute later</td>
</tr>
<tr>
<td><strong>Nocturnal or morning erection</strong></td>
<td>Generally present</td>
<td>Generally absent or reduced in frequency and intensity</td>
</tr>
<tr>
<td><strong>Associated Features</strong></td>
<td>Onset temporarily related to specific psychosocial stress</td>
<td>Onset temporally related to disease</td>
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Case 1

- 46 y/o M w/ intractable szs partial w/ 2ndary generalization since age 7
- CC: Wife left him
- Prior hx: Physically abused as child, 1st sexual encounter age 12, then highly promiscuous throughout teen years
- Current sexual issues: Highly fearful of having a seizure during sexual relations
- Pt’s perception of epilepsy & sexuality: No woman other than his abusive wife would want to marry him.
- Therapist’s perception: Sexuality influenced by early abuse and paternal abandonment age 5. Unconscious issues of dependency, shame exacerbated by epilepsy.
Case 2

- 35 y/o F w/ intractable szs controlled after L temporal lobectomy
- Current issues: Fear of intimacy, no relationships, deficits in self-esteem
- Pt’s perception epi & sexuality: Epi caused her to w/draw from male peers
- Therapist: Onset of epi during menarche led to associating epi w/ sexuality and fear of loss of control over her behavior. She believes she damaged herself by masturbation.
Case 3

- 35 y/o M w/ intractable szs, CP w/ secondary generalization since age 9
- Current issue: Never had sexual relations
- Pt’s perception: Epi has ruined my life “Can’t drive, can’t take the train, can’t have a life”
- Therapists perception: Severe epi impeded education, emotion, social and sexual growth. Immaturity and very low self-esteem. Sense of peer rejection during adolescence and maternal overprotection
Bibliography


Long After Kinsey, Only the Brave Study Sex

By BENEDICT CAREY

From the movie "Kinsey," opening in theaters, government agents seize a box of studying shipped by Dr. Alfred C. Kinsey, the pioneer researcher, and impound the contents as obscene.

The story portrays a time in American history, the 60s, when marital relations were rarely discussed and reporting about sex was greeted with a society verging on horror. In 1948, when Dr. wrote "Sexual Behavior in the Human Male," a pervert, a menace and even a Communist. The world has changed in the years since then. But science has remained constant: Americans' views about the scientific study of sexuality.

After the sexual revolution, sex researchers still operate in a kind of scientific underground, cataloging behavior is like keeping a field guide to sin.

... and Present

1959 Should birth control information be available to anyone who wants it? 
YES 73%
NO 14%

1970 Would you approve if sex education classes discussed birth control?
YES 55%
NO 45%

1971 Should an adult be able to follow his views on having homosexual relations with a consenting adult, or be required to conform to society's standards?
FOLLOW VIEWS 39%
CONFORM 48%

1973 Do sexual materials lead people to commit rape?
NO 43%
YES 59%

2003 Is it morally acceptable to use birth control pills or condoms?
YES 94%

2003 How important is it to have sex education as part of the school curriculum in your community?
VERY 89%
FINALLY 21%