Cystic Fibrosis and Male Sexuality: The Good News

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Emeritus Professor, UCSF
I read in one of the papers that couples can get pregnant without sex. Is that true?

A patient, 1998
2. A 3-kg object is released from rest at a height of 5m on a curved frictionless ramp. At the foot of the ramp is a spring of force constant $k = 100 \text{ N/m}$. The object slides down the ramp and into the spring, compressing it a distance $x$ before coming to rest.

(a) Find $x$.

(b) Does the object continue to move after it comes to rest? If yes, how high will it go up the slope before it comes to rest?

$U = \frac{1}{2}kx^2$

$\therefore$ there is an elephant in the way.

CF and male fertility is an easier problem!
Basic Male Evaluation

History

Physical

Semen Analysis

Hormones

Genetic Tests

Other Tests

Medical Therapy

Surgery

Sperm Processing

ART
<table>
<thead>
<tr>
<th>Medications</th>
<th>Habits</th>
<th>Exposure</th>
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<tbody>
<tr>
<td>Nitrofurantoin</td>
<td>ETOH</td>
<td>Radiation</td>
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<tr>
<td>Sulfasalazine</td>
<td>Tobacco</td>
<td>Heat</td>
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<tr>
<td>Cimetidine</td>
<td>Steroids</td>
<td>Pesticides</td>
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<tr>
<td>β-blockers</td>
<td>Marijuana</td>
<td>Lead</td>
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<td>Ca+ Chann. Block.</td>
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<td>Antipsychotics</td>
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</table>
Normal Male Anatomy
Physical Examination

“Natural Vasectomy”
Infertility M.D. Provider (Male or Female)

Medical Evaluation

- Y microdeletions

Genetic Counseling

- Karyotype
- CFTR/5T

Post-Test Counseling

Treatment Plan
Major Human Y-linked Loci

11.32
Testis Determining Factor (TDF) (anti-sense)

11.31
Inability to See/Hear Obvious (ISHO)

Gadgetry Locus (GAD)
Macintosh Computers (MAC)
Random Electrical Devices

11.2
Inability to Express Affection over the Telephone (ME TOO)

Bullshitting (BS)

11.1
Posturing in the Presence of Other Males (POSH)
Male Answer Syndrome
Beer Consumption Controlling Factor (BCCF; may be amplified)
Vehicular Attraction Cluster (VRoom)
Refusal to ask for Directions When Lost (ANTI-STOP)
Channel Flipping (FLIP)
Variable Violence Region (VVR)

11.23
Pseudo-Self Confidence (psi SC)

Ability to Remember and Tell Jokes (JOKE)
Rock Throwing Region (RAR)
Pre-Adolescent Fascination with Arachnida, Reptilia and Rodenta (ARR)

q
Male Bonding Locus (MB)
Softball Teams (ST)
Sports Page (SP)
Football Teams (FT)
Air Guitar (AIR)
Addiction to Death & Destruction Movies (Terminator)
The CFTR Gene

The Gene: CFTR, located 7q31.2
5T IVS8 (5T variant)

Function: Encodes the cyclic adenosine monophosphate-regulated chloride channel in secretory epithelia

Problem: 1500+ mutations described
Mullerian and Wolffian Duct Relationships
Congenital Absence of the Vas Deferens (CAVD)

• Unilateral: most azoospermic
• Bilateral: all azoospermic
• Involves any segment of Wolffian duct
• Seminal vesicle agenesis, cysts
• Can have ejaculatory duct obstruction
• Prostatic and utricular cysts
• If ipsilateral kidney absent: No CFTR mutations
• If ipsilateral kidney present: 80% have CFTR mutations

“Form fruste” of CF: CF: Pneumonia, pancreatic insufficiency, bowel obstruction, sinusitis, nasal polyps.
Nonobstructive Azoospermia (36%)

CAVD

Idiop. Obstruction (12%)

Other (3%)

Oligospermia (49%)
An immaculate misconception
by Carl Djerassi
Produced and directed by William Archer
Yerba Buena Center for the Arts
San Francisco, California
6 October 1998, 8:00 pm.

What makes one a parent? Love, genetics, giving birth? This question lies at the center of Carl Djerassi’s newest play TABOOS. Returning to his scientific roots, Djerassi explores the other side of planned parenthood. When a lesbian couple and an infertile fundamentalist Christian couple each look to have a child, more than biology gets in the way of the idea of the “perfect family.” TABOOS explores the unexpected, and often messy, results that arise when emotions and science collide.

Praise for the London premiere:
“Having grappled with such issues as test-tube reproduction and scientific fraud, Djerassi now explores the implications of modern fertility techniques or, as one character describes it, ‘a spectacularly complicated reproductive mess among adults, not all of them consenting...’ a comedy fertilized by a ‘what if?’ case study.” — Ian Johns, The Times (London)

“A stage full of scientific and ethical viewpoints... Djerassi manages to make this comedy of genetic muddle strangely gripping.” — Fiona Mountford, Evening Standard (London)

“Rugby ball theatre... there are exciting complications at every turn. In the ethical crossfire that follows, Djerassi seems to have weighted the arguments as evenly as possible.” — Kieron Quirkie, Time Out (London)
Sperm Retrieval Procedures

Techniques for Obstructive Azoospermia

Vasal sperm
Epididymal sperm
  PESA
  MESA
Testis sperm
  TESA
  TESE
Obstructive Azoospermia

Vasal (MVSA; PVSA)

Epididymal (MESA, PESA)

Testicular (TESA, TESE, Microdissection TESE)
Obstructive Azoospermia

**Guideline:** Least invasive, least damaging, best yield.

Since assisted reproduction (IVF-ICSI) does not have a 100% success rate, it behooves reproductive urologists to develop and use sperm-retrieval techniques that are not only reliable and of low morbidity, but that also have the potential to harvest sufficient sperm to enable multiple IVF-ICSI attempts without repeat surgery.

Turek et al. Ass Reprod Rev. 1999, 9: 60-64
Epididymal sperm

• Microscopic/magnified epididymal sperm aspiration (MESA)
  – Open incision
  – Use of optical magnification
  – High yield

• Percutaneous sperm aspiration (PESA)
  – No incision
  – No magnification
  – Low yield
Microscopic Epididymal Sperm Aspiration (MESA)
The Mini-MESA

- Local +/- sedation
- 1-2 hours
- 6-10 million TMC
- Freeze-all approach

- Mean 2 pain pills
- Recovery 1-2 days
- <1% complication
- 1% need repeating
Percutaneous Epididymal Sperm Aspiration (PESA)
Why MESA and not PESA?
Testicular sperm

• Testicular sperm extraction (TESE)
  – Open incision
  – High yield

• Percutaneous sperm aspiration (TESA)
  – No incision
  – Low yield

• Percutaneous biopsy of testis
  – No incision
  – Moderate yield
  – Risk for hematoma
Testicular Sperm Extraction (TESE)

Window Biopsy Technique
Testicular PercBiopsy
The Problem of Azoospermia

5% of infertile men

- History
- Physical Exam
- Hormones
- Semen Analysis

Obstructive

Non-obstructive

Repair

ICSI

ICSI
Nonobstructive Azoospermia

Testicular (TESA, TESE, MicrodissectionTESE)

Surgeon beware!!
How “Patchy” or “Focal” is Sperm Production?²⁰

- Bx-FNA Discrepancy
  - Bx
  - 27% FNA +

- Intratestis Variability
  - -
  - 25% of testes

- Intertestis Variability
  - +
  - 19% of testes
Testis FNA Mapping

Office FNA Map

Sperm Found?

Yes

IVF/ICSI
"Directed" TESE

No

Donor Sperm Adoption
Fine Needle Aspiration (FNA) Mapping Template

R

1  2  3
10 5  6
11 8  9

L

12 13 14
15 16 17
18 22 20
19
Biologically, it appears to.....

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<tr>
<th></th>
<th>Motility</th>
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<th>*Viability</th>
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<tr>
<td></td>
<td>Fresh</td>
<td>Thawed</td>
<td>Fresh</td>
<td>Thawed</td>
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<tr>
<td>Testis, NOA</td>
<td>5%</td>
<td>0.2%</td>
<td>86%</td>
<td>46%</td>
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<tr>
<td>Epididymis, OA</td>
<td>22%</td>
<td>7%</td>
<td>57%</td>
<td>24%</td>
</tr>
<tr>
<td>Vas deferens, fertile</td>
<td>71%</td>
<td>38%</td>
<td>91%</td>
<td>51%</td>
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*Vital Stains: carboxyfluorescein, 0.08mg/mL; propidium iodide, 20mg/mL
Epididymal Sperm: Evidence-Based Guidelines

• For epididymal vs. testicular sperm in obstructive azoospermia:
  There is insufficient evidence of a difference in outcome.

• For fresh vs. frozen thawed epididymal sperm:
  There is no difference in clinical outcome (FR, OPR, IR)

Other Sexual Dysfunction:

- Erectile dysfunction
- Premature ejaculation
- Retrograde ejaculation
- Low libido (sex drive)
Massachusetts Male Aging Study: Relationship of Prevalence/Degree of ED to Age

DEGREE OF ED

<table>
<thead>
<tr>
<th>AGE (yr)</th>
<th>PROBABILITY</th>
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<tr>
<td>40</td>
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<td>45</td>
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<td>65</td>
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Mechanism of Erection

- Arterial Dilation
- Sinusoids fill
- Venous compression
Evaluation of Erectile Dysfunction

History + Physical exam + Lab

Appraise pt’s goal, expectation & profile
Discuss diagnostic and treatment options

Therapeutic trial

Further diagnostic testing

Definitive treatment
The penis does not obey the order of its master, who tries to erect or shrink it at will. Instead, the penis erects freely while its master is asleep. The penis must be said to have its own mind, by any stretch of the imagination.

Leonardo da Vinci
CF and Male Sexual Function

The problem is well defined.
The solution is well defined.
Fertility: Planning is important.