

CENTER FOR DRUG EVALUATION AND RESEARCH

ADVISORY COMMITTEE: NONPRESCRIPTION DRUGS
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DATE OF MEETING: 4/15/97

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SLIDES (AND HANDOUTS)

**NONPRESCRIPTION DRUGS
ADVISORY COMMITTEE**

with representation from:
Repro. Health, Anti-infective,
CDRH Ob-Gyn Devices Panel,
and the CFSAN Panel.
TUESDAY, APRIL 15, 1997
VAGINAL DOUCHING

APPEARS THIS WAY
ON ORIGINAL

HISTORY AND REGULATORY ASPECTS OF VAGINAL DOUCHE DRUGS

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ON ORIGINAL

ON ORIGINAL

Helen Cothran
Division of OTC Drug Evaluation,
Center for Drug Evaluation and Research
Food and Drug Administration

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**ADVISORY REVIEW PANEL ON OTC
CONTRACEPTIVES AND OTHER VAGINAL
DRUG PRODUCTS
(FEDERAL REGISTER OF OCTOBER 13, 1983)**

**VAGINAL DOUCHE -- A
LIQUID PREPARATION USED
TO IRRIGATE THE VAGINA
OVER AN INDETERMINATE
PERIOD FOR ONE OR MORE OF
THE FOLLOWING PURPOSES:**

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- 1. CLEANSING**
- 2. PRODUCING SOOTHING AND REFRESHING EFFECTS**
- 3. DEODORIZING**
- 4. RELIEVING MINOR IRRITATIONS**
- 5. REDUCING THE NUMBER OF PATHOGENIC ORGANISMS**
- 6. ALTERING THE pH SO AS TO ENCOURAGE THE GROWTH OF NORMAL VAGINAL FLORA**
- 7. PRODUCING AN ASTRINGENT EFFECT**
- 8. LOWERING SURFACE TENSION**
- 9. PRODUCING A MUCOLYTIC EFFECT**
- 10. PRODUCING A PROTEOLYTIC EFFECT**

FEDERAL FOOD, DRUG, AND COSMETIC ACT

DRUG - An article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals or intended to affect the structure or any function of the body.

COSMETIC - An article intended to be applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance.

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I. Ingredients classified by the Panel as safe and effective (Category I) for the relief of minor irritations of the vagina:

Indication: “For the (temporary) relief of minor vaginal itching, irritation, and soreness

calcium propionate	20 % gel
sodium propionate	20 % gel
potassium sorbate	1 to 3 % as a douche
povidone-iodine	.15 to .3 % as a douche

II. Ingredients classified by the Panel as safe and effective to lower surface tension and produce a mucolytic or proteolytic effect:

Indication: “Removes vaginal discharge, removes vaginal secretions, mild detergent action, thins out vaginal mucus discharge”

dioctyl sodium sulfosuccinate	.02 % douche
nonoxynol 9	.0176 % douche
octoxynol 9	.088% douche
sodium lauryl sulfate	.01 to .02 % douche

**III. Ingredients classified by the Panel
as safe and effective to alter vaginal
pH:**

**Indication: “Helps keep vagina in its
normal acid state”**

No ingredients classified in Category I

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ON ORIGINAL

**IV. Ingredients classified by the Panel
as safe and effective to produce an
astringent effect:**

Indication: “Astringent”

No ingredients classified in Category I

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ON ORIGINAL

V. The Panel also recommended professional labeling (labeling provided to health professionals, but not to the general public) for the following ingredients:

- **propionates for the treatment of Candida albicans.**
- **Povidone-iodine (.15 to .3 % and 10 % concentration) as a microbicidal douche, and as part of a treatment regimen for Candida, Trichomonas, and nonspecific vaginitis.**
- **Sodium lauryl sulfate and docusate sodium for the treatment of Trichomonas**

PANEL'S RECOMMENDED LABELING

- **“Does Not Prevent Pregnancy.”**
- **“Do not use during pregnancy except upon the advice and under the supervision of your physician.”**
- **“Keep this and all drugs out of the reach of children.”**
- **“If vaginal itching, redness, swelling, or pain develop, stop douching. Consult your physician if these symptoms persist.”**

APPEARS THIS WAY
ON ORIGINAL

PANEL'S RECOMMENDED LABELING

For products for the relief of minor irritation only:

- “If minor irritation has not improved after 1 week of use, consult your physician.”
- “If symptoms continue or redness, swelling, or pain develop, stop douching. Consult your physician if these symptoms persist.”

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PANEL'S RECOMMENDED LABELING

Methods for douching:

- **“Do not press the lips of the vagina around the nozzle. Overfilling the vagina may force fluid into the uterus (womb) and cause inflammation.”**
- **“Douching does not prevent pregnancy.”**
- **“If douching results in pain, soreness, itching, excessive dryness, or irritation, stop douching. If symptoms persist, consult a physician.”**

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PANEL'S RECOMMENDED LABELING
Methods for douching - other
information concerning directions
for use

- **Directions for mixing**
- **Instructions for use of a douche in sitting, standing, and reclining position**
- **Douche bag should not be more than 3 feet above the vagina**
- **Expel air from the tubing**
- **Do not occlude vaginal opening, allow free outflow of the solution**
- **Rinse and drain douche equipment before storing**
- **Gently insert nozzle and allow gentle flow of solution into the vagina**

PREAMBLE TO 1983 PANEL'S REPORT

**FDA DID NOT ALLOW MARKETING
OF:**

- ◆ **CALCIUM PROPIONATE**
- ◆ **SODIUM PROPIONATE**
- ◆ **POTASSIUM SORBATE**

**THESE INGREDIENTS ARE NEW
DRUGS**

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Remaining Ingredients:

Indication: “For relief of minor vaginal irritation. . . .”

- ~~◆ **calcium propionate**~~
 - ~~◆ **sodium propionate**~~
 - ~~◆ **potassium sorbate**~~
 - ◆ **povidone-iodine**
-

Indication: “Removes vaginal discharge,. . . vaginal secretions, mild detergent action,. . . “

- ◆ **dioctyl sodium sulfosuccinate**
- ◆ **nonoxynol 9**
- ◆ **octoxynol 9**
- ◆ **sodium lauryl sulfate**

PREAMBLE TO 1983 PANEL'S REPORT

- ◆ **DOUCHING EQUIPMENT IS A
DEVICE, NOT A DRUG**

- ◆ **PANEL'S COMMENTS ON
DOUCHING EQUIPMENT
REFERRED TO CDRH
(FORMERLY BUREAU OF
DEVICES)**

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FEDERAL REGISTER OF FEBRUARY 3,
1994:

- **FDA WITHDREW THE PANEL'S 1983 REPORT**
- **FDA DETERMINED THAT MOST CLAIMS REVIEWED BY THE PANEL WERE COSMETIC, NOT DRUG CLAIMS**
- **THERE WILL BE NO SEPARATE OTC DRUG MONOGRAPH FOR VAGINAL DRUG PRODUCTS**

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FEDERAL REGISTER OF FEBRUARY 3,
1994 (continued):

- **MINOR VAGINAL IRRITATION, ITCHING, AND SORENESS CLAIMS AND PROFESSIONAL LABELING CLAIMS FOR POVIDONE-IODINE WILL BE REFERRED TO OTHER RULEMAKINGS (SUCH AS ANTIMICROBIAL)**
- **INTENDED USE OF A PRODUCT IS PRIMARY FACTOR WHETHER A PRODUCT IS DRUG OR COSMETIC**
- **HOWEVER, THE PRESENCE OF A PHARMACOLOGICALLY ACTIVE INGREDIENT COULD MAKE A PRODUCT A DRUG IN THE ABSENCE OF EXPLICIT DRUG CLAIMS.**

SUCH INGREDIENTS/CLAIMS WILL BE ADDRESSED IN APPROPRIATE RULEMAKINGS

CURRENTLY:

- **POVIDONE-IODINE .15 TO .30 % DOUCHE IS THE ONLY CATEGORY I INGREDIENT TO RELIEVE MINOR IRRITATIONS OF THE VAGINA**
- **A TENTATIVE FINAL MONOGRAPH FOR POVIDONE-IODINE HAS NOT PUBLISHED; THEREFORE, THESE CLAIMS HAVE NOT BEEN EVALUATED BY FDA**
- **POVIDONE-IODINE AS A DOUCHE FOR OTC AND PROFESSIONAL LABELING USES WILL BE ADDRESSED IN A FUTURE FEDERAL REGISTER NOTICE**
- **OTHER INGREDIENTS AND CLAIMS, AS NECESSARY, WILL BE ADDRESSED IN FUTURE FEDERAL REGISTER NOTICES**

COSMETIC LAWS AND REGULATIONS

Presented at the Meeting of the Non-Prescription Drugs Advisory Committee
on Vaginal Douches, April 15, 1997.

Cosmetics marketed in the United States, whether manufactured here or imported from abroad, must be in compliance with the provisions of :

The Federal Food, Drug, and Cosmetic Act (FD&C Act),

The Fair Packaging and Labeling Act (FPLA),

and the regulations published under the authority of these laws.

The regulations published by the Food and Drug Administration (FDA) are all codified in 21 CFR 700 to 740.

*

The FD&C Act (Section 201); Definition: COSMETIC

"articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for **cleansing, beautifying, promoting attractiveness, or altering the appearance.**" Cosmetic products include: *Skin creams, lotions, perfumes, lipsticks, fingernail polishes, eye and facial make-up preparations, shampoos, permanent waves, hair colors, toothpastes, deodorants, vaginal douches.*

Products that are cosmetics but are also intended to **treat, mitigate, or prevent disease, or otherwise affect the structure or functions** of the human body, are considered both drugs and cosmetics and must comply with both the drug and cosmetic provisions of the law. These include many over-the-counter drugs:

Anticaries toothpastes, sunscreen preparations, antiperspirants that are also deodorants, antidandruff shampoos, medicated douches.

*

The law provides only limited regulatory oversight for cosmetics.

The cosmetic industry has been given the direct responsibility for assuring the safety of their products before they are marketed.

No requirement for pre-market approval of cosmetic products or ingredients.

Cosmetic manufacturers may use essentially any ingredient in their products with the exception of color additives and a few prohibited or restricted ingredients.

No requirement for safety testing.

FDA strongly urges manufacturers to substantiate the safety of their products. It is the responsibility of each manufacturer to select and conduct appropriate tests.

No requirement for establishing product efficacy.

No requirement to register cosmetic establishments or their products.

No requirement to report consumers' injuries or adverse reactions.

*

COSMETIC PRODUCT REGULATORY REQUIREMENTS

Product identity statement.

(With a descriptive name or illustration of the nature or use of the product).

Declaration of ingredients and net quantity of contents.

Name and place of business of manufacturer, packer, or distributor.

Tamper-resistant packaging.

(for cosmetic liquid oral hygiene products and vaginal products; 21 CFR §700.25)

*

FD&C Act Sec. 601-Adulterated Cosmetics

A cosmetic shall be deemed to be **adulterated-**

(a) If it bears or contains any poisonous or deleterious substance which may render it injurious to users **under the conditions of use prescribed in the labeling** thereof, or, **under such conditions of use as are customary or usual:**

(b) If it consists in whole or in part of any filthy, putrid, or decomposed substance.

(c) If it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health.

(d) If its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health.

(e) If it is not a hair dye and it is, or bears or contains, a color additive which is unsafe...

It is the Agency's responsibility:

to identify hazards and take appropriate actions, and

to find harmful products and remove them from the marketplace.

*

FD&C Act Sec. 602-Misbranded Cosmetics

A cosmetic shall be deemed to be **misbranded-**

If its labeling is false or misleading,

if it does not bear the required labeling information, or

if the container is made or filled in a deceptive manner.

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Vaginal Douching

FDA Review of Epidemiologic Studies

**Roselie A. Bright, Sc.D.
CDRH, FDA**

**Pamela Scott
CDRH, FDA**

**Lark Lambert
CFSAN, FDA**

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Epidemiology of Douching

Consider published, only

No clinical trials

No randomization

No cohort studies

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All case control

All temporal cross-sectional

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Organization of This Talk

Panel members have:

List of abbreviations

For papers in bibliography that I am not discussing, the reasons

For each of the following elements I will first discuss PID then ectopic pregnancy and infertility finally cervical carcinoma outcomes

--Study design

--Main effect

--Could main effect be due to bias? Does infection explain the main effect?
Effect in spite of ascertainment bias (Pap)
Reason for douching
Number of sexual partners
Role of race

--Dose response:

Frequency and history of douching

--Specificity of douche product:

Relative effects of solution and device type

Abbreviations

PID	Pelvic Inflammatory Disease	HPV	Human Papilloma Virus
RR	Relative Risk	OC	Oral contraceptive
FR	Fecundity Ratio	IUD	Intrauterine Device
<i>C t</i>	<i>Chlamydia trachomatis</i>	DDES	Diethylstilbestrol
<i>N g</i>	<i>Neisseria gonorrhoeae</i>	BMI	Body Mass Index
<i>T v</i>	<i>Trichomonas vaginalis</i>	MD	Physician
STD	Sexually Transmitted Disease	D&C	Dilation of cervix & curettage of endometrium

Studies from Bibliography that are not Presented

Brinton	Matched sets were broken due to nonresponse, so only one matching factor, age, could be controlled in the analysis. Although suggestive, this is the only study on vaginal carcinoma.
Joesoef	This is a cross-sectional study that did not attempt to ascertain whether douching preceded the outcome, STD.
Jossens (1996)	Most analyses ignored the matching factors and are not presented in the talk.
Llahi-Camp	This is a cross-sectional study that did not attempt to ascertain whether douching preceded the outcome, bacterial vaginosis, and provided no information on overall douching prevalence.
Mueller	All analyses on ectopic pregnancy ignored the matching factors and are not presented in the talk.
Scholes (1992)	This study focused on cigarette smoking. The other Scholes paper had the full analysis of douching and is presented.
Stergachis	This is a cross-sectional study that did not attempt to ascertain whether douching preceded the outcome, <i>Chlamydia trachomatis</i> infection.

PID Study Designs

Author	Cases	Controls
Aral	National probability sample, self report, any past PID	Other women in sample
Mueller	Among confirmed non-congenital primary tubal infertility, self report of MD-diagnosed PID	All others in group of confirmed noncongenital primary tubal infertility
Pairsarn-tantiwong	PID hospital cases, with cervical <i>C t</i>	Outpatient service, sexually active, no PID signs, with cervical <i>C t</i>
Jossens	PID cases in a clinical antimicrobial trial, 1986-1989	Hospital Women's Clinic, 1981-1985
Scholes	First PID or acute salpingitis, treated as in- or outpatients	HMO enrollees, no prior PID diagnosis
Wolner-Hanssen	Surgically confirmed PID in trial enrollees, recruited from STD-, Women's-, or Viral Disease Clinic, or emergency dept.	1. Trial enrollees with PID signs or symptoms, but diagnosis ruled out surgically ("PID-like controls") 2. Patients with new problems presenting at an STD clinic ("random controls")

Ectopic Pregnancy Study Designs

Author	Cases	Controls
Phillips	Surgical tubal pregnancies	Intrauterine pregnancies
Kendrick	Surgical ectopic pregnancies	Pregnancies with fetus $\geq 500g$, and induced abortions
Chow JM	Surgical ectopic pregnancies	Uncomplicated pregnancies
Chow W-H	Surgical tubal pregnancies	Pregnancies
Daling	Hospital ectopic pregnancies	Sexually active, childbearing age women from health plan

Infertility Study Design

Baird: Relative time to pregnancy among population mothers.

Cervical Carcinoma Study Designs

Author	Cases	Controls
Peters	Registry cervical cancer cases	Random, in person selected from neighborhood
Herrero	Hospital, newly diagnosed invasive cervical cancer	Hospital and community
Gardner	Cervical cancer cases found through pathology labs and state registry	Random digit dialed from population
Slattery	(Same as Gardner)	(Same as Gardner)

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Strength of Main Association for PID

Author	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Aral	1.6			
Mueller	0.68 (0.30-1.5)			
Jossens		NS	age, race	
Pairsarn-tantiwong	3.4 (1.2-9.7)	10 (2.0-73)	(all had cervical C t), age, T v	
Scholes		1.7 (1.0-2.9)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhoea
Wolner-Hanssen	2.2 (1.3-3.7)	1.9 (1.02-3.5)	(PID-like controls), age, race, years, employment status, current smoking	
Wolner-Hanssen	2.7 (1.7-4.1)	1.7 (1.04-2.8)	(random controls), age, race, parity, education, current smoking, age at 1st intercourse, frequency of intercourse, history of C t or N g infection or PID, and birth control method	

Strength of Main Association for Ectopic Pregnancy

Author	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Phillips	1.1 (0.6-2.1)			
Kendrick	2.8 (1.0-7.7)			
Chow JM	2.7 (1.8-3.6), matched	2.1 (1.3-3.5)	age, race, ethnicity, hospital, age at 1st intercourse, lifetime # of sexual partners, past infertility, nulliparity, chlamydial infection	
Daling		1.3 (0.9-1.8)	age, race, year, county, health plan membership, gravidity, lifetime # of sexual partners	current smoking, ever used IUD, education, income, current contraception, past barrier contraception, history of STD, marital status, frequency of intercourse, age at 1st intercourse
Baird*	1.5 (1.3-1.7)	1.5 (1.3-1.7)	age, smoking, frequency of intercourse, menstrual cycle length, breast feeding, oral contraceptives as last birth control method, history of ovarian cysts, history of LSD use	race, education, income, prenatal DES exposure, history of PID, endometriosis, STDs, BML, prior OC use, prior IUD use, pregnancy history, age at 1st intercourse, # sexual partners, frequency of intercourse, beverages, other recreational drugs, spouse's lifestyle, menstrual cycle regularity

* Infertility, RR = 1/FR

Strength of Main Association for Cervical Carcinoma

Author	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Gardner	2.5 (1.8-3.6)	1.3 (0.8-1.9)	age, race, lifetime # sexual partners, cigarette smoking, religious activity, education	age at 1st intercourse, birth control method, vaginal infections
Herrero		1.4 (1.1-1.9)	age, number of sexual partners, age at first intercourse, HPV, interval since last Pap smear, gravidity, # of household facilities	
Peters		1.008 (1.004-1.012)**	age, race, neighborhood, language, years since last Pap smear, years from menarche to first intercourse, education, smoking, barrier contraceptives, sexual partners before age 20, genital warts	

** For each extra year and time per month

For PID, Effect of Infection

Author	Infection	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Pair'-wong	Among (+) cervical <i>C t</i>	3.4 (1.2-9.7)	10 (2.0-73)	age, <i>T v</i>	
Wolner-Hanssen	Cases also have <i>C t</i> only	<u>1.7 (0.3-8.7)</u> 3.3 (0.9-12)		(PID-like controls) (random controls)	
Wolner-Hanssen	Cases also have <i>N g</i> only	<u>5.4 (0.8-37)</u> 3.8 (0.8-18)		(PID-like controls) (random controls)	
Wolner-Hanssen	Cases also have bacterial vaginosis only	<u>6.4 (1.2-35)</u> 5.7 (1.2-27)		(PID-like controls) (random controls)	
Scholes	Douche due to MD- or self-diagnosed infection		7.9 (2.6-24)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhea
Wolner-Hanssen	Cases do not have <i>C t</i> , <i>N g</i> , or bacterial vaginosis	<u>2.1 (0.6-7.6)</u> 2.7 (0.8-8.6)		(PID-like controls) (random controls)	

Scholes: Among controls, (+) *C t* serology had simple RR of 3.9 (1.5-10) for douching.

For Infertility and Cervical Carcinoma, Effect of Infection

Author /Outcome	Infection	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Baird /Infertility	Never douched due to infection or odor	unchanged [from 1.5 (1.3-1.7)*]	unchanged [from 1.5 (1.3-1.7)*]	age, smoking, frequency of intercourse, menstrual cycle length, breast feeding, oral contraceptives as last birth control method, history of ovarian cysts, history of LSD use	race, education, income, prenatal DES exposure, history of PID, endometriosis, STDs, BML, prior OC use, prior IUD use, pregnancy history, age at 1st intercourse, # sexual partners, frequency of intercourse, beverages, other recreational drugs, spouse's lifestyle, menstrual cycle regularity
	History of genital infections	17% of douchers and 20% of nondouchers			
Slattery on Gardner /Cervical carcinoma	Douche ≥ 4 /mo (y/n): Pap test $> 1/2$ yr Pap test $\leq 1/2$ yr		2.7 (1.0-7.2) 9.5 (2.2-41.9)	age, race, lifetime # sexual partners, cigarette smoking, religious activity, education	age at 1st intercourse, birth control method, vaginal infections

* RR = 1/FR

Douched for "cleanliness"

Outcome	Author	Reason	Simple RR (95% CL)	Adjustment factors
PID	Wolner-Hanssen	Cleanliness	2.5 (1.3-4.9) 4.1 (2.5-6.9)	(PID-like controls), years (random controls)

Douche after menses

Outcome	Author	Adjusted RR (95% CL)	Adjustment factors	Not confounders
PID	Scholes	1.3 (0.5-3.4)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhoea

Effect of Lifetime # Sexual Partners

Author /Outcome	# partners	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Wolner-Hanssen /PID	Among douched in prior 2 mo: <10 partners 11-25 partners >25 partners	3.5 (1.9-6.4) 2.4 (0.8-6.9) 1.8 (0.8-4.0)		(random controls)	
Daling /Ectopic pregnancy	Measures of douche history, solution, and device for: All subjects >1 partner		[1.2 (0.8-1.9)] - [1.5 (1.0-2.5)] [1.5 (0.8-2.1)] - [1.7 (1.1-2.8)]	age, race, year, county, health plan membership, gravidity, lifetime # of sexual partners	current smoking, ever used IUD, education, income, current contraception, past barrier contraception, history of STD, marital status, frequency of intercourse, age at 1st intercourse
Gardner /Cervical carcinoma	Douche >4/mo, vs. <10 times ever, for: <1 partner >1 partner		27 (4.1-170) 1.9 (0.4-10)	age, race, lifetime # sexual partners, cigarette smoking, religious activity, education	age at 1st intercourse, birth control method, vaginal infections

Role of Race in Douching Effects

Author /Outcome	Race	Simple RR (95% CL)	Adjustment factors
Aral /PID	White Black	1.6*** 1.4***	
Wolner-Hanssen /PID	Douched in prior 2 mo (y/n): White Black Other	2.9 (1.4-6.1) 0.6 (0.2-1.8) 4.5 (0.6-35)	(PID-like controls), age, race, signs and symptoms of PID, years, employment status, current smoking
Wolner-Hanssen /PID	Douched in prior 2 mo (y/n): White Black Other	3.5 (1.9-6.4) 1.1 (0.5-2.1) 3.8 (1.0-15)	(random controls), age, race, parity, education, current smoking, age at 1st intercourse, frequency of intercourse, history of C t or N g infection or PID, and birth control method

*** Calculated from reported %s.

APPEARS THIS WAY
ON ORIGINAL

For PID, Dose Response: Douching Frequency

Author	Frequency	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Mueller	Never (ref) ≤2/yr >2/yr	0.69 (0.25-1.9) 0.67 (0.27-1.7)		(all have 1° tubal infertility)	
Scholes	Never (ref) In prior 2-3 mo: 1-3/mo ≥4/mo		1.8 (1.0-3.4) 3.9 (1.4-11)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhea
Wolner-Hanssen	<1/mo (ref) 1-2/mo ≥3/mo	3.3 (1.1-9.7) 2.9 (1.02-8.4)	4.7 (1.2-19) 3.9 (1.1-14)	(PID-like controls), age, race, years, employment status, current smoking	
Wolner-Hanssen	<1/mo (ref) 1-2/mo ≥3/mo	2.5 (1.04-6.0) 3.6 (1.5-8.7)	1.6 (0.6-4.9) 3.4 (1.1-10)	(random controls), age, race, parity, education, current smoking, age at 1st intercourse, frequency of intercourse, history of C t or N g infection or PID, and birth control method	

For Ectopic Pregnancy, Dose Response: Douching Frequency

Author	Frequency	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Phillips	<1/mo (ref) ≥1/mo		0.8 (0.3-2.2)	race, education, prior PID, current smoking, parity, past ectopic pregnancy	income, past smoking, marital status, young age at 1st intercourse, ≥3 lifetime sexual partners, prior gonorrhea or trichomoniasis, prior OC use, prior infertility, prior abdominal surgery, prior abortion, prior D&C, endometriosis
Chow W-H	Never (ref) Occasionally Weekly		1.4 (0.93-2.2) 2.0 (1.03- 4.0)	race, gravidity, smoking, yr of index pregnancy, Dalkon Shield use, condom use by partner	age, income, education, occupation, # sexual partners, age at 1st regular intercourse, hx of pelvic infection, planned status of index pregnancy
Daling	Never (ref) ≤2/yr Every few mo 1/mo 1/wk	0.9 (0.6-1.4)	1.2 (0.8-1.8) 1.5 (1.0-2.2) 1.3 (0.8-2.2)	age, race, year, county, health plan membership, gravidity, lifetime # of sexual partners.	current smoking, ever used IUD, education, income, current contraception, past barrier contraception, history of STD, marital status, frequency of intercourse, age at 1st intercourse
Baird*	<2/yr (ref) 3/yr to <2/wk ≥2/wk	1.7 6.3 no relationship		(all <25 y) (all ≥ 25 yr)	race, education, income, prenatal DES exposure, history of PID, endometriosis, STDs, BMI, prior OC use, prior IUD use, pregnancy history, age at 1st intercourse, # sexual partners, frequency of intercourse, beverages, other recreational drugs, spouse's lifestyle, menstrual cycle regularity

* Infertility, RR = 1/FR

For Cervical Carcinoma, Dose Response: Douching Frequency

Author	Frequency	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Gardner	<10 ever (ref) <1/mo 1-2/mo 3-4/mo >4/mo	1.0 (0.6-1.6) 1.2 (0.7-2.1) 1.1 (0.5-2.2) 4.7 (1.9-11)	age, race, lifetime # sexual partners, cigarette smoking, religious activity, education	age at 1st intercourse, birth control method, vaginal infections
Herrero	Never (ref) Not regular Regular, <1/wk 1-2/wk >2/wk	1.1 (0.8-1.5) 1.8 (1.0-3.3) 1.1 (0.7-1.8) 1.6 (1.0-2.4)	age, number of sexual partners, age at first intercourse, HPV, interval since last Pap smear, gravidity, # of household facilities	
Peters	1-4/mo >4/mo	1.5 (0.9-2.3) 3.4 (1.7-6.8)	age, race, neighborhood, language	

For PID, Dose Response: Douching History

Author	History	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Scholes	Never (ref) Only before prior 2-3 mo Prior 2-3 mo		1.4 (0.7-2.8) 2.1 (1.2-3.9)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhoea
Wolner-Hanssen	Age began douching Age at study Douching interval	No difference No difference No difference			

For Ectopic Pregnancy, Dose Response: Douching History

Author	History	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Daling	Never (ref) 1-5yr ≥6 yr	1.3 (0.9-1.8) 1.3 (0.8-2.3)	age, race, year, county, health plan membership, gravidity, lifetime # of sexual partners.	current smoking, ever used IUD, education, income, current contraception, past barrier contraception, history of STD, marital status, frequency of intercourse, age at 1st intercourse
Daling	Never (ref) 1-5yr ≥6 yr	1.6 (1.1-2.3) 1.6 (0.9-2.8)	(all >1 lifetime sexual partner), others as above	as above

For Cervical Carcinoma, Dose Response: Douching History

Author	History	Adjusted RR (95% CL)	Adjustment factors
Herrero	Never (ref) Age started regular use Months regular use	No trend No trend	age, number of sexual partners, age at first intercourse, HPV, interval since last Pap smear, gravidity, # of household facilities
Peters	<2yr (ref) 2-19 yr >20 yr	1.5 (0.9-2.6) 2.0 (1.1-3.7)	age, race, neighborhood, language

For PID, Effect of Douche Solution

Author	Solution	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Scholes	Never (ref) Noncommercial Commercial		2.0 (1.0-4.4) 2.0 (1.0-4.0)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhoea
Wolner- Hanssen	Among douched in prior 2 mo: Other methods (ref) Commercial solution with disposable device	1.2 (0.5-2.8) <hr/> 2.4 (1.3-4.4)		(PID-like controls) <hr/> (random controls)	

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For Ectopic Pregnancy, Effect of Douche Solution

Author	Solution	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Chow W-H	Never (ref) Wkly with: Water Noncommercial Commercial		1.5 (0.4-5.3) 1.2 (0.4-3.2) 4.4 (1.6-13)	race, gravidity, smoking, yr of index pregnancy, Dalkon Shield use, condom use by partner	age, income, education, occupation, # sexual partners, age at 1st regular intercourse, hx of pelvic infection, planned status of index pregnancy
Daling	Never (ref) Water solution^ Commercial <hr/> With >1 lifetime partner: Never (ref) Water solution^ Commercial		1.3 (0.8-2.0) 1.3 (0.9-2.0) <hr/> 1.7 (1.1-2.8) 1.5 (0.9-2.3)	age, race, year, county, health plan membership, gravidity, lifetime # of sexual partners.	current smoking, ever used IUD, education, income, current contraception, past barrier contraception, history of STD, marital status, frequency of intercourse, age at 1st intercourse
Baird*	<2/yr (ref) Water Water & vinegar Commercial	1.5 (1.1-2.2) 1.7 (1.3-2.3) 1.7 (1.4-2.2)			race, education, income, prenatal DES exposure, history of PID, endometriosis, STDs, BML, prior OC use, prior IUD use, pregnancy history, age at 1st intercourse, # sexual partners, frequency of intercourse, beverages, other recreational drugs, spouse's lifestyle, menstrual cycle regularity

^ Water with or without vinegar or soda * Infertility, RR = 1/FR

For Cervical Carcinoma, Effect of Douche Solution

Author	Solution	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Gardner	Never (ref)	0	age, race, lifetime # sexual partners, cigarette smoking, religious activity, education	age at 1st intercourse, birth control method, vaginal infections
	Household cleaner and water	2.3 (1.1-4.7)		
	Water/vinegar	1.3 (0.3-5.2)		
	Water/soda	1.3 (0.6-3.0)		
	Water only			
	Douched >4/mo:			
	Never (ref)	0		
	Household cleaner and water	0.3 (0.05-2.1)		
Peters	Commercial	27 (1.5-480)		
	Water/vinegar	infinity		
	Water/soda	0.3 (0.04-2.7)		
	Water only			
Peters	Water-vinegar only	1.2 (0.7-2.0)	age, race, neighborhood, language	
	Preparation	2.4 (1.4-4.0)		

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For PID, Effect of Douche Device

Author	Device	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not confounders
Scholes	Never (ref)		1.9 (0.9-4.0) 2.1 (1.1-4.3)	age, race, marital status, gravidity, # sexual partners	income, education, smoking, current contraception, history of gonorrhea
	Disposable				
Wolner-Hanssen	Not disposable				
	In prior 2 mo:			(PID-like controls) (random controls)	
Other methods (ref)	1.2 (0.5-2.8)				
	Prefilled disposable	2.4 (1.3-4.4)			

For Ectopic Pregnancy and Infertility, Effect of Douche Device

Author /Outcome	Device	Simple RR (95% CL)	Adjusted RR (95% CL)	Adjustment factors	Not con-founders
Daling /Ectopic pregnancy	Never (ref) Disposable Bag		1.5 (1.0-2.5) 1.2 (0.8-1.9)	age, race, year, county, health plan membership, gravidity, lifetime # of sexual partners	current smoking, ever used IUD, education, income, current contraception, past barrier contraception, history of STD, marital status, frequency of intercourse, age at 1st intercourse
	With >1 lifetime partner: Never (ref) Disposable Bag		1.6 (1.0-2.8) 1.5 (0.8-2.1)		
Baird* /Infertility	<2/yr (ref) Disposable Bag	1.9 (1.3-2.6) 1.7 (1.4-2.0)			race, education, income, prenatal DES exposure, history of PID, endometriosis, STDs, BMI, prior OC use, prior IUD use, pregnancy history, age at 1st intercourse, # sexual partners, frequency of intercourse, beverages, other recreational drugs, spouse's lifestyle, menstrual cycle regularity

* RR = 1/FR, calculated from graph

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Summation of Studies (Table 1)

Consideration	Outcome*		
	PID	Ectopic pregnancy /Infertility	Cervical cancer
Main effect	00++++	0++++	+++
<i>Could main effect be due to bias?</i>			
♦ Does infection explain the main effect?: --Main effect present among infected pts --Main effect present among uninfected pts --Infection itself related to douching	++ + ++	- 0	
♦ Effect in spite of ascertainment bias (Pap)			+
♦ Effect among those douching to "clean"	+		
♦ Effect among those douching after menses	0		
♦ Effect stronger with fewer sexual partners	+	0	+
♦ Role of race (effect absent among blacks)	0+.		

* Each relevant study is represented with a mark indicating its evidence against (-), neutral (0), or supporting (+) a positive association with douching.

Summation of Studies (Table 2)

Consideration (these are supportive if present, but not necessary)	Outcome*		
	PID	Ectopic pregnancy / Infertility	Cervical cancer
<i>Dose response</i>			
♦ Frequency of douching	00+	000++	0++
♦ History of douching	0+	0	0+
<i>Specificity of douche product</i>			
♦ Effect relative to other solutions:	0+	0++	-+
--Commercial		00	0
--Water		0	0+
--Water and vinegar		0	0
--Water and soda		0	
♦ Effect relative to other devices:			
--Disposable	00	00	
--Reusable bag	00	00	

* Each relevant study is represented with a mark indicating its evidence against (-), neutral (0), or supporting (+) a positive association with douching.

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Conclusions

Consistent moderate or null effect, in spite of:

- poor study power
- low douching prevalence
- different study designs
- difficulty of getting douche history for unknown relevant time period

Moderate effects are difficult to study with epidemiologic tools.

Moderate effects often turn out to be spurious. Similar patterns of douching effects for PID/ectopic pregnancy/infertility and cervical cancer support this concern.

Confounding could be either over- or undercontrolled.

If effect real:

- may be subject to competing risk factors
- may be independent of douche solution or device

Evidence is suggestive, but no more than suggestive, that douching independently raises the risk of PID, ectopic pregnancy, infertility, and cervical carcinoma.

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**Pressure and Flow Measurements
in Different Types of Vaginal Douches**

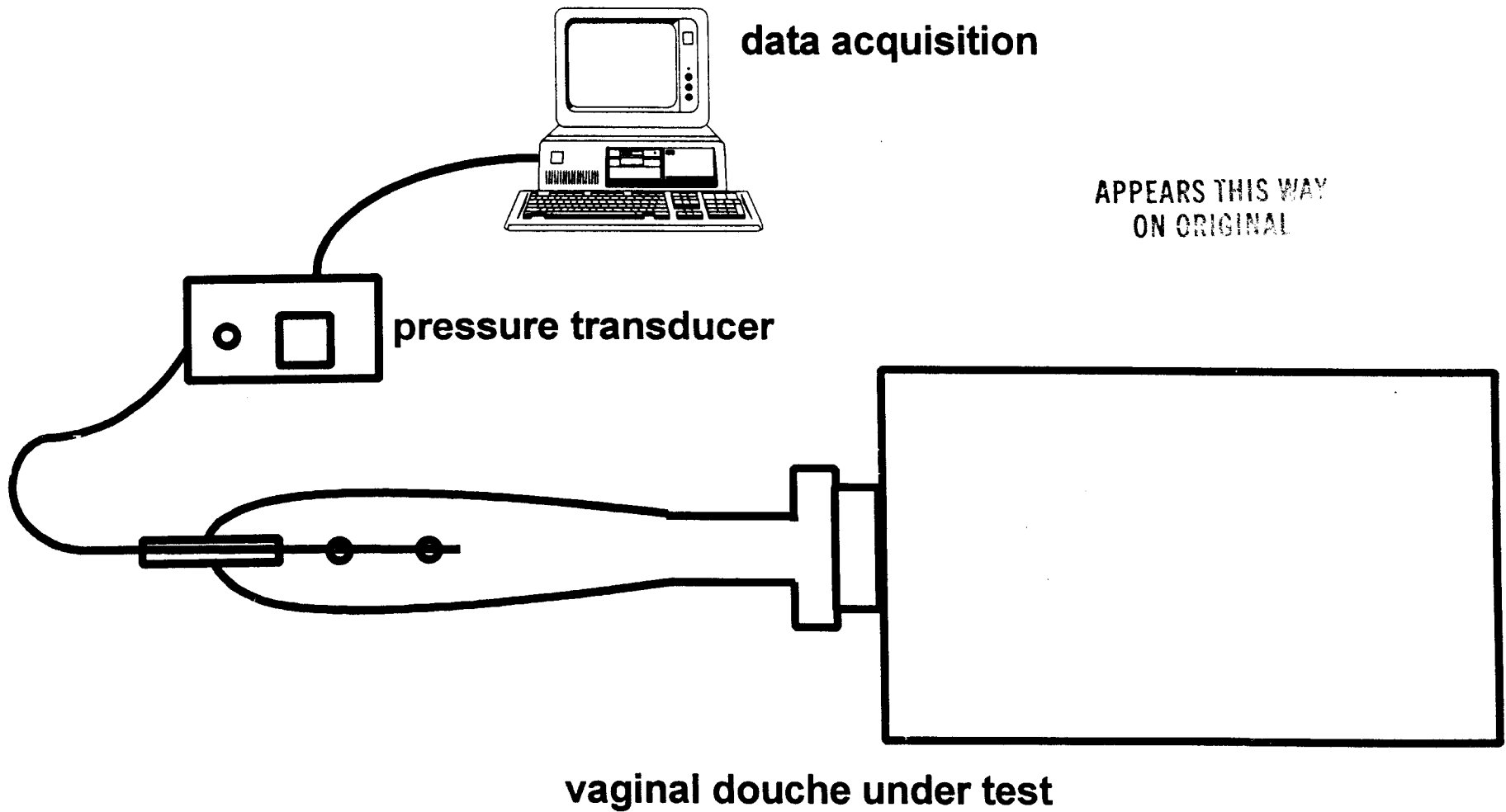
**Jean E. Rinaldi
Biomedical Engineer
FDA/CDRH
Office of Science and Technology**

**Acknowledgements to:
Ronald F. Carey
Stephen M. Retta
Jeffrey M. Porter**

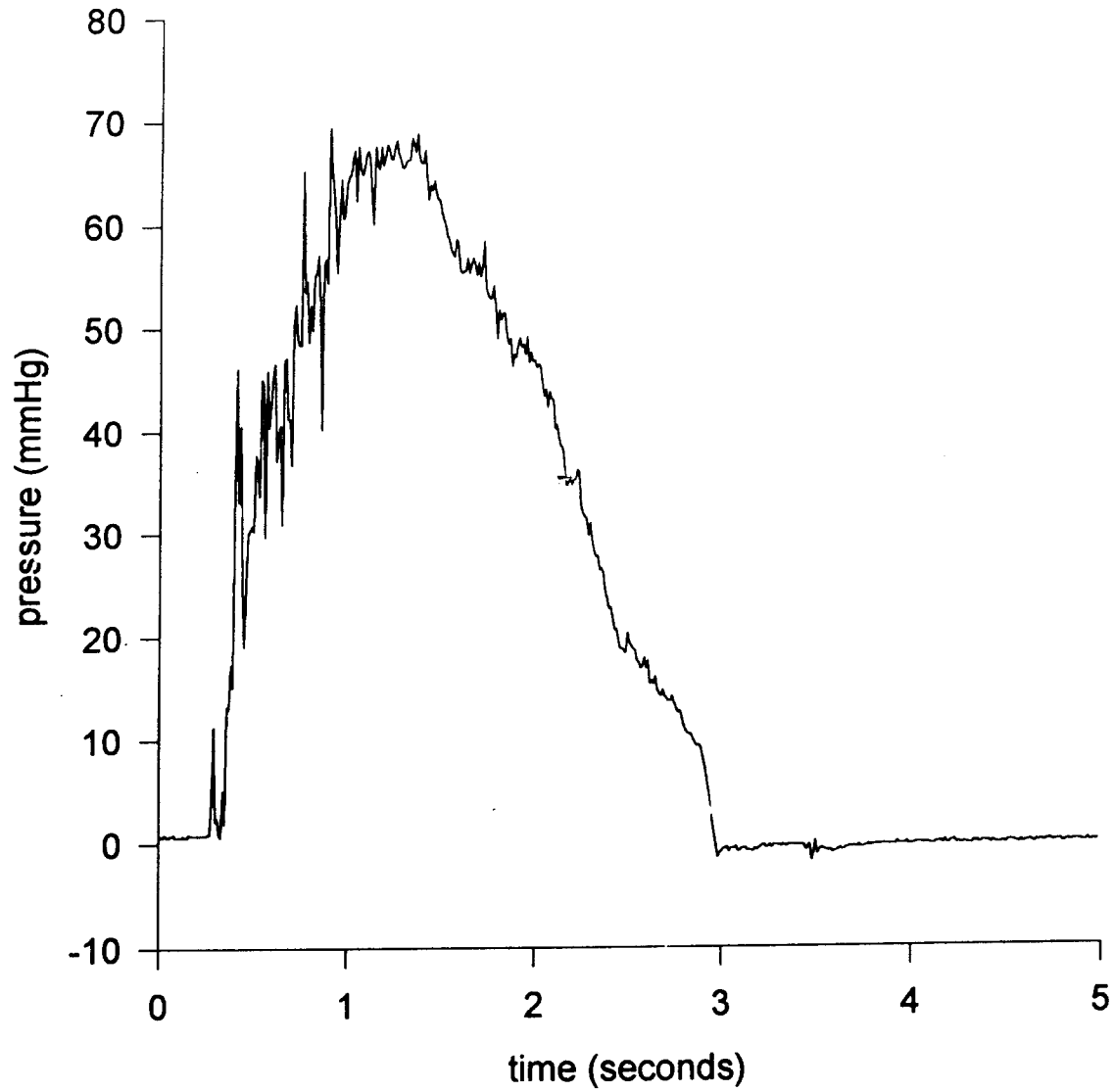
Important Caveats

- (1.) Only *ONE* sample of each type tested.**
- (2.) Only *ONE* “user” performing all tests.**
- (3.) *NO* in vitro physiologic model or human environment.**
- (4.) *NO* temperature effects.**
- (5.) No clear way to tie results obtained to any clinical effect.**

Pressure Measurement Experimental Set-Up

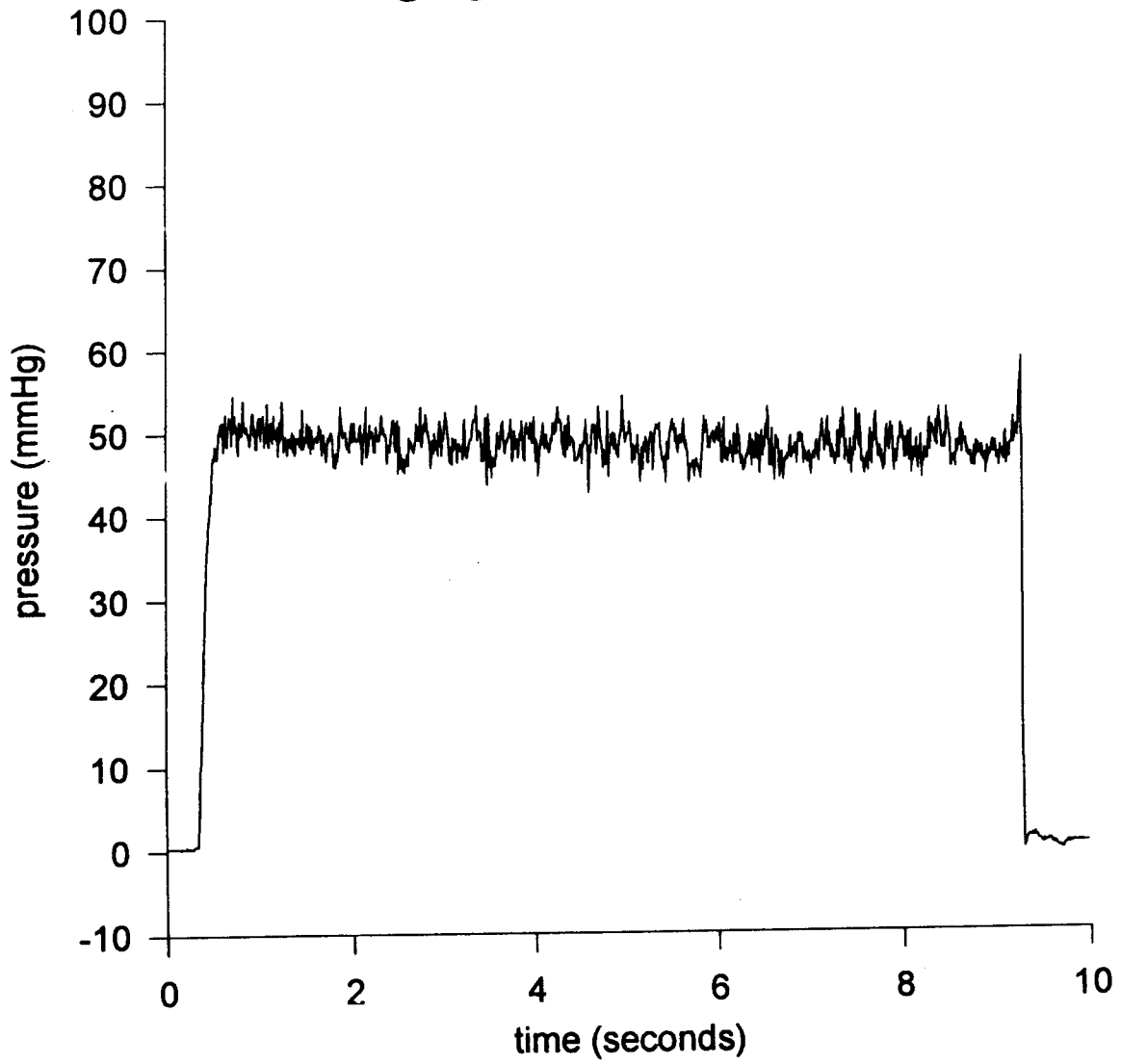


Disposable Bottle: Pressure vs. Time



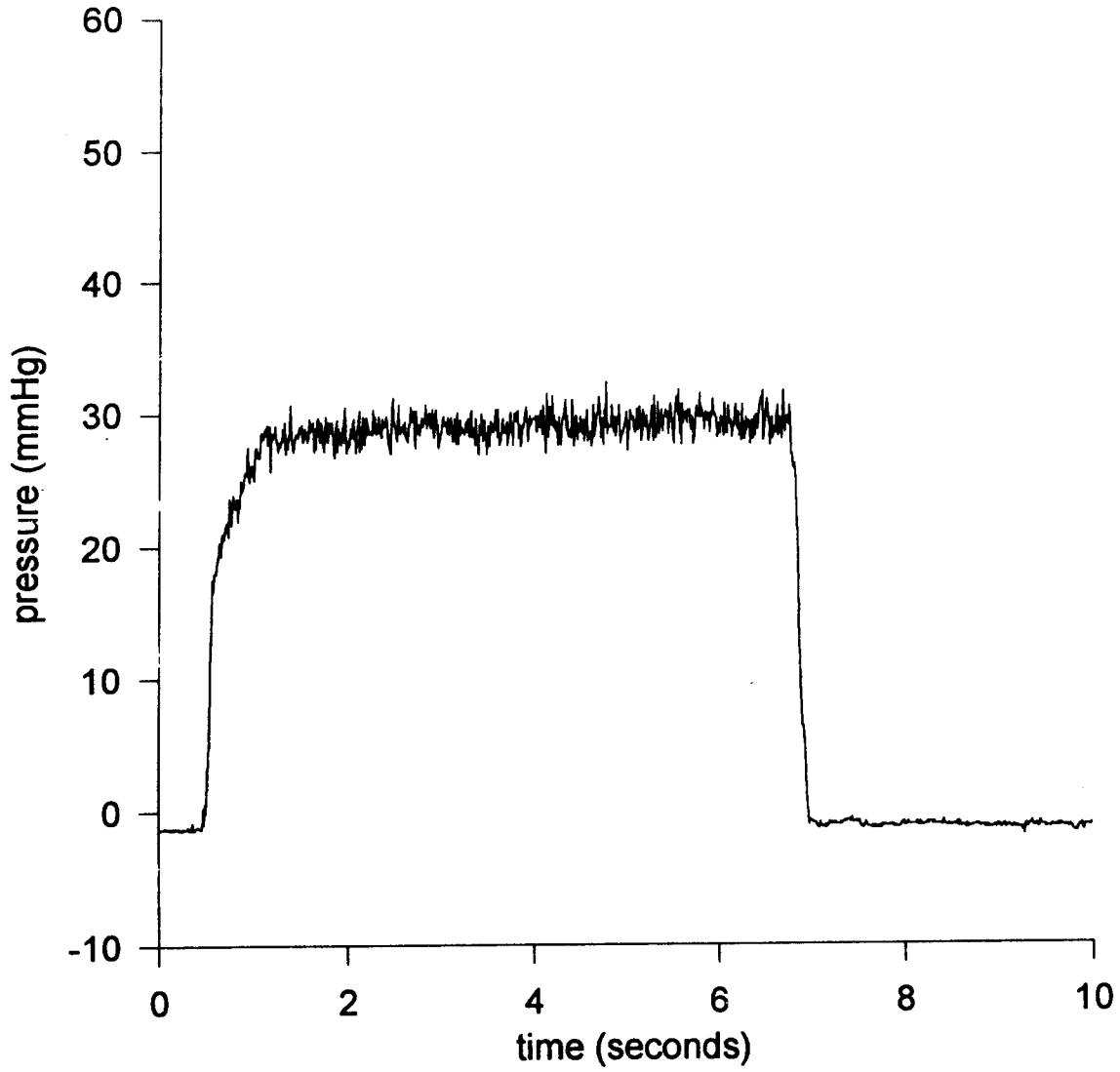
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Hanging Bag: Pressure vs. Time



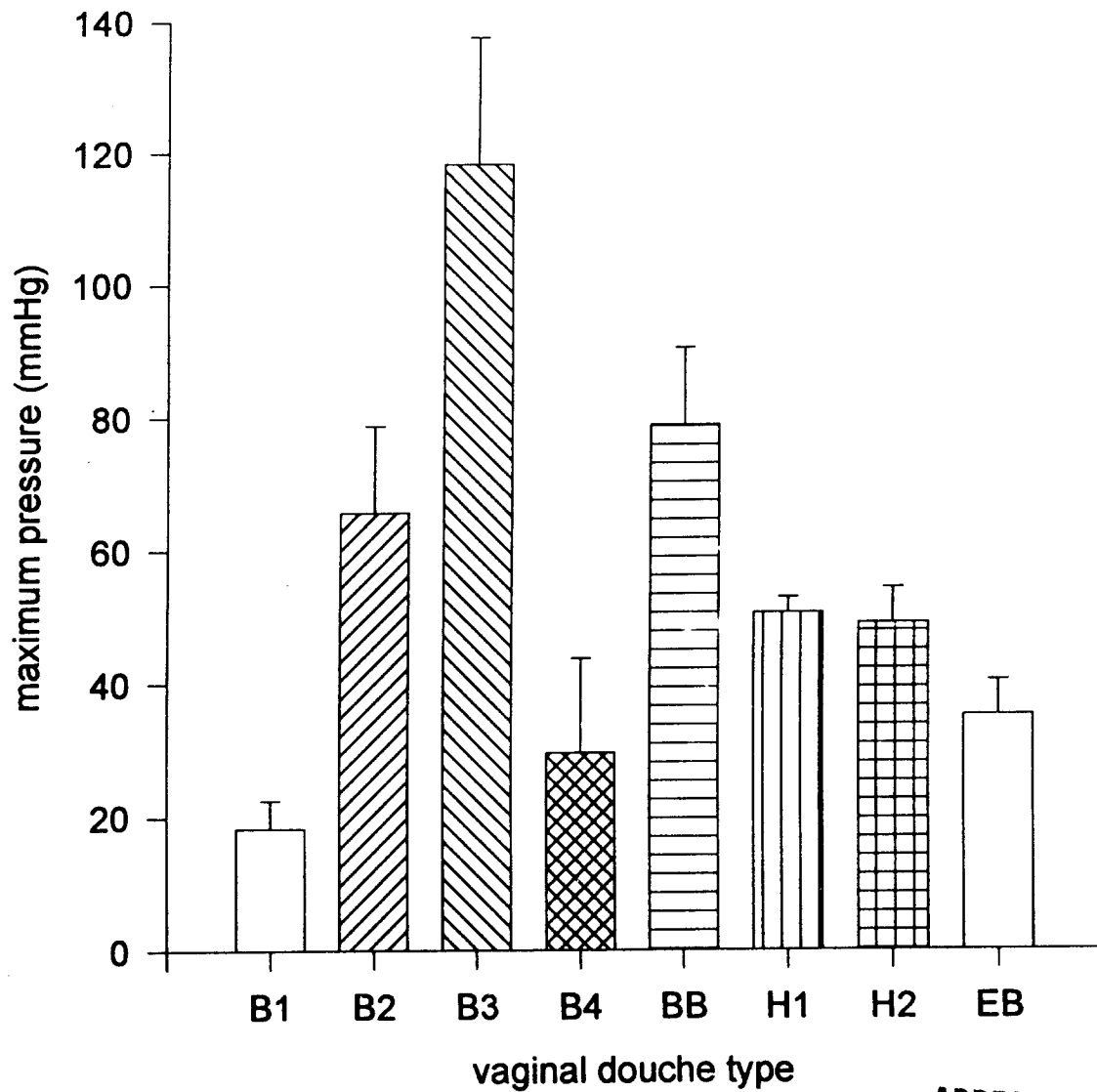
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Expandable Bag: Pressure vs. Time



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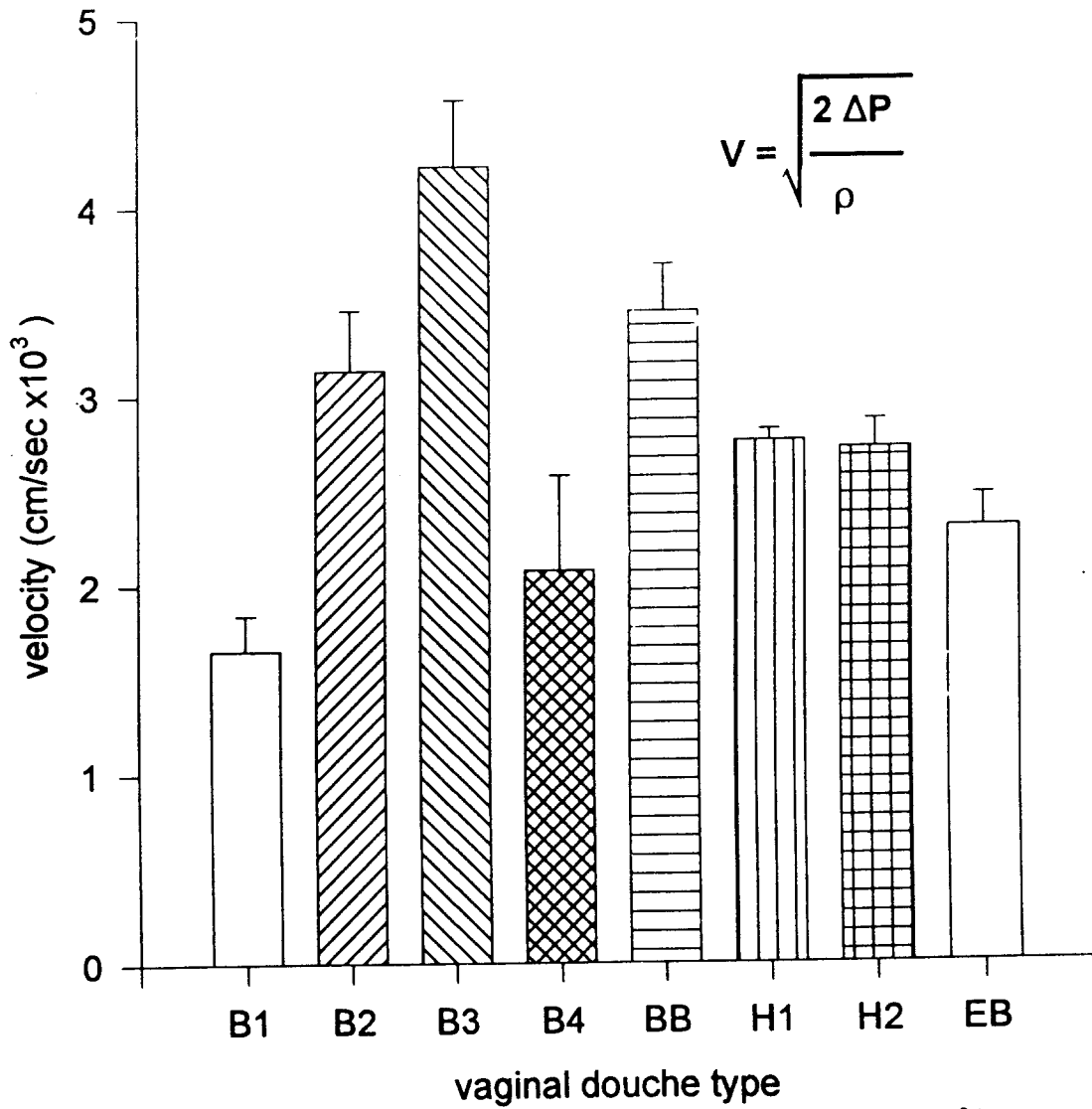
Maximum Pressure vs. Douche Type



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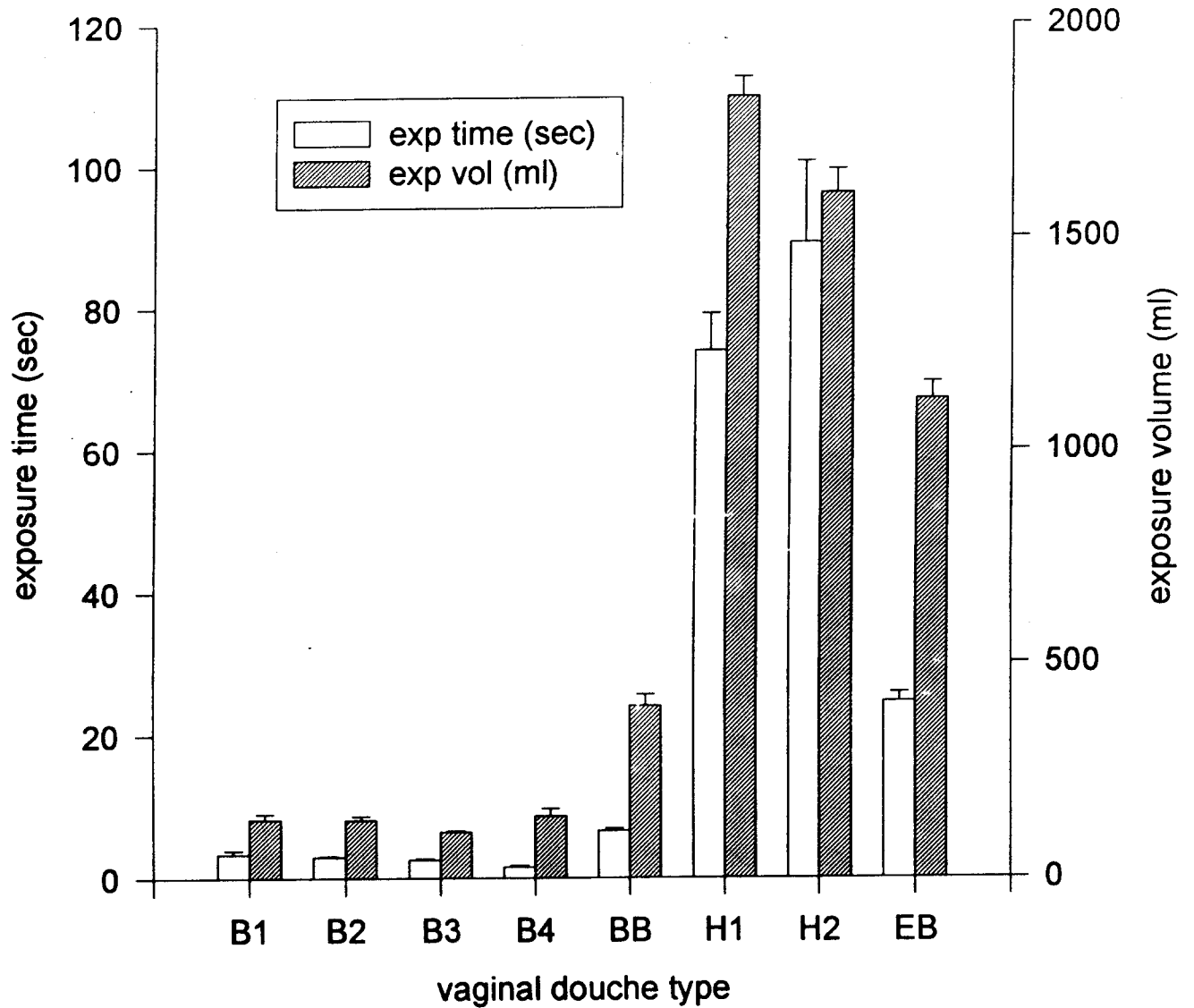
Velocity vs. Douche Type

Exit velocities determined by Bernoulli Equation:



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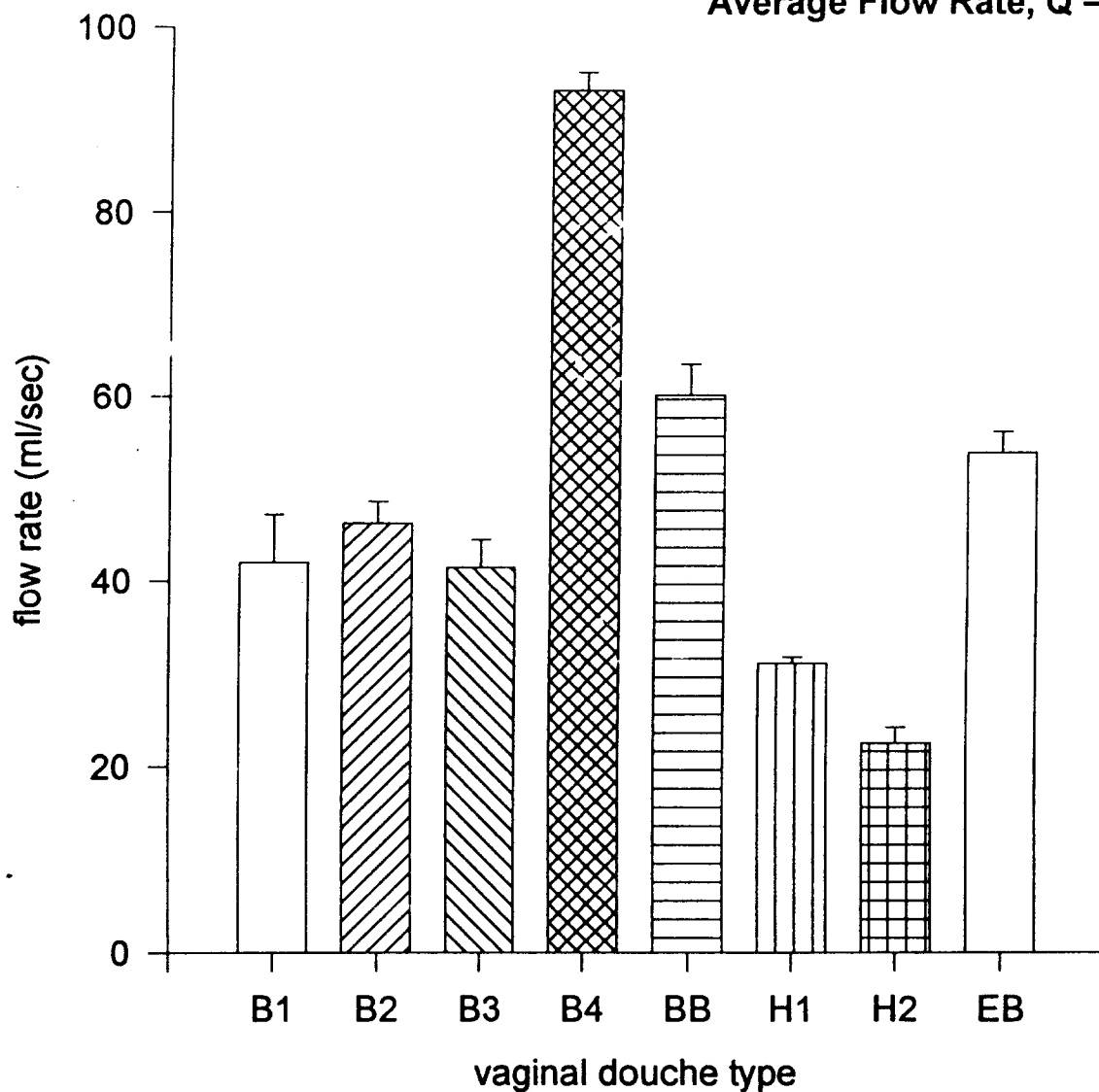
Exposure Times and Volumes for Different Douche Types



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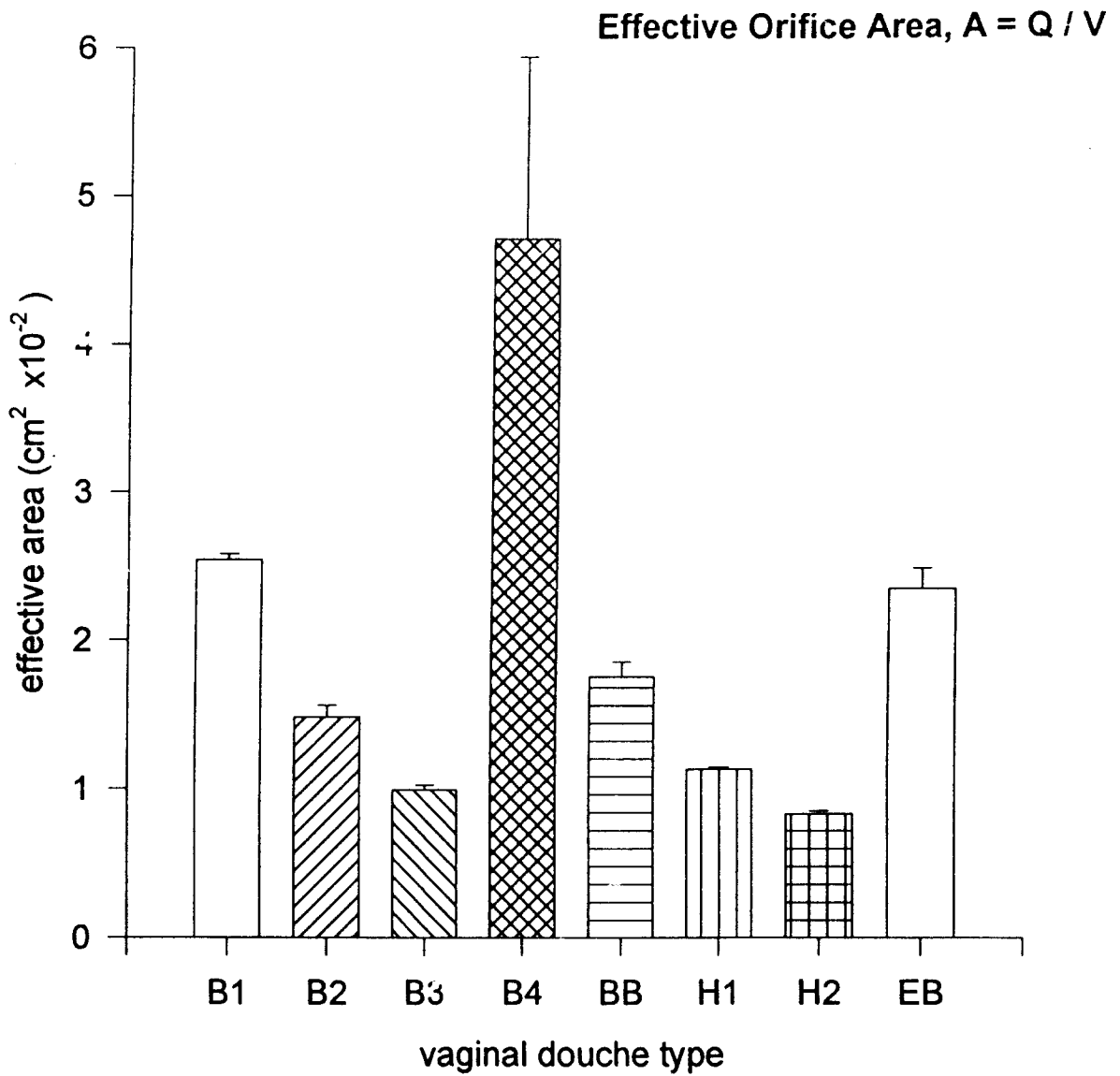
Flow Rate vs. Douche Type

Average Flow Rate, $Q = v / t$



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Effective Orifice Area vs. Douche Type



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Summary

- (1.) Human anatomical variety including cervical os, uterine angle, vaginal conditions, temporal changes, parity, age.**
- (2.) Douching use variety including postural effects, nozzle placement, nozzle angle, nozzle design.**
- (3.) Other variables including reuse, solution effects, temperature.**

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Topics of Discussion

- Labeling on Current Vaginal Douche products
 - ◆ Actual labels
 - ◆ Overview of OTC label elements among the various products
 - ◆ Describe language used
 - ◆ Relate to OTC Review

Labels Reviewed: Caveats

- Labels from retail purchase
- D.C. metropolitan area only
- Not comprehensive
- Not representative

Product Categories

- Vinegar & Water
- Baking Soda & Water
- Other Ingredients
- O-9 Containing
- Povidone-Iodine Containing

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Show Labels

Summary: Current Labeling

- Among different company's products, language is variable
 - ◆ by amount of information provided
 - ◆ by type of information provided
- Products containing different ingredients from the same company bear the same labeling

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Show Tables

	Summer's Eve Vinegar & Water	Generic Super G Fresh & Free	Massengill	Trichotine (conc)	Zonite (conc)
Indication (What To Use For)	No (Yes)	No (Yes)	No (Indirect)	No (Yes)	No (Indirect)
- When To Use	Yes	Yes	No	No	No
Warnings:					
- Frequency	Yes	Yes	Yes	Yes	Yes
- Contraception	Yes	Yes	Yes	No	Yes
- PID Assoc.	Yes	No	Yes	No	No
- MD Referral	Yes	No	Yes	No	No

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	Summer's Eve Touch of Spring	Yeast-Gard Medicated	Generic CVS Bala Floor	Betadine Medicated	Generic Medicated
Indication (What To Use For)	No (Yes)	Yes (Yes)	No (Yes)	No (Yes)	No (Yes)
- When To Use	Yes	No	Yes	No	No
Warnings:					
- Frequency	Yes	Yes (Directions)	Yes	Yes	Yes (Directions)
- Contraception	Yes	Yes	Yes	Yes	Yes
- PID Assoc.	Yes	No	No	Yes	No
- MD Referral	Yes	No	Yes	Yes (Insert)	No

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WHEN TO USE	
Vinegar & Water:	
Summer's Eve	After menstrual period, using contraceptive jellies and creams, and anytime you want to feel clean & refreshed.
Generic	A likely time to douche is after menstruation. But you may want to ... wash away built-up secretions that cause odor, clean away contraceptive jellies, or to feel clean & fresh
Baking Soda & Water:	
Massengill	None
O/S Containing	
Yeast-Gard	None
Generic	The most obvious time is after menstruation. But you'll want to use it other times as well-after nervous tension, to clean away contraceptive jellies and creams, wash away built-up secretions that cause odor, anytime to feel clean & fresh.
Iodine Containing	
Betadine	None
Generic	

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Vinegar & Water:	
Summer's Eve	To clear out normal accumulations of vaginal secretions, ... to feel clean & refreshed.
Generic	To wash away built-up secretions that cause odor, to clean away contraceptive jellies or creams, or to feel clean & fresh
Baking Soda & Water:	
Massengill	Use this product only as directed for routine cleansing. (Directions)
Other	
Trichotine	Cleans thoroughly, thins out and removes discharge and mucous debris. Helps to prevent disagreeable odor. Use for routine feminine hygiene or as directed by your physician.
Zonite	... leaves you feeling fresh, clean, odorfree..and confident. For the external vaginal area, Zonite can be used undiluted, as often as required, as a cleansing and deodorizing agent.
O/S containing	
Yeast-Gard	For prompt symptomatic relief of vaginal discharge with minor irritation and itching.
Iodine containing	
Betadine	For prompt symptomatic relief of minor vaginal irritation, itching and soreness. For deodorizing and cleansing. For other uses, see your physician.

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Vinegar & Water	
Summer's Eve, Generic	None.
Baking Soda & Water:	
Massengill	If vaginal dryness or irritation occurs discontinue use.
Other:	
Trichotine	If irritation occurs, discontinue use.
9-Containing:	
Yeast-Gard	If symptoms persist for more than 2 weeks, or if redness, swelling or pain develops, discontinue use and consult a physician.
Generic	If vaginal dryness or irritation occurs, discontinue use.
Iodine-Containing:	
Betadine	If symptoms persist after five days of use, or redness, swelling or pain develops, discontinue use and consult a physician.
Generic	If symptoms persist after 7 days of use, or redness, swelling or pain develops, discontinue use and consult physician.

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Vinegar & Water	
Summer's Eve	Do not douche more than twice weekly except under the advice and supervision of a physician.
Generic	Vaginal douches should not be used more than twice weekly except when advised by a doctor.
Baking Soda & Water	
Massengill	You should douche no more than twice a week except on the advice of your doctor.
Other	
Trichotine Zonite	Do not douche more often than twice weekly unless directed by your physician.
9-Containing	
Yeast-Gard	Use two bottles per week. (Directions)
Generic	Vaginal douches should not be used more often than twice a week.
Iodine-Containing	
Betadine	Use once daily for five days (for symptoms). Use up to twice weekly (for deodorizing & cleansing).
Generic	Use one bottle per day until symptoms disappear, but no more than 7 days. (Directions)

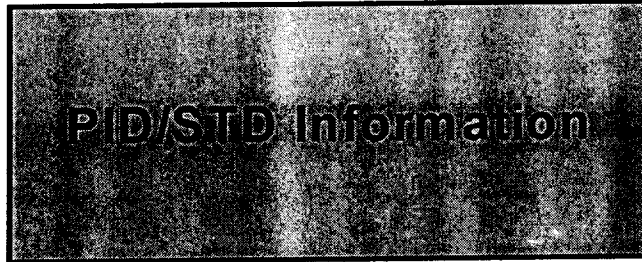
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Warnings - Use During Pregnancy	
Vinegar & Water:	
Summer's Eve (Massengill)	Do not douche during pregnancy except under the advice and supervision of a physician.
Generic	Vaginal douches should not be used during pregnancy except when advised by a doctor.
Other:	
Trichotone	None.
Zonite	If you are pregnant or nursing a baby, seek the advice of a health professional before using this product.
O-9-Containing:	
Yeast-Gard	Do not use during pregnancy or while nursing except with the approval of a physician.
Generic	Do not use vaginal douches when pregnant except when advised by a physician.
Iodine-Containing:	
Betadine	Do not use during pregnancy or while nursing except with the approval of your physician.
Generic	Do not use during pregnancy except with the approval of your physician.

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Warnings - Use During Pregnancy	
Vinegar & Water:	
Summer's Eve	Douching does not prevent pregnancy.
Generic	A douche is only a cleanser, not a contraceptive.
Baking Soda & Water:	
Massengill	Douching does not prevent pregnancy.
Other:	
Trichotone	None.
Zonite	Douching does not prevent pregnancy.
O-9-Containing:	
Yeast-Gard	Douching does not prevent pregnancy.
Generic	A douche is not a contraceptive and should not be used to prevent pregnancy.
Iodine-Containing:	
Betadine, Generic	Douching does not prevent pregnancy.

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Vinegar & Water	
Summer's Eve	... nor will it cure or prevent any sexually transmitted disease (STD). ... Douching should not be used for self treatment or if you have symptoms of PID or STD.
Generic	None.
Baking Soda & Water	
Massengill	Douches should not be used for the self treatment of any STDs or PID.
Other	
Trichotine, Zonite	None.
Yeast-Containing	
Yeast-Gard	None.
Generic	Douches should not be used as treatment for sexually transmitted diseases (STD) or pelvic inflammatory disease (PID).
Iodine-Containing	
Betadine, Generic	None.

WARNINGS Association with PID	
Vinegar & Water:	
Summer's Eve	An association has been reported between frequent douching and pelvic inflammatory disease (PID), a serious infection of the reproductive system. It is not currently known whether frequent douching is causally related to PID, but women should be aware of this association.
Generic	None.
Baking Soda & Water:	
Massengill	An association has been reported between douching and pelvic inflammatory disease (PID), a serious infection of your reproductive system which can lead to sterility and/or ectopic (tubal) pregnancy.
Other:	
Trichotone, Zonite	None.
O-9-Containing:	
Yeast-Gard, Generic	None.
Iodine-Containing:	
Betadine	Douching is reported to be associated with Pelvic Inflammatory Disease, a serious infection of the reproductive system.
Generic	None.

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WARNINGS Association with PID		
Vinegar & Water:		
Summer's Eve	PID symptoms include lower abdominal pain, fever, chills, nausea, vomiting, and/or a pus-like yellow cervical discharge. STD symptoms include vaginal discharge of an unusual amount, color or odor, painful and/or frequent urination; and genital sores or ulcers.	
Baking Soda & Water:		
Massengill	PID's most common symptoms are pain and/or tenderness in the lower part of the abdomen and pelvis. You may also experience a vaginal discharge, vaginal bleeding, nausea or fever. Other sexually transmitted diseases (STDs) have similar symptoms and/or frequent urination, genital sores, or ulcers.	
O-9-Containing:		
Generic	If you are experiencing frequent and painful urination, lower abdominal pain, genital sores or ulcers or if your sexual partner has genital symptoms, or if your vaginal discharge is an unusual amount, color, or odor, you should discontinue using this product and contact your physician. You may have a serious medical condition.	
Vinegar & Water	O-9-Containing	Iodine-Containing
Generic: None.	Yeast-Gard: None.	Betadine, Generic: None.

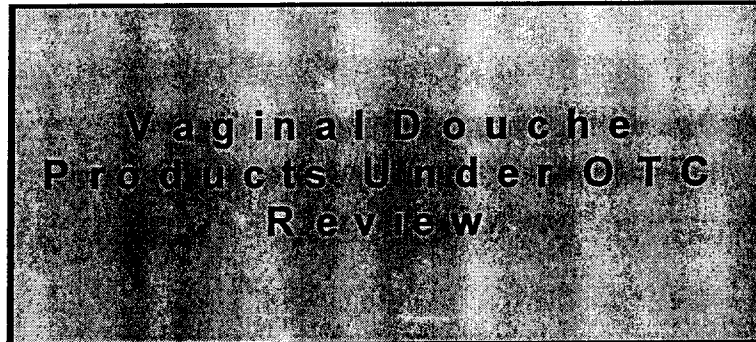
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WARNINGS: Related to Physician for STD/AIDS Symptoms	
Vinegar & Water:	
Summer's Eve	If you have any of these symptoms or suspect you may have been exposed to a STD, do not use this product, or any douche, and consult a physician immediately.
Generic	None.
Baking Soda & Water:	
Massengill	PID requires immediate medical attention. ... If you suspect you have one of these infections or PID, stop using this product and see your doctor immediately.
Other:	
Trichotone, Zonite	None.
Q-9-Containing:	
Yeast-Gard	None.
Generic	If you think you have an STD or PID, do not douche and contact your physician immediately.
Iodine-Containing:	
Betadine, Generic	None.

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Massengill
What you should know about Pelvic Inflammatory Disease
Warning: Association with PID
Table: six common sexually transmitted diseases and their symptoms
A special note about HIV & AIDS
When to see your doctor
Preventing STDS and AIDS
Infections that don't cause long-term health problems (yeast infection, trichomoniasis, bacterial vaginosis)
About Massengill (when to douche, how to douche, Q&A)
Betadine
Vaginitis
3 most common: Candidiasis, Trichomoniasis, Bacterial Vaginosis
Gonorrhoea, Chlamydia, Syphilis, AIDS, Genital Herpes, Genital Warts
Pelvic Inflammatory Disease, Douching and PID
See your Doctor

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Panel Recommendations: 1983 Specific language for:

- Not using during pregnancy
- Not using as a contraceptive
 - ◆ *Trichotine*
- How to douche:
 - (mixing, insertion, position, non-occlusion, gentle flow, not overfilling, when to stop using)
 - ◆ *No one label used all elements*
 - ◆ *Trichotine, Zonite (mixing instructions)*

Panel's Report: 1983 Indications

- Relief of minor vaginal itching, irritation and soreness
 - ◆ Povidone-iodine: 0.15 to 0.3% douche
 - ◆ Ca propionate: 20% gel
 - ◆ Na propionate: 20% gel
 - ◆ K sorbate: 1 to 3% douche
- *P-I Containing products have this claim*
- *Yeast-Gard included this claim (no P-I)*

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Panel's Report: 1983 Indications

- Removes vaginal discharge, vaginal secretions, mild detergent action, thins out vaginal mucus discharge
 - ◆ Nonoxynol-9: 0.0176% douche
 - ◆ Octoxynol-9: 0.088% douche
 - ◆ Dioctyl Na sulfosuccinate: 0.02% douche
 - ◆ Na lauryl sulfate: 0.01 to 0.02% douche
- *Most all douche products have this claim*
- *Yeast-Gard (O-9) discharge, minor irritation & itching*

Panel's Report: 1983 Professional Labeling

- Treatment of *Candida albicans*
 - ◆ Propionates
- Treatment of *Trichomonas*
 - ◆ Sodium lauryl sulfate
- Treatment Regimen for *Candida*,
Trichomonas, Nonspecific vaginitis
 - ◆ Povidone-iodine: 0.15 to 0.3% and 10%
- *Trichotine* (as directed by physician)
- *Betadine* (for other uses, see your physician)

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Current Standing: 1994

- Panel's report withdrawn
- Most are cosmetic, not drug claims
- No separate OTC Drug Monograph for Vaginal Drug Products
- Minor vaginal irritation, itching, and soreness claims will be referred to other rulemakings, (e.g. Antimicrobial Monograph)

Current Standing: 1994

- TFM for povidone-iodine in vaginal douche products not published
- P-I claims for relief of vaginal irritation, itching and soreness under review
- Professional labeling claims will be addressed in a future FR notice

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Vaginal Douching and the Risk of Ectopic Pregnancy Among Black Women

**Juliette S. Kendrick
Hani K. Atrash
Lilo T. Strauss
Paul M. Gargiullo
Young W. Ahn**

in press
**American Journal of Obstetrics and Gynecology
May 1997**

Reasons for Study

- ▣ **Incidence of ectopic pregnancy increasing, U.S. and worldwide**
 - ▣ **Ectopic pregnancy more common in African-American women**
 - ▣ **Could vaginal douching be an important risk factor?**
 - ▣ **Previous studies include few African-American women**
-

Methods

- * Major metropolitan hospital in GA
 - * October 1988 to August 1990
 - * Women ages 18-44
 - * Questionnaire by interviewer
 - * Cases: confirmed ectopic pregnancy
 - * Controls: 2 sources combined
 - Obstetric controls: delivering infant \geq 500 gm
 - Abortion controls: seeking abortion
-

Methods

- * Exclusions:
 - previous ectopic pregnancy
 - previous tubal surgery
 - current IUD use
 - limited to black, non-Hispanic
 - * Douching: "At any time before this pregnancy, did you ever douche?"
 - reason, frequency, timing, apparatus, solution
 - * Analysis:
 - logistic regression modeling
 - confounders: age, parity, marital status, education, infertility, smoking, sex partners, IUD, PID, STDs
-

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Characteristics of Cases and Controls

	% Cases (n=197)	% Controls (n=1119)
Age 18-24 years	46	64
Education <12 years	26	25
Married	42	28
Nulliparous	30	25
History of infertility	14	3
History of PID	21	13
Ever smoker	44	26
≥ 5 sex partners	58	45
Ever douched	97	89

Main reason for douching

- * Routine cleanliness (78% controls)
 - * Unusually heavy vaginal discharge (3% controls)
 - * Vaginal itching or burning (0.5% controls)
 - * Both itching and discharge (0.1% controls)
 - * Other (7.4% controls):
 - I just do it
 - my mother said to
 - it's a habit
 - it's the thing to do
 - my doctor told me to
 - bad odor or bad smell
 - after sex
 - after my period.
-

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Risk of Ectopic Pregnancy Associated with Douching

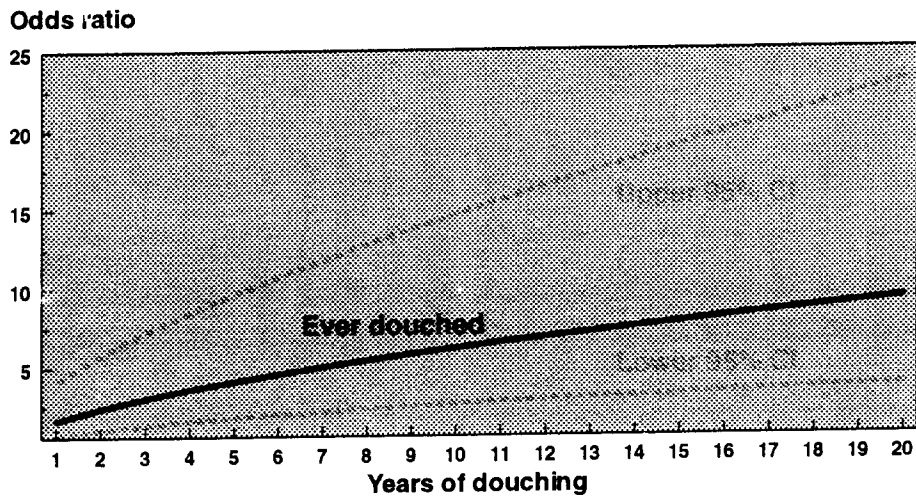
	Adjusted OR	95% CI
Never douched	1.0	referent
Ever	3.6	1.6- 8.9
Reason		
Habit	3.6	1.5- 8.4
Symptoms	4.5	1.7-11.8
Frequency		
≤ once per month	3.8	1.6- 9.3
Once per 2-3 weeks	3.9	1.6- 9.5
Once per week	2.9	1.1- 7.4
> once per week	4.3	1.7-10.9
Solution		
Vinegar and water - home made	3.1	1.3- 7.9
Vinegar and water - store bought	3.9	1.6- 9.3
Povidone iodine	4.5	1.6-12.9
Other store bought	3.7	1.5- 9.0

Risk of Ectopic Pregnancy Associated with Douching

	Adjusted OR	95% CI
Never douched	1.0	referent
After intercourse		
	4.5	1.9-10.8
	3.2	1.3- 7.6
During menses		
No	3.7	1.6- 8.8
Yes	5.1	1.6-16.6
After menses		
No	5.2	1.8-15.3
Yes	3.7	1.6- 8.8
Month of conception		
Not that month	4.4	1.7-11.1
Douched that month	3.6	1.5- 8.6

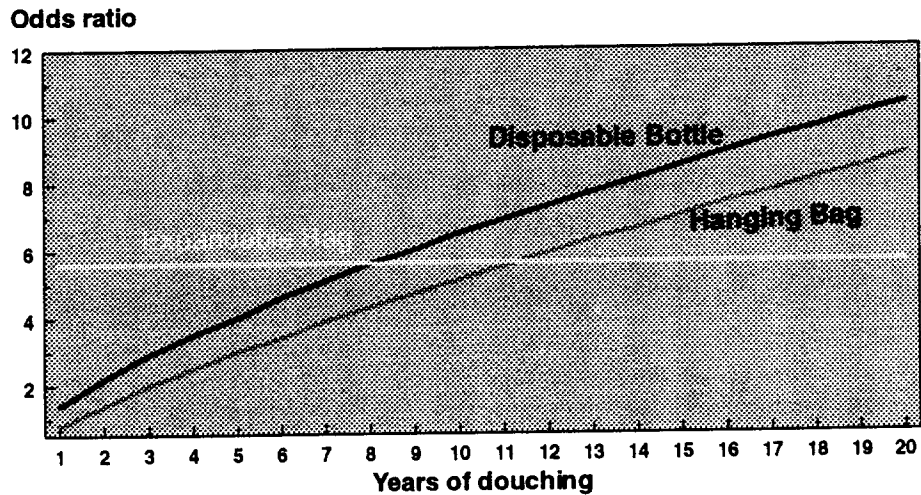
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Risk of Ectopic Pregnancy by Years of Douching at Least Once Per Month



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Risk of Ectopic Pregnancy by Years of Douching and Type of Apparatus Used



Methodologic Considerations

- Strengths:

- **designed for this issue**
- **detailed douching information**
- **high exposure prevalence**
- **control selection**

- Limitations:

- **self reported PID, STDs**
 - **temporal sequence**
 - **select population**
-

APPEARS THIS WAY
ON ORIGINAL