



Treatment With Cryotherapy by Mid-Level Clinicians In Low-Resource Settings

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Outpatient Treatment Options

Procedure	Outpatient	Anesthesia	Electrical Power	Nonphysicians	Cost
Cryotherapy	Yes	No	No	Yes	Low
Electrocautery	Yes	Yes (Local)	Yes	Yes	Low
Cold Cautery (100°C)	Yes	Yes (Local)	Yes	Yes	Low
LEEP ¹	Yes	Yes (Local)	Yes	No	High
Laser Vaporization	Yes	Yes (Local)	Yes	No	High
Cone Biopsy	No	Yes (General or regional)	Yes ²	No	High
Hysterectomy	No	Yes (General or regional)	Yes ²	No	High

Low = < \$500; Moderate = \$500-\$1500; High = > \$1500

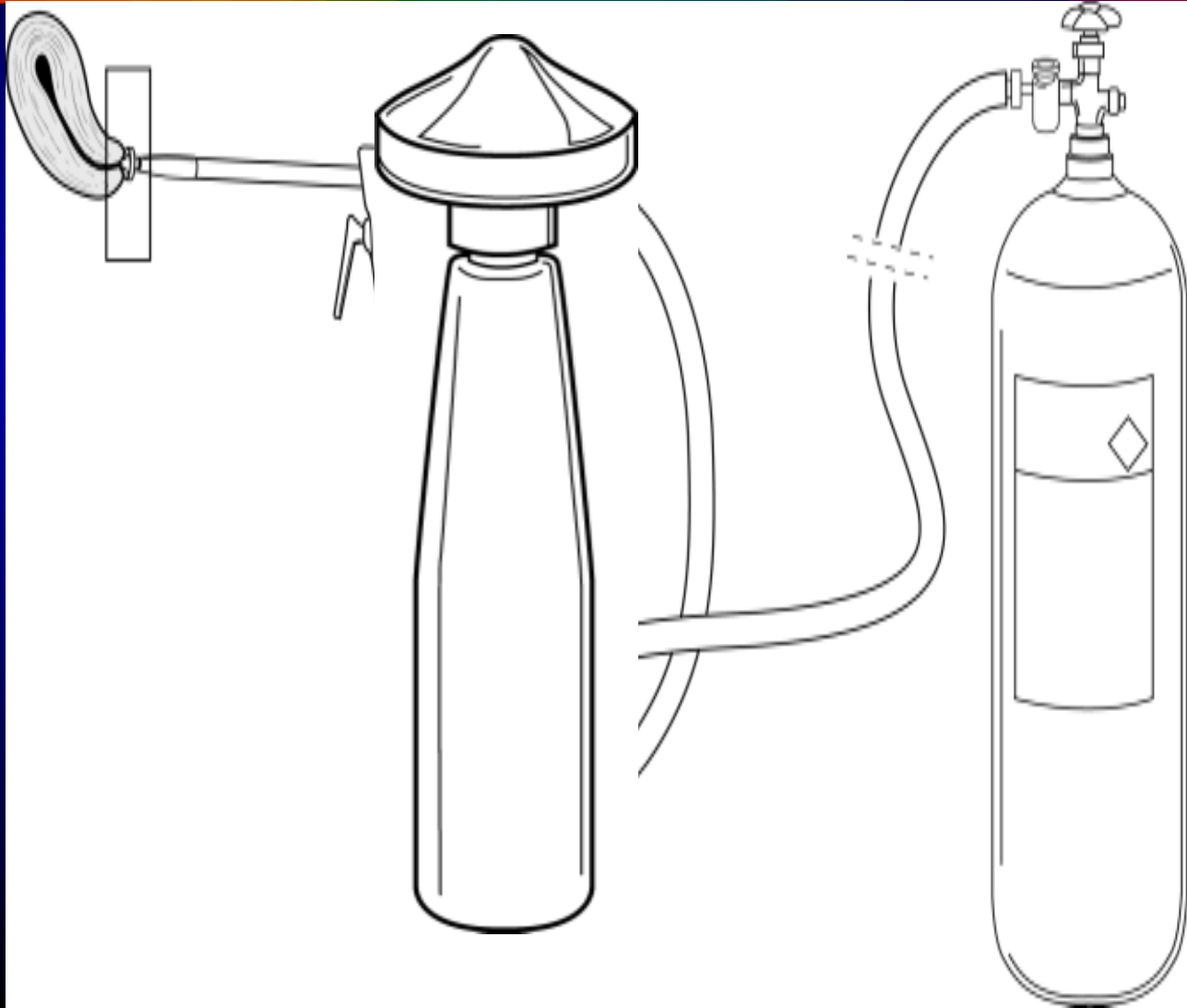
¹ Loop electrosurgical excision procedure

² Requires use of operating room lighting and equipment

Cryotherapy: Background

- Over 40 years of worldwide experience—mostly in developed countries
- Majority of experiences and research conducted in '70s and '80s
- In the US, nurses/nurse practitioners have routinely performed cryotherapy as part of cervical cancer prevention programs since the 1980s.

Cryotherapy: Equipment



Cryotherapy: Before and After



ACCP: Cryotherapy Literature Review

- Objective: comprehensive assessment of
 - Safety
 - Acceptability
 - Effectiveness
- Selection criteria
- Number of papers

Literature Review: Methodology

- OVID MEDLINE search (1955 to 2001) Search Terms: Cryo -therapy, -surgery...
- 435 articles: > 102 judged relevant
- Eligibility filters for Effectiveness (9 criteria total)
 - Randomized trial or observational follow-up study
 - Lost to f/u <20%
 - Diagnostic criterion met (colpo/biopsy or 2 abnormal cytologies)
 - Results are explicit for each group

Outcomes Reported in Literature

- Effectiveness
- Complications
 - Major
 - Minor
- Side effects
- Long-term sequelae
 - Fertility
 - Fecundity
 - Obstetric complications of labor and delivery

Literature Review: Definitions

- Acceptability - side effects @ <1 month
 - (pain, vasomotor, discharge, spotting)
- Safety - complications @ <1 month
 - (PID, bleeding, necrotic plug)
- Effectiveness - lesion-free @ ≥ 1 year
- Long term sequelae - problems after 1 month
 - (stenosis, infertility, obstetrical problems)

Effectiveness: Best Evidence

- 32 studies reviewed; 7 randomized trials
- Cure rates after one treatment: 86-95 percent
- Cure rates typically lower for patients with more severe lesions and/or larger lesions
- Generally less effective for lesions that extend into the endocervical canal

Literature Review: Safety/Complications*

- 38 papers assessed/discussed complications
- 19 papers overall reported a complication
- 2 randomized trials with active follow-up (Mitchell '98; Berget '87)

*within 1 month post-treatment

Literature Review: Safety/Complications

- PID - < 1%
 - (Mitchell '98; Berget '87),
 - higher in adolescents (~10%)
- Severe bleeding - none reported
 - (Mitchell '98; Berget '87; Kwikkel '85; Kirwan '85; Jobson & Homesley '84; Townsend '83;)
- Necrotic plug syndrome - <3%
 - (Creasman '73; Schantz '84; Berget '87;)
 - Suspect this is due to high endocervical freeze

Complications: PID

- Does cryotherapy cause pelvic infection?
 - \approx 19 cases specifically identified out of 14,240 who received cryotherapy
- Methodological problems
 - “PID” poorly defined: PID may not have been a specific outcome variable of the study
 - Follow-up is not uniform

Literature Review: Acceptability

- 45 studies reported assessing one or more side effects
- 13 actively assessed side effects
- Limited data on women's experiences with cryotherapy and its side effects

Acceptability

Best evidence

- Vasomotor - 10 to 20%
 - (Townsend '71, '83)
- Pain - \leq menstruation or early labor,
 - ~4 (scale of 0 to 10)
 - (Sammarco '93, Harper '97)
- Spotting - $< 25\%$, ~3 days (Berget '87)
- Discharge - universal,
 - ~30 50% malodorous, usually < 1 month
 - (Berget '87; Harper 2000)

Experience with Discharge after Cryotherapy Treatment

- Profuse, watery, clear, yellowish, sometimes malodorous,
 - Heaviest during first 6 days post-treatment
 - 2-5 pads/day for first 10 days
 - May last from 2-6 weeks
- Summary:
 - Discharge is an expected side effect
 - Few data about *patient* perspectives

Sequelae

- Stenosis –
 - < 2% ‘needed’ dilation in the clinic
 - ~3% inability to insert cotton-tip swab at 3 mos.
- Obstetrical problems - No differences in rapid labor, C-S, abortion rates (Benrubi ‘84; Hemmingsson ‘82)
- Infertility - No association with reduced fertility

Complications: Cervical Stenosis

- Frequently described as *theoretical* concern
- Poorly defined
 - External os narrowing
 - Narrowing of isthmus
 - Inability to obtain cytology
 - May be related to “long nipple”
- Clinical correlation: studies have found no effects
 - On fertility
 - On intrapartum performance
 - On dysmenorrhea

Cryotherapy: Logistics

The devil is in the details

- Gas Supply can be a rate-limiting step
 - CO₂ vs. Nitrous Oxide
 - Local suppliers must be identified and relied upon
- Machines break
 - Must create local capacity for common repairs
 - “RAM” workshops recently conducted in Thailand

Cryotherapy: Mid-level Providers

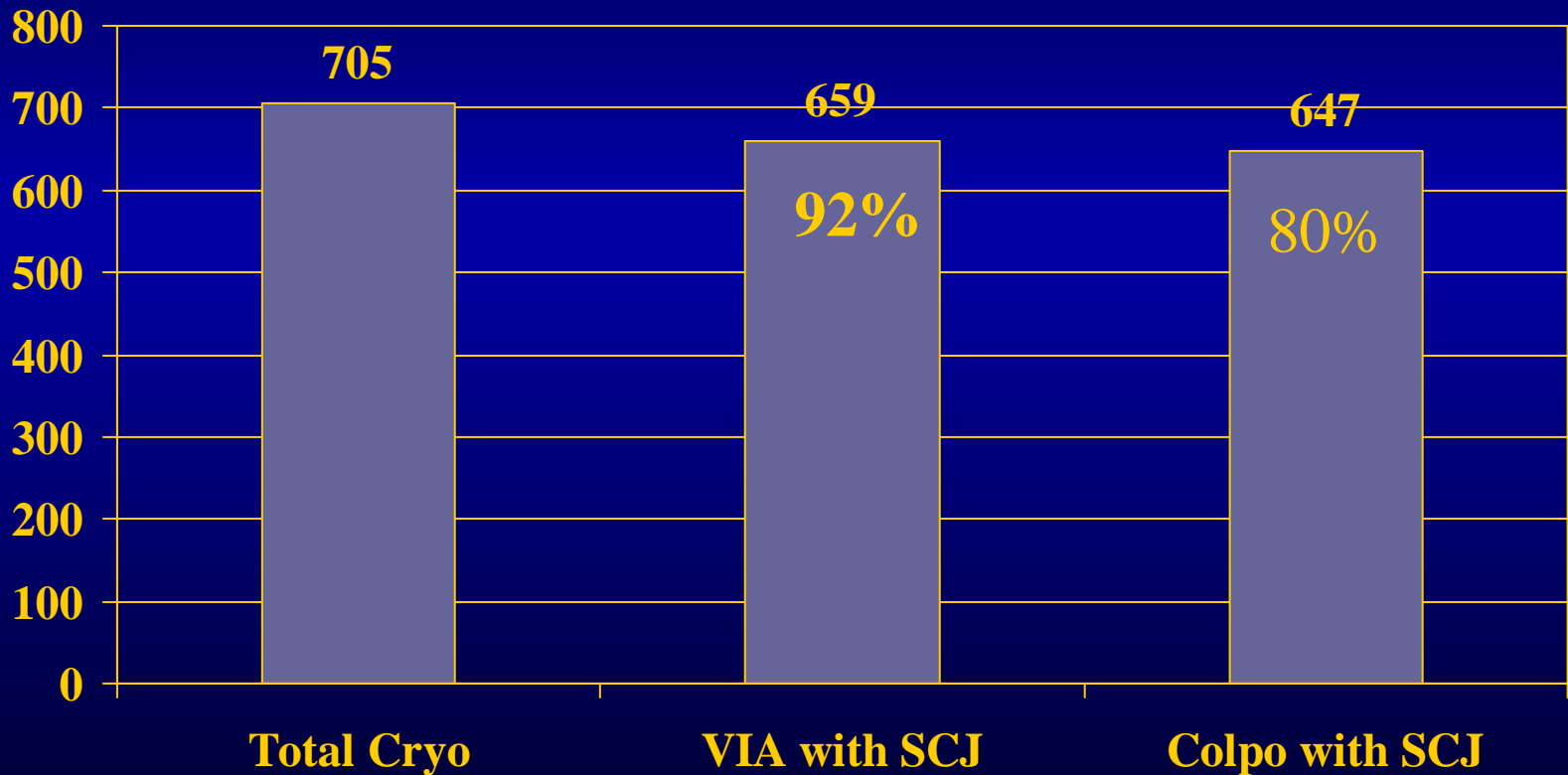
Training Parameter	EH	IARC	JHPIEGO	PATH
Number of Physicians	0	119	12	11
Number of Non-Physicians	5	47	110	4
Time to Competency (cases)	N/A 5	2 2	2 4	N/A
Degree of Difficulty	easy	easy	easy	easy
Hardest Aspect	“arms”	attitude	“pessure”	“criteria”
Number Performed in Projects	N/A 949	<500 3500	50 ~1500	N/A 40

SAFE Project: Thailand

Selected Results

	<u>Mobile</u>	<u>Hospital</u>	<u>Total</u>
VIA	3490	2506	5999
Test Positive Rate	12%	16%	13.6%
Cryotherapy	443	296	739
Problem Visit	4	32	36
Minor Complications			28
Major Complications	0	0	0
Percent Positive at 1 year	N/A	4.8%	
Cases of HGSIL at one year		4	
Cancers at One year		1	

One Year Follow-up—Visibility of SCJ

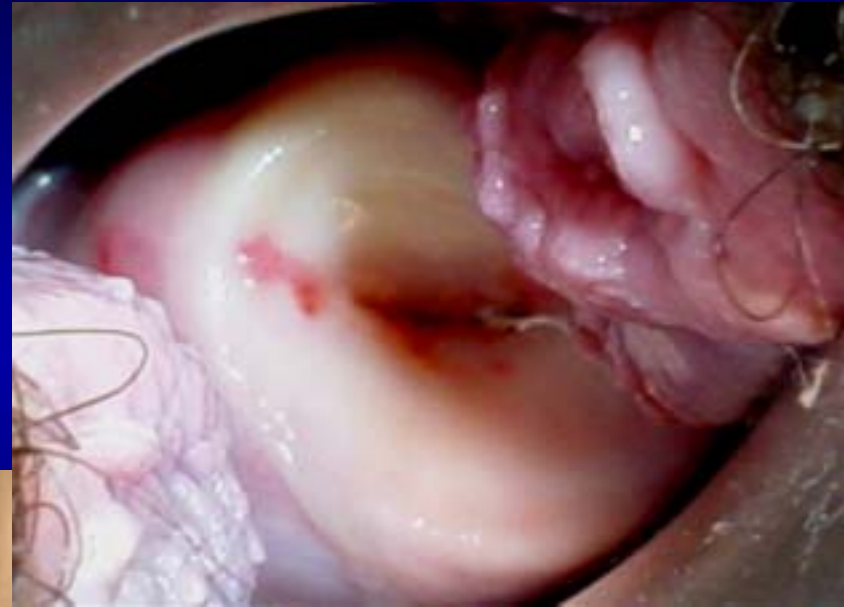


Cryotherapy: Mid-level Providers

- ACCP results:
 - Major Complications: 2 cases (~6000 procedures)
 - Minor Complications: ~2-4%
 - Patient Acceptability (satisfaction, etc): >80%
 - Throughput: ~ 40 minutes (includes VIA)



Cryotherapy in Rural Thailand



Conclusions

- Cryotherapy is a well-established safe and effective means of treatment for cervical precancer
- Cryotherapy can be competently provided by midlevel practitioners in low-resource settings
- With good training, it is likely that effectiveness will be comparable to the published literature to date