

Cervical Dysplasia and Invasive Cervical Cancer

**Satellite Conference and Live Webcast
Friday, October 10, 2008
1:00 - 3:00 p.m.**



**Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division**

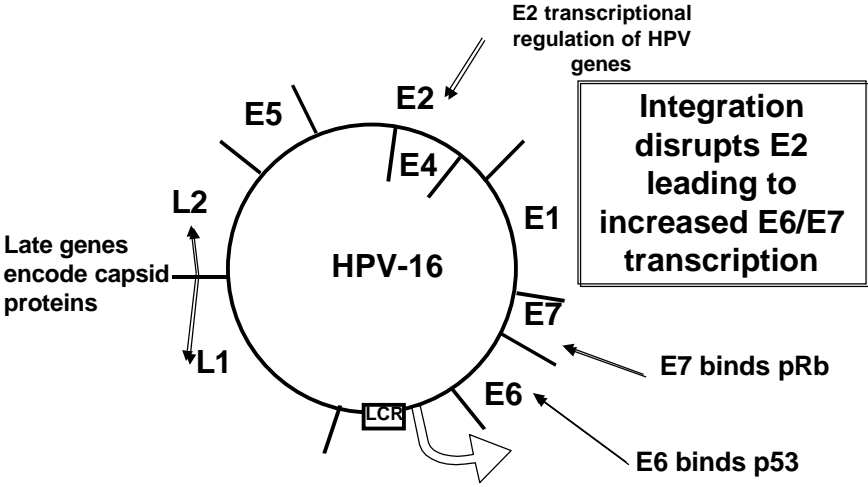
Faculty

**Michael A. Finan, M.D., F.A.C.S.
Chief, Gynecologic Oncology**



Human Papilloma Virus

- Non-enveloped DNA encased in capsid



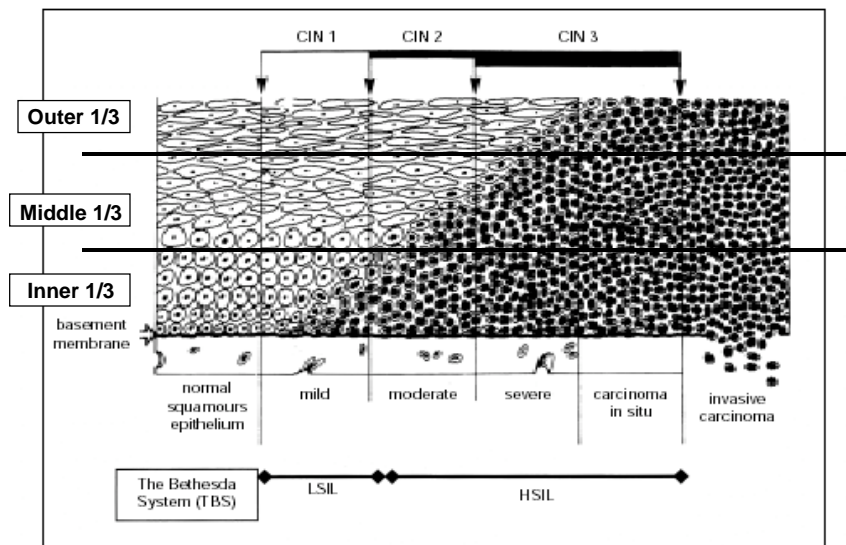
HPV Types

High Risk HPV Testing

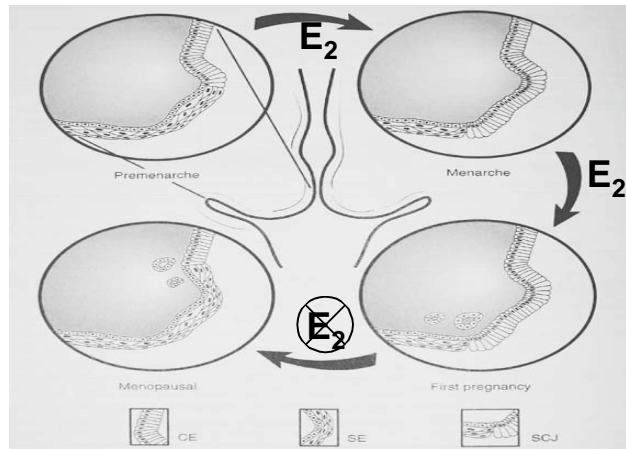
Low Risk	Intermediate Risk	High Risk
6, 11, 26, 42, 44, 54, 70, 73	31, 33, 35, 39, 51, 52, 55, 58, 59, 66, 68	16, 18, 45, 56

- Low Risk: never found alone in invasive cancer
- HPV-16: more common in squamous lesions
- HPV-18: more common in endocervical lesions

Cervical Dysplasia Schematic



Understanding The Cervical Transformation Zone



From: Practical Gynecologic Oncology 3rd Ed. Berek & Hacker

Dysplasia Natural History

Biopsy	Regress	Persist	Progress to CIN 3	Progress to Cancer
CIN1	57%	32%	11%	<1%
CIN2	43%	35%	22%	5%
CIN3	32%	56%	N/A	12%



Ostor AG. Int J Gyn Path. 1993

Infectious Or Neoplastic?

Normal \longleftrightarrow Infection \longleftrightarrow Neoplasia

- No Neoplasia
- No Infection

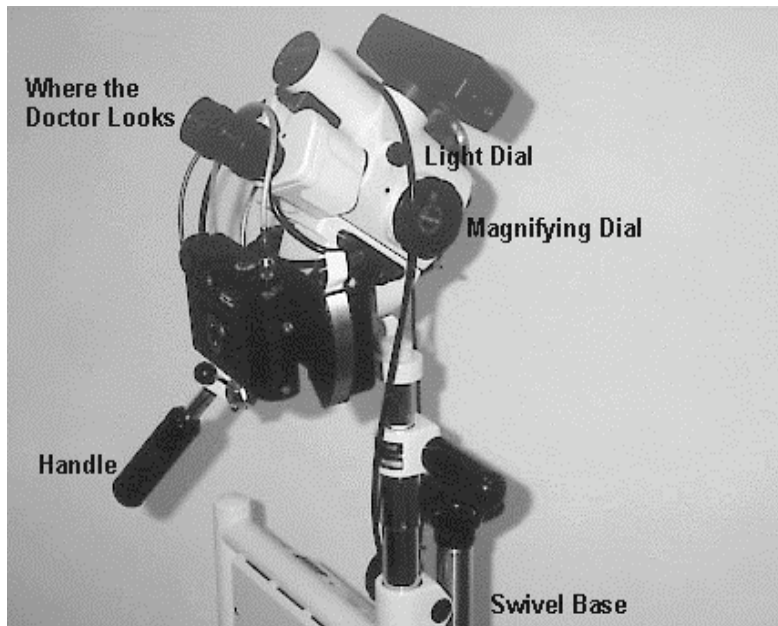
Pap Normal
ASCUS
LSIL

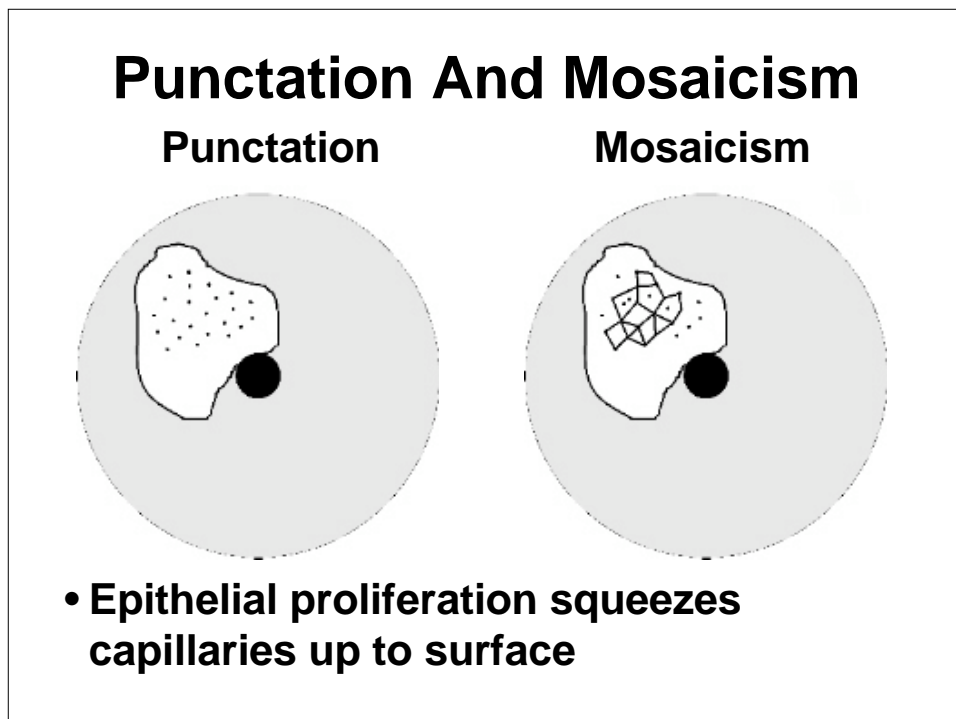
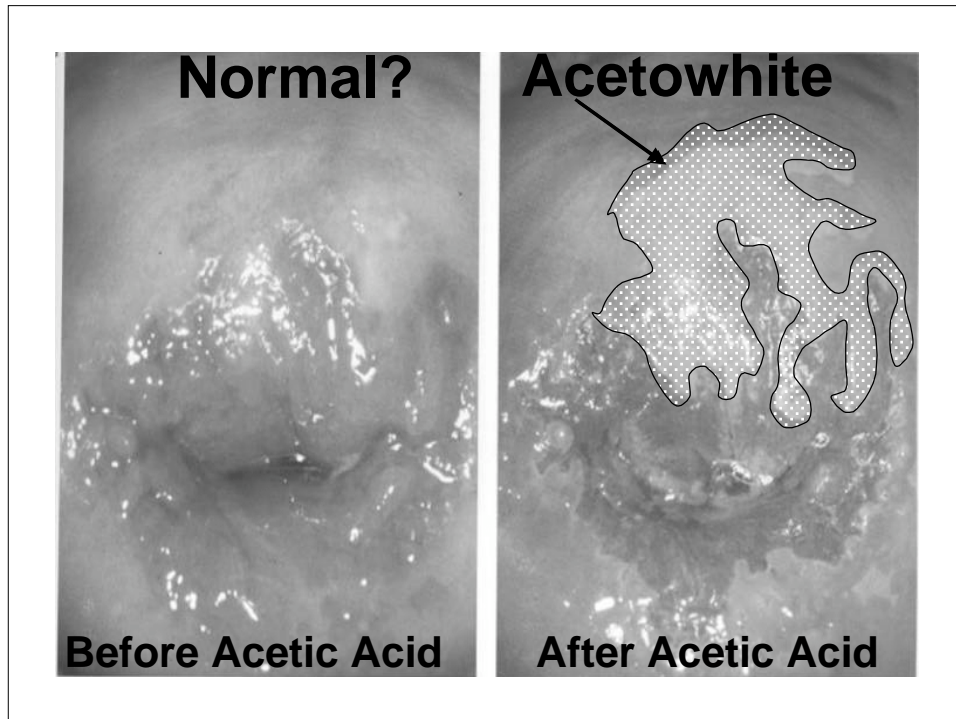
- Infection (HPV)
- No Neoplasia

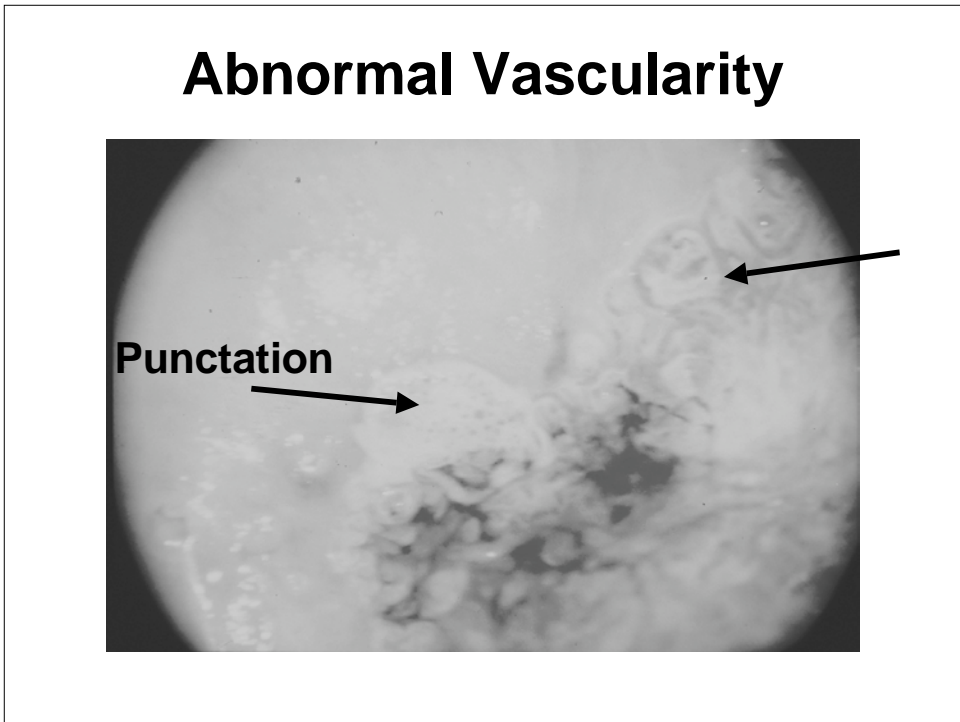
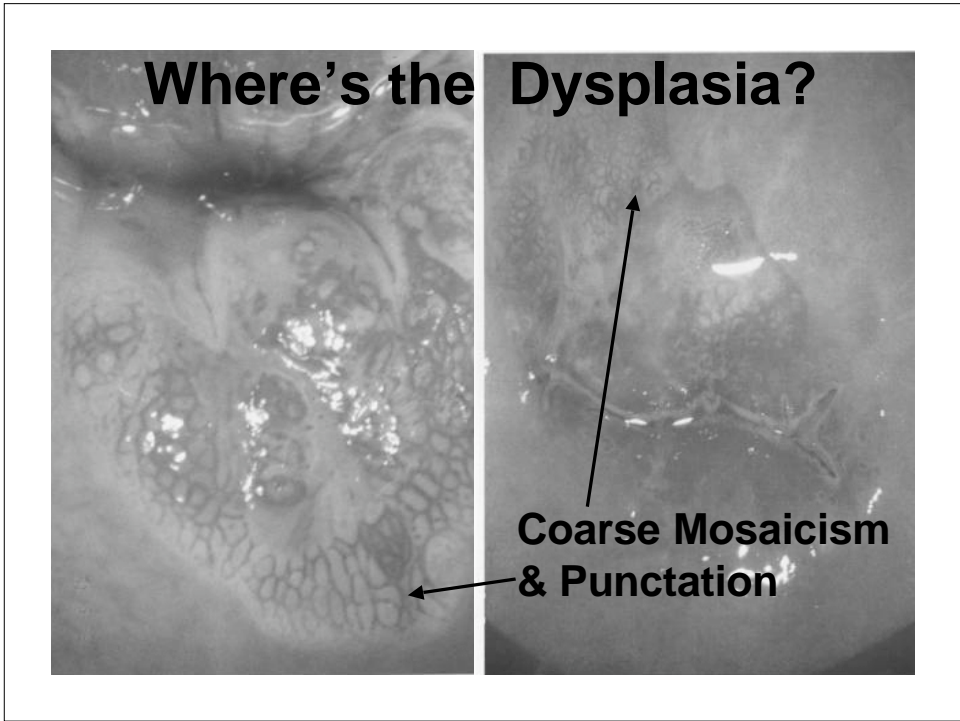
Normal
ASCUS
LSIL
HSIL

- Neoplasia
- Infection

ASCUS
LSIL
HSIL

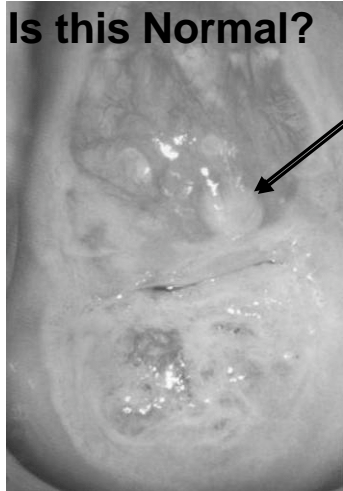




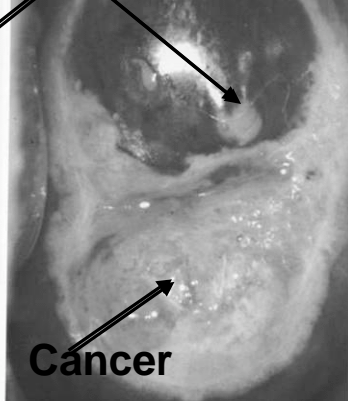


Lugol's

Is this Normal?



Nabothian Cyst



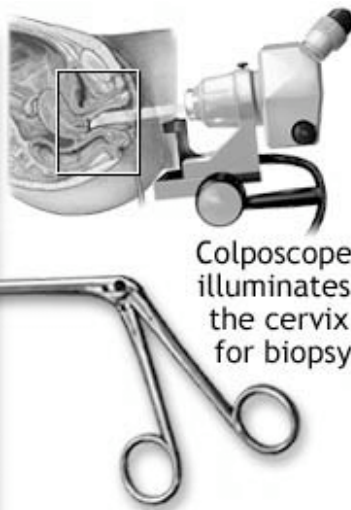
Lugol's Iodine Application

Tischler Biopsy Instrument





Biopsy forceps are used to sample the cervix



Colposcope illuminates the cervix for biopsy

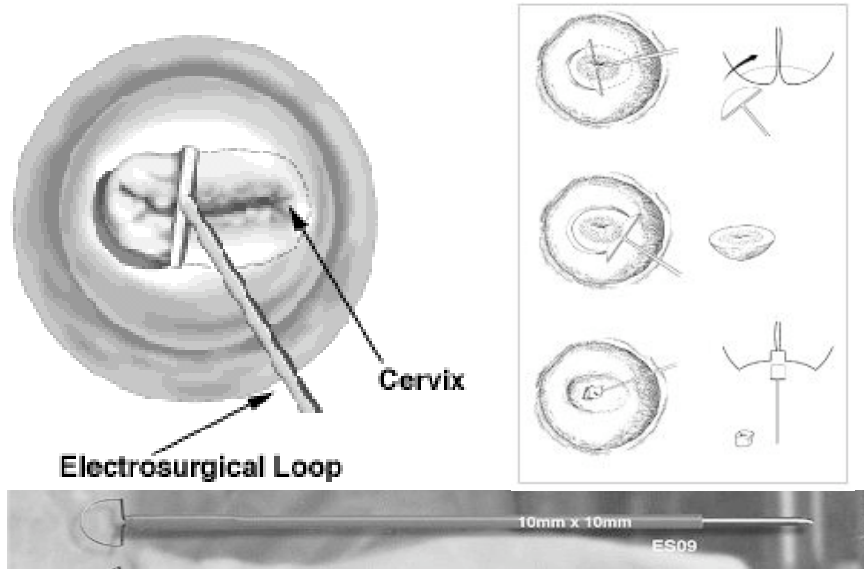
ADAM.

Cold cone biopsy:
a large area of tissue around the cervix is excised for examination



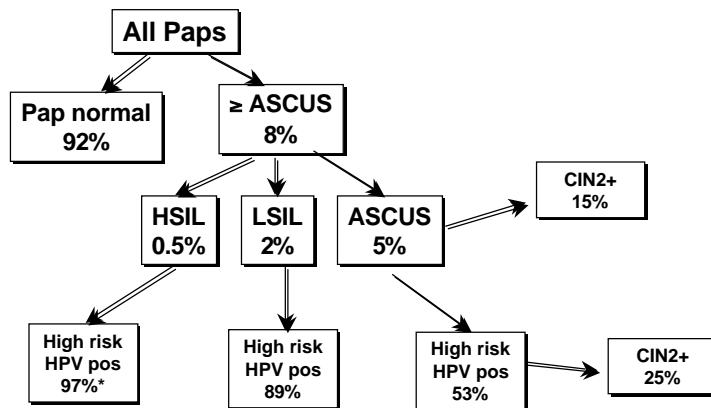
Cervix viewed through speculum with patient in lithotomy position

LEEP Diagram



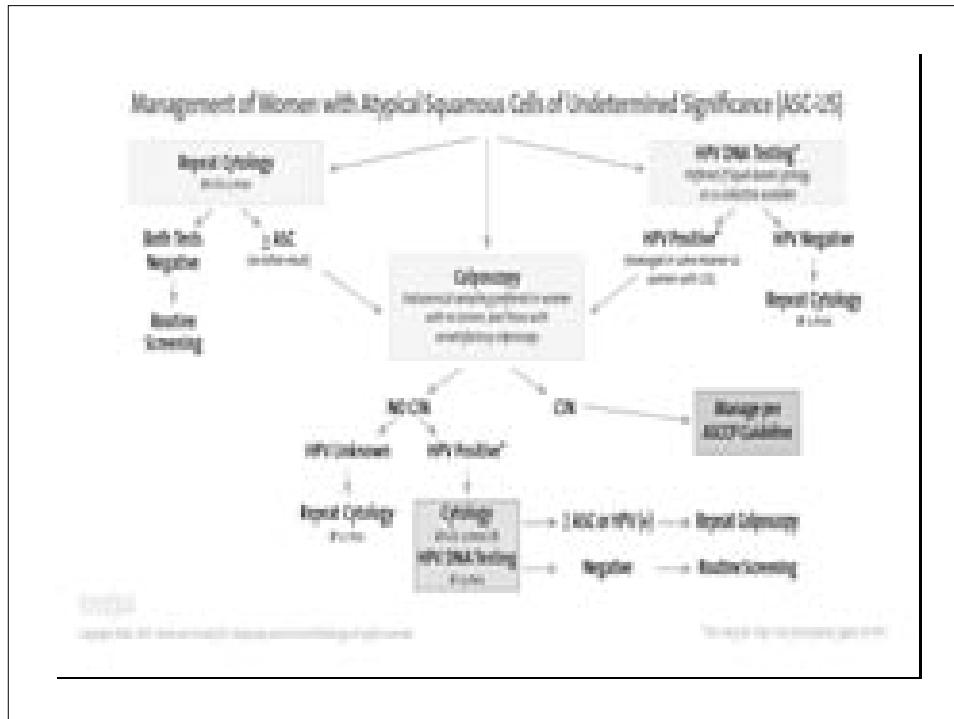
ASC-H Slide
LSIL Algorithm

HPV Testing- ALTS Distribution



*Missing or false neg values

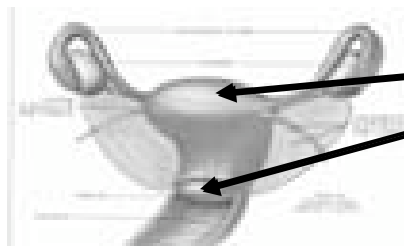
HPV Triage reduces
Colpo of ASCUS by 50%

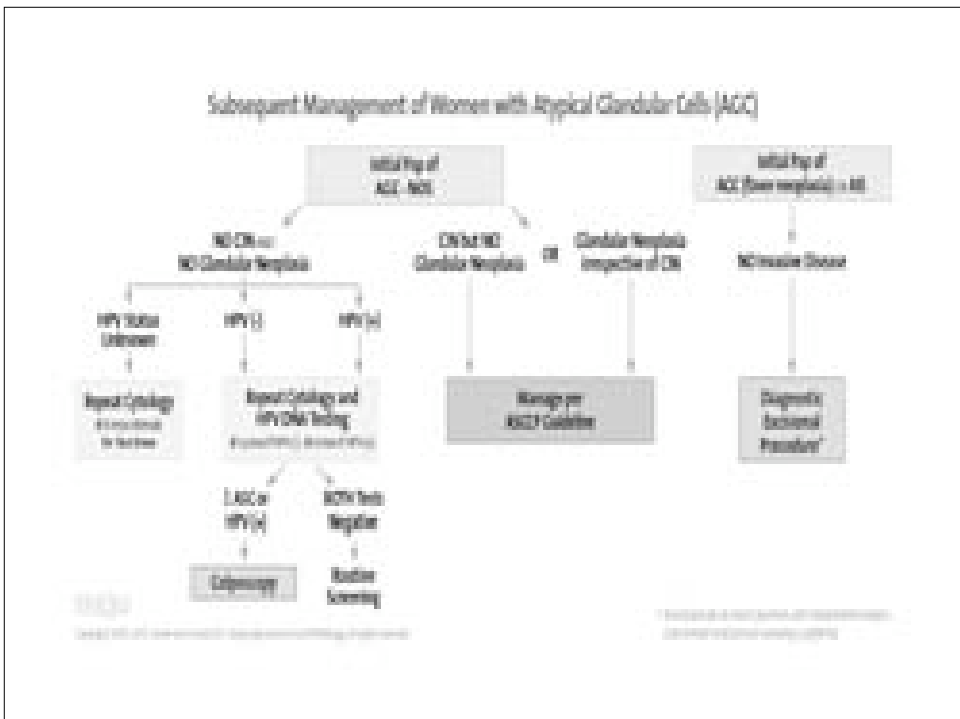
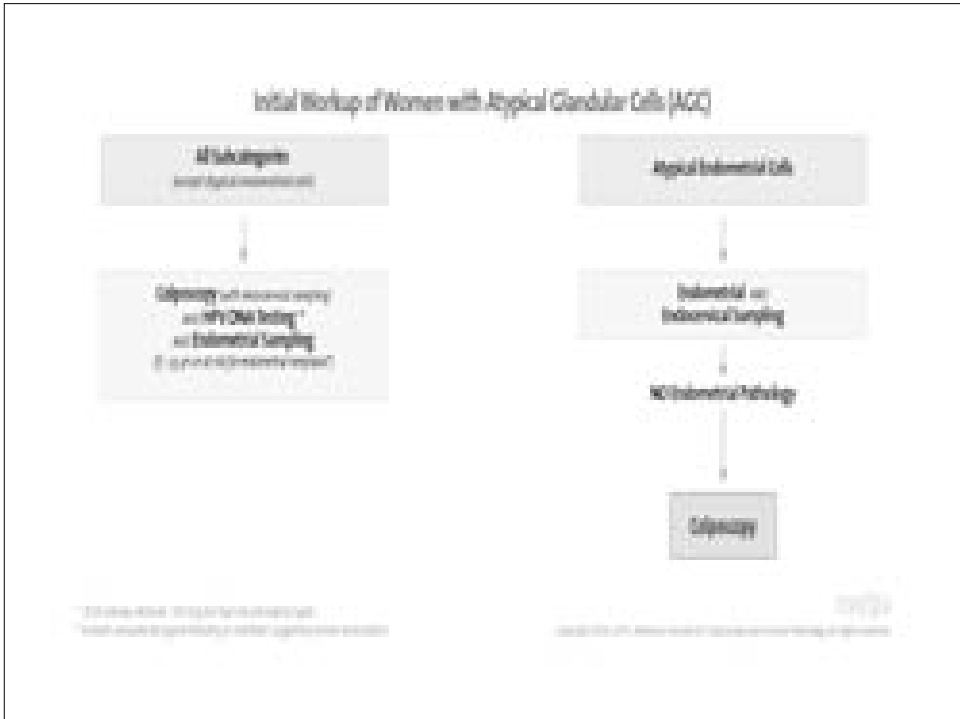


Atypical Glandular Cells of Undetermined Significance (AGUS)

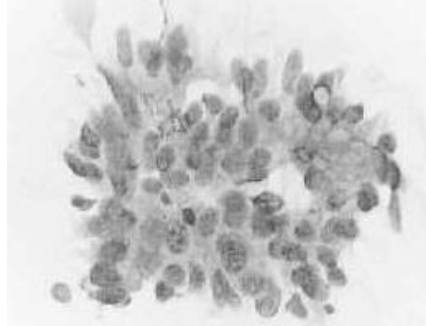
• Where are glandular cells?

- Endometrium
- Endocervix

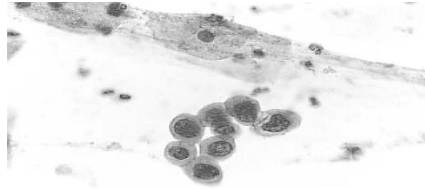




AGUS



AGUS



HSIL

**Difficult to differentiate HSIL from AGUS
on Pap**

Significance Of AGUS

Pap	Any HSIL (including squamous)	High Grade Glandular Lesion
AGUS Reactive	5-39%	1-8%
AGUS NOS	9-41%	0-15%
AGUS favor neoplasia	27-96%	10-93%

Management of Adolescent Women with Either Atypical Squamous Cells of Undetermined Significance (ASC-US) or Low-grade Squamous Intraepithelial Lesion (LSIL)

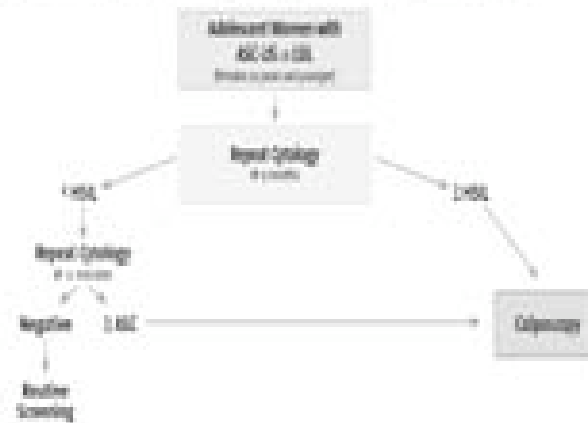


FIGURE 2

Copyright © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins

Management of Women with Atypical Squamous Cells Cannot Exclude High-grade SIL (ASC-H)

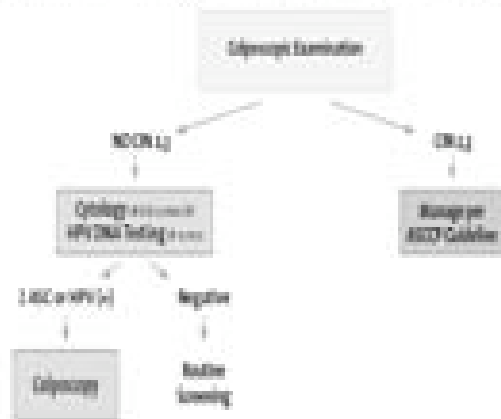
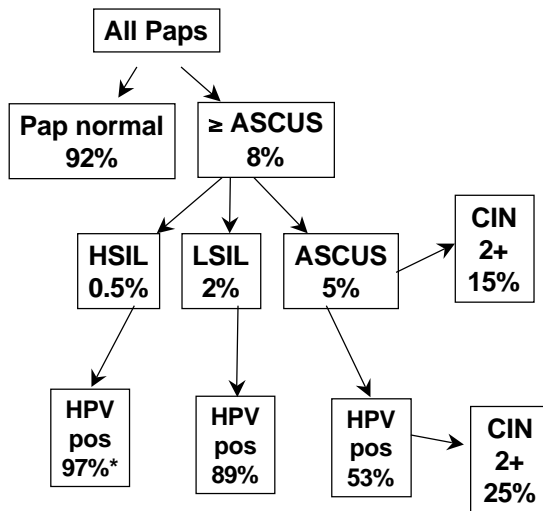


FIGURE 3

Copyright © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins

ASC-H

- ASC- Can't rule out high grade lesion
 - 87% High-risk HPV positive
 - 30% CIN2 or CIN3 on biopsy

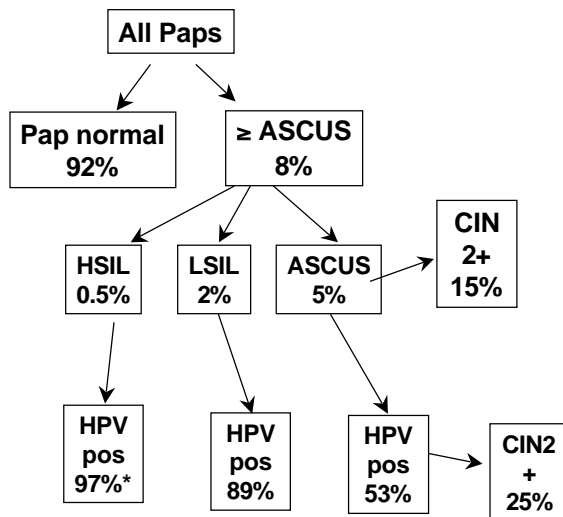


- Immediate Colposcopy

See www.asccp.org

LSIL

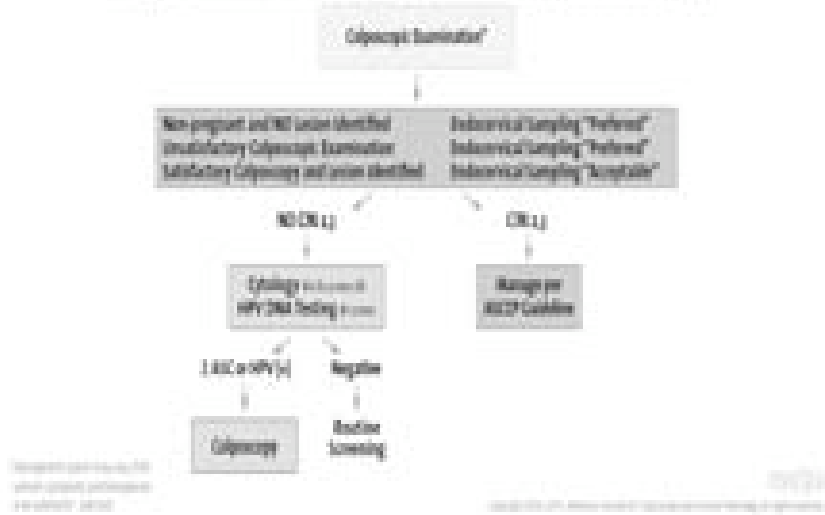
- Almost all High Risk HPV positive
 - HPV testing useless
- 30% CIN2/3



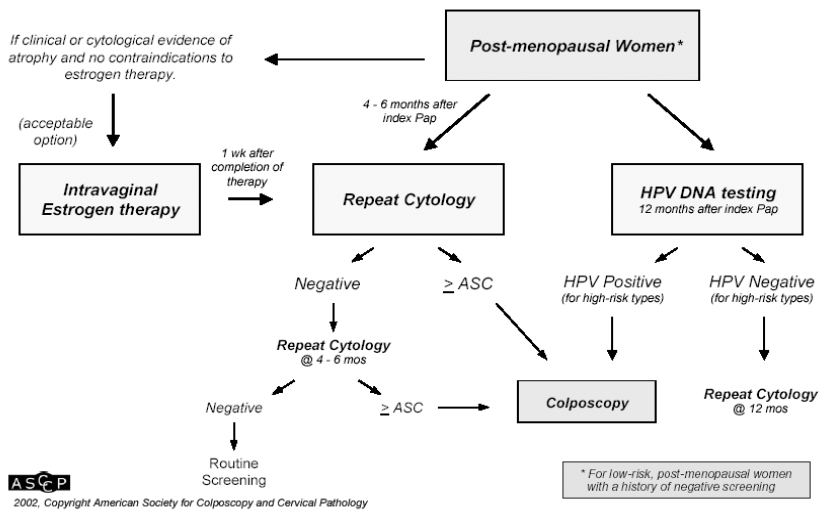
- Immediate Colpo

See www.asccp.org

Management of Women with Low-grade Squamous Intraepithelial Lesion (LSIL)*



Management of Women with Low-grade Squamous Intraepithelial Lesions In Special Circumstances



Management of Pregnant Women with Low-grade Squamous Intraepithelial Lesion (LSI)

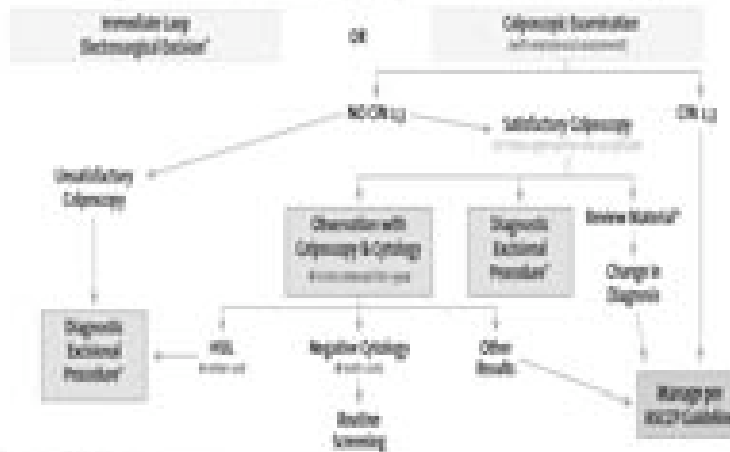


ASCC3

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Management of Women with High-grade Squamous Intraepithelial Lesion (HSIL)[†]



* ASC[†] Guidelines preferred if available

[†] ASC = American Society for Colposcopy and Cervical Pathology

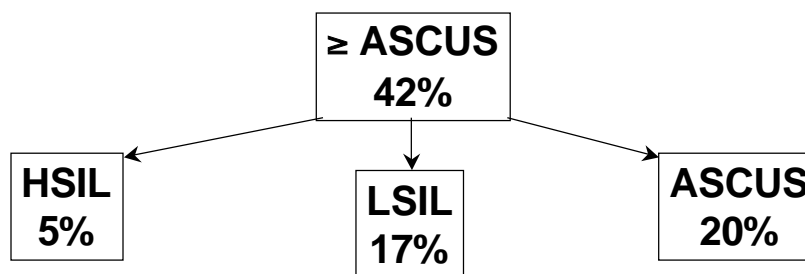
† Management of pregnant women with cervical intraepithelial neoplasia is covered

ASCC3

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HIV Patients

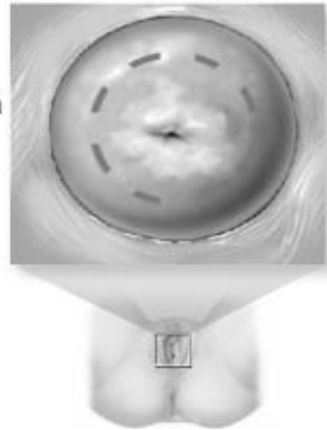
- Pap every 6 months
- Colpo for all abnormalities \geq ASCUS
- Higher risk for severe dysplasia and cancer
- More likely to have abnormal cytology



CIN2 or CIN3

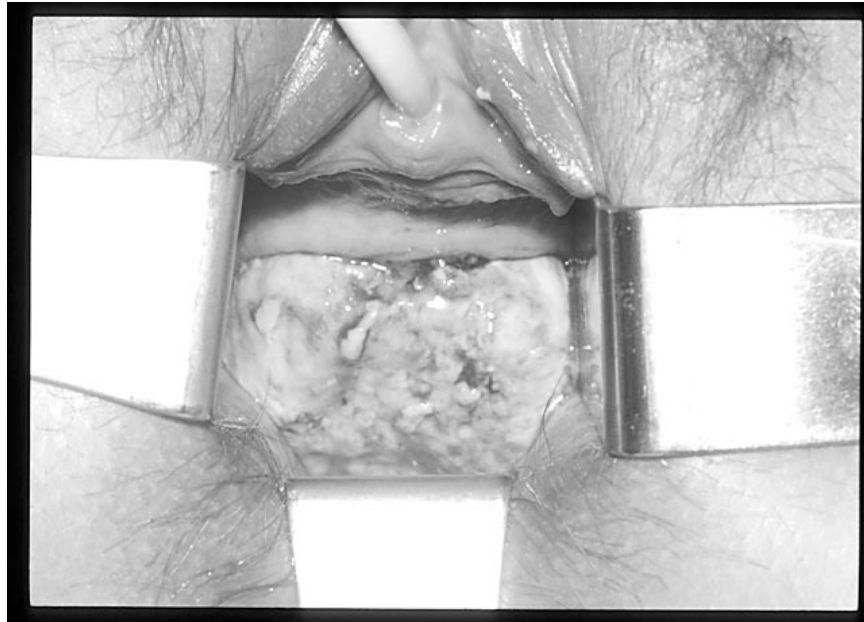
BX	Regress	Persist	CIN 3	Cancer
CIN1	57%	32%	11%	<1%
CIN2	43%	35%	22%	5%
CIN3	32%	56%	N/A	12%

Compressed nitrogen gas flows through a cryo probe making the metal cold enough to freeze and destroy the abnormal cervical tissue

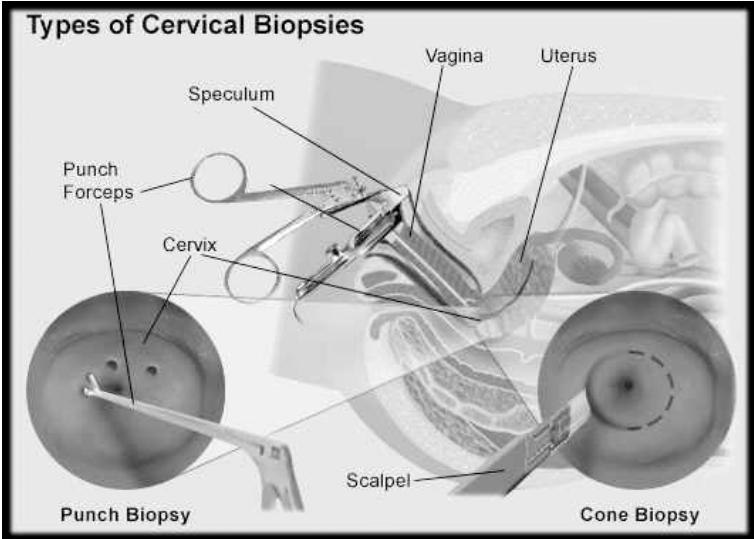


Cervix as viewed through speculum with patient in lithotomy position

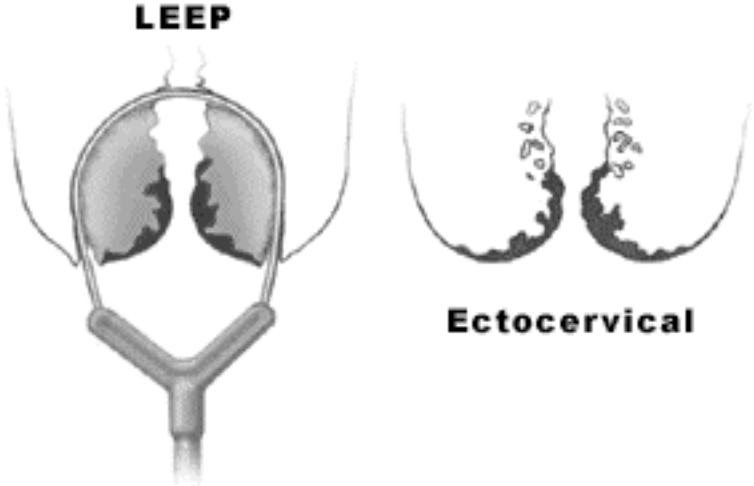
ADAM.

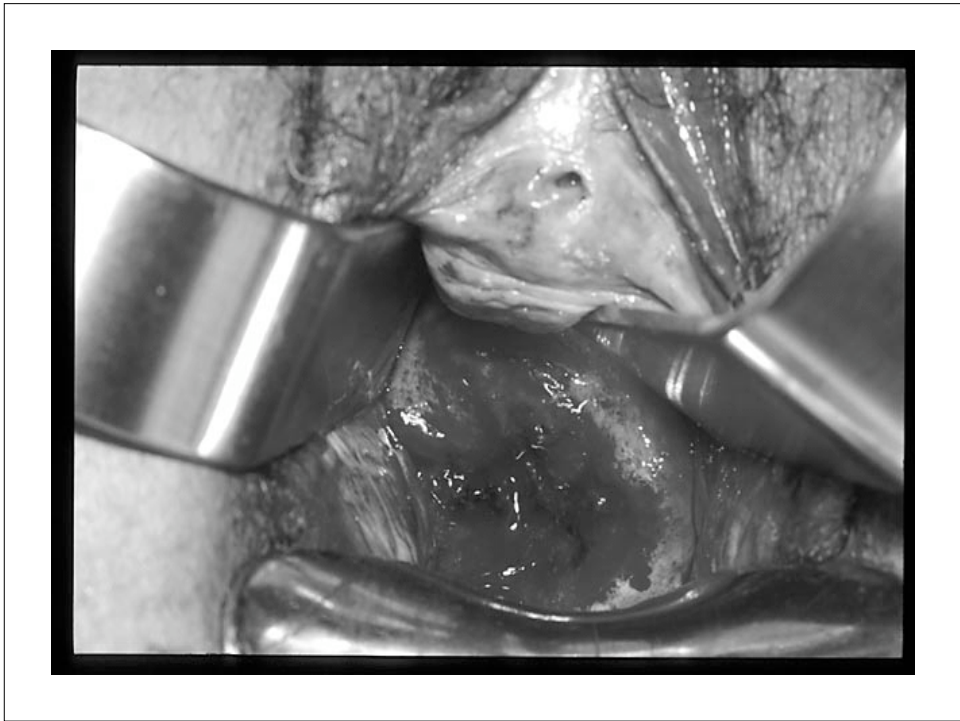


Diagnosis

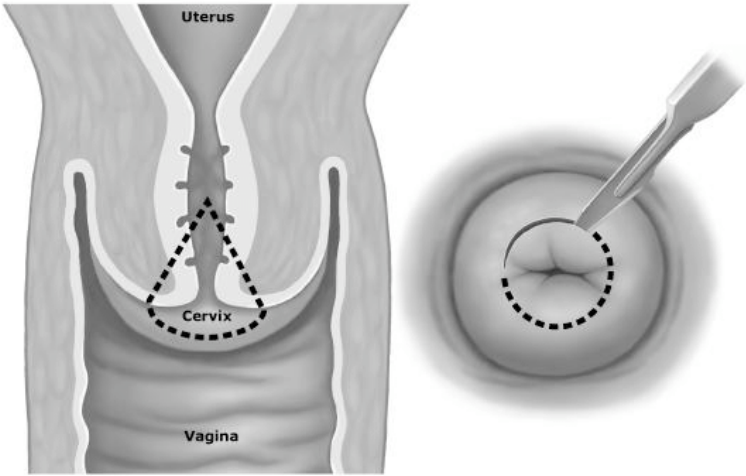


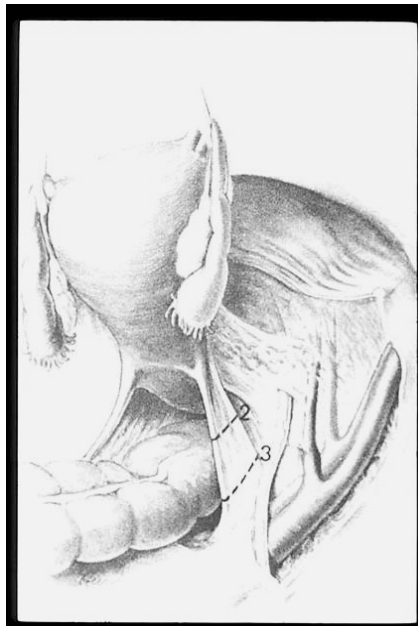
LEEP

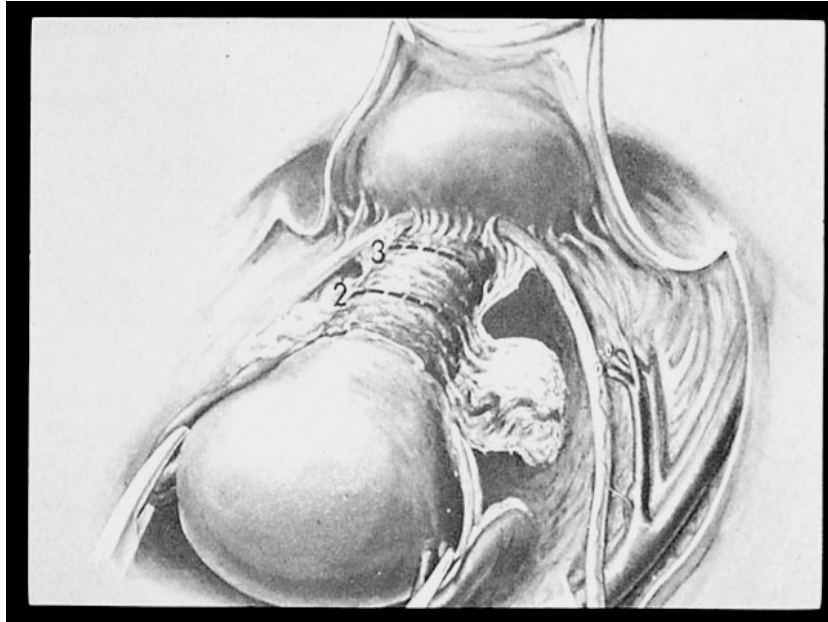




Cervical Conization







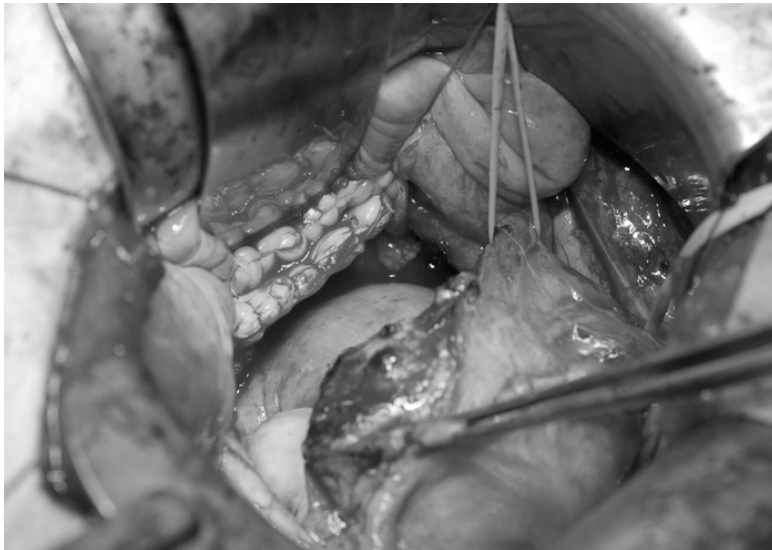
Radical Trachelectomy



Radical Trachelectomy



Radical Trachelectomy



Radical Trachelectomy



IB1 VS IB2 CERVICAL CANCER

COMPLICATIONS of Radical Hysterectomy

	IB1 n (%)	IB2 n (%)
None	91 (50.3)	25 (52.1)
Thromboembolic event	9 (5.0)	1 (2.1)
Medical minor	78 (43.1)	19 (39.6)
Surgical major	1 (0.5)	3 (6.2)
Other major	2 (1.1)	0 (0.0)

p = 0.0775 (NS)

Finan MA et al, Gynecol Oncol 1996

Locally Advanced Cervical Cancer

	Bulky Tumor > 4 cm	Smaller Tumor < 4 cm
Nodal metastases	80%	16%
Local recurrences	40%	5 %
Distant metastases	50%	1%

Chung, et al: Am J Obstet Gynecol, 138, 1980

Cervical Cancer

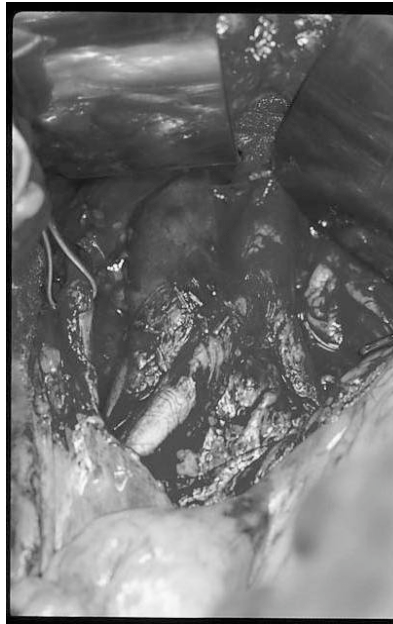
Pelvic Nodal Involvement

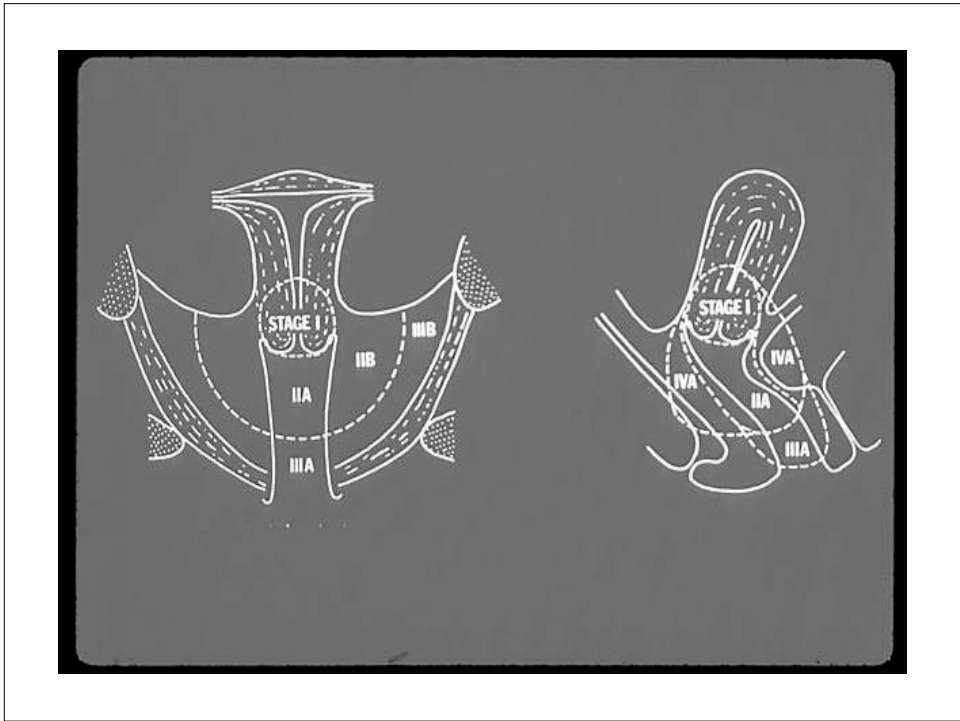
Stage	Patients% + Pelvic Nodes	
IB	1160	20
IIA	90	26
IIB	341	36
III	96	43
IVA	23	55

Cervical Cancer

Para-aortic Nodes

Stage	Patients	% + Para-aortic Nodes
IB	1579	4
IIA	212	11
IIB	602	20
III	546	27
IVA	80	31





Cervical Cancer

Nodal Metastases (cont.)

Risk Groups

Number of <u>Nodes</u>	<u>Lesion size</u>		
	<u>< 1 cm</u>	<u>1.1 - 4 cm</u>	<u>> 4 cm</u>
≤ 2	LR	LIR	HIR
> 2	LIR	HIR	HR
		<u>10 yr survival</u>	<u>Postop XRT</u>
Low Risk (n=13)		92%	61%
Low Intermediate Risk (n=66)		70%	56%
High Intermediate Risk (n=66)		56%	50%
High Risk (n=20)		13%	85%

Alvarez RD, et al. Gynecol Oncol, 35: 130-135 (1989)

IB Cervical Cancer

- 100 patients, Radical Hysterectomy, randomly selected
- Studied prognostic factors:

Histopathologic

Grade

Stromal Reaction

Depth of invasion

CLS

Character of Tumor - Stromal Border

Number of mitoses

Clinical

Age

Race

Lesion size

- Purpose was to define "risk groups" to classify patients

Gauthier P, et al. Obstet & Gynecol, 66: 569 (1985)

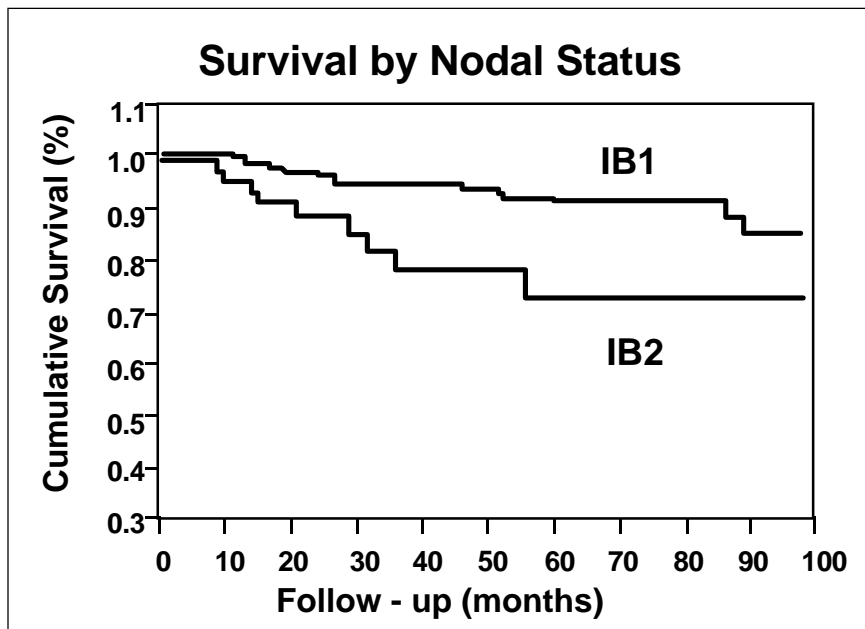
IB Cervical Cancer

3 risk groups identified:

	<u>Tumor diameter</u>	<u>Depth of invasion</u>
Low Risk:	< 2 cm	any depth
	2.1 - 3 cm	depth ≤ 1.5 cm
Intermediate Risk:	2.1 - 3 cm	> 1.5 cm
	> 3.0 cm	≤ 1.5 cm
High Risk:	> 3.0 cm	> 1.5 cm

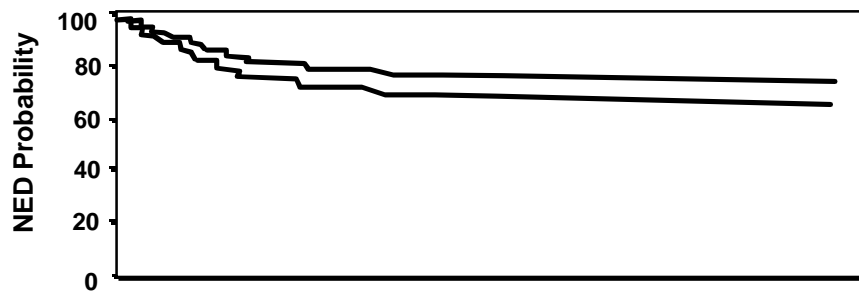
<u>Risk Group</u>	<u>Pos Nodes</u>	<u>Recurrence</u>	<u>5 yr %</u>
	(n)	(%)	survival
Low	75	20	8
Intermediate	14	29	36
High	11	36	64

Gauthier P, et al. Obstet & Gynecol, 66: 569 (1985) UAB, Birmingham



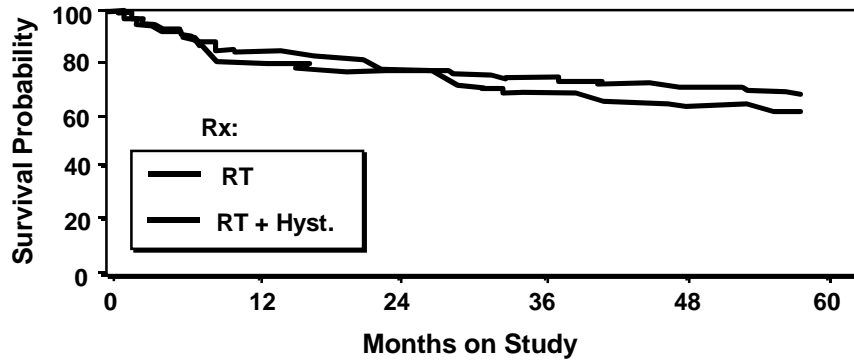
Finan MA, et al; Gynecol Oncol 1996

Progression-Free Interval



Keys, H et al, GOG, Abstr, SGO, 1997

Survival Time



Keys, H et al, GOG, Abstr, SGO, 1997

Cervical Cancer

Adenocarcinoma: Is it really worse?

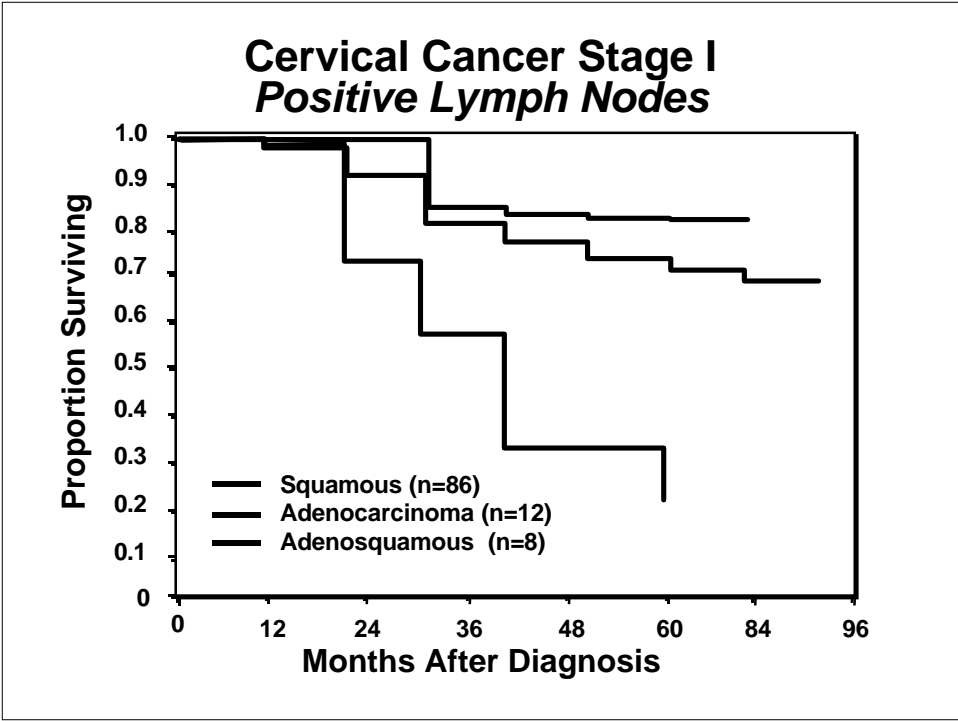
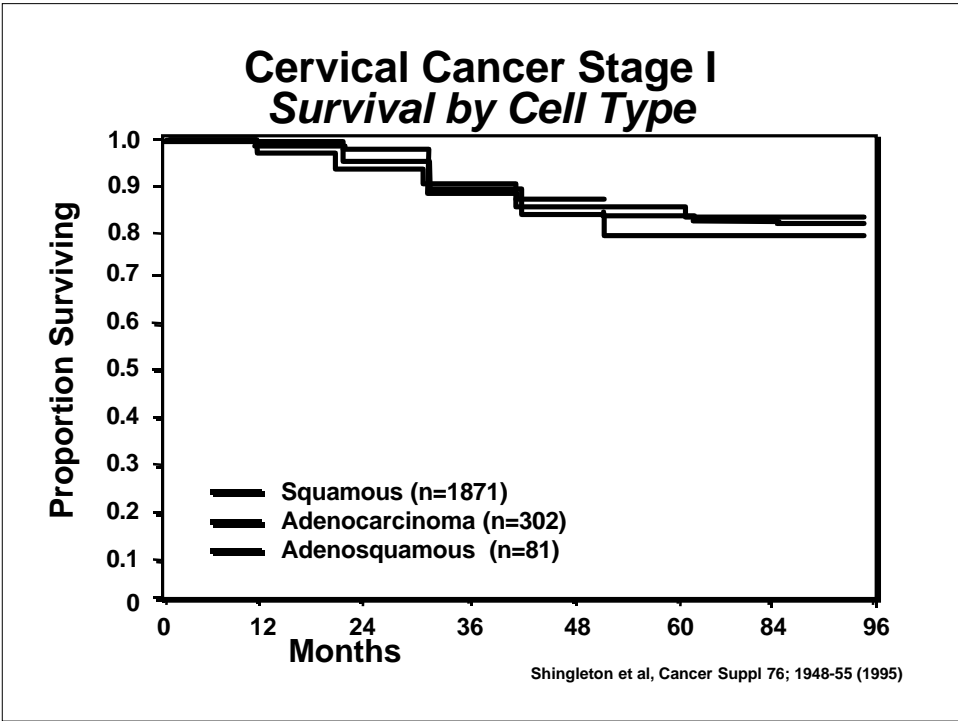
Stage IB analysis of survival by treatment:

5 year survival

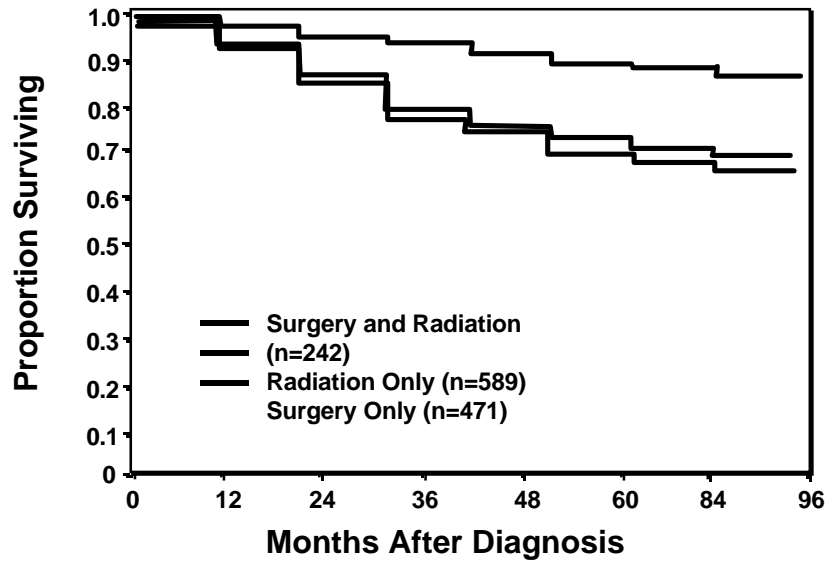
	<u>Surgery alone</u>	<u>Surgery & XRT</u>	<u>XRT alone</u>
Squamous cell	93%	73%	76%
Adenocarcinoma	95%	66%	71%
Adenosquamous	69%	87%	79%

- SCCa and Adenocarcinoma patients treated with Surgery alone had a significantly better survival than women treated with Surgery and XRT or XRT alone ($p < 0.001$).
- Adenosq patients had similar survival in all treatment groups ($p = 0.5$).

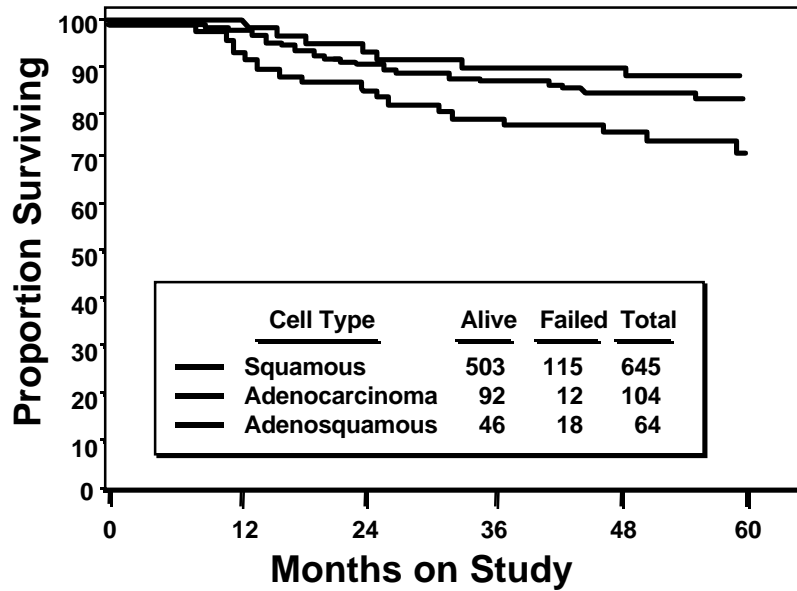
Shingleton HM, et al. Cancer Suppl, 76: 1948-1955 (1995)

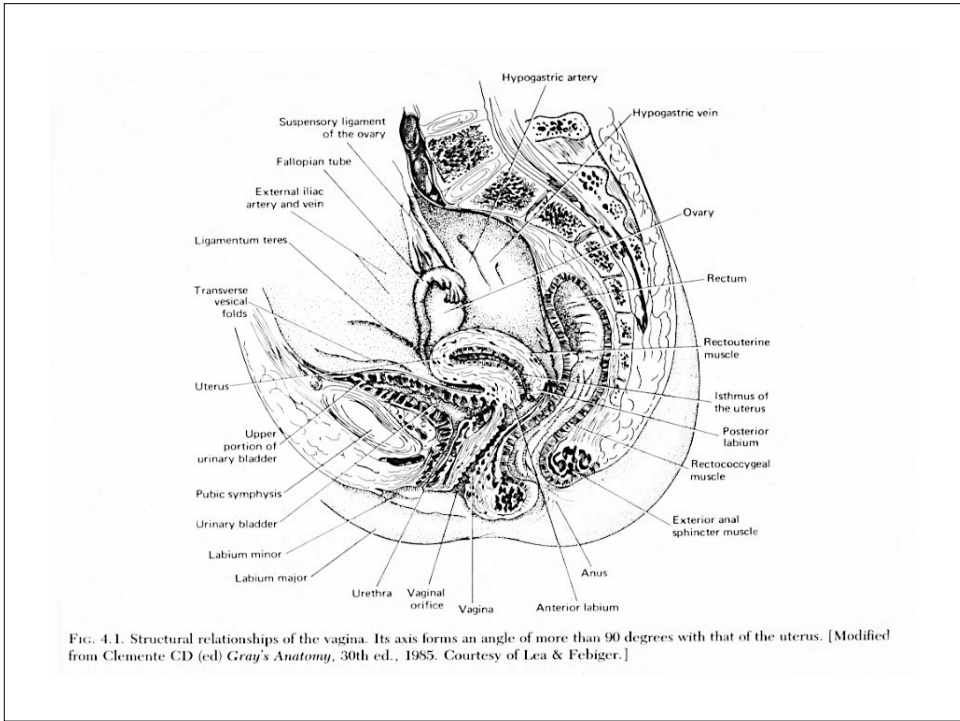


Squamous Carcinoma of Cervix Stage Ib *Survival by Treatment*



Cervical Cancer- Survival by Cell Type





Brachytherapy For Cervical Cancer

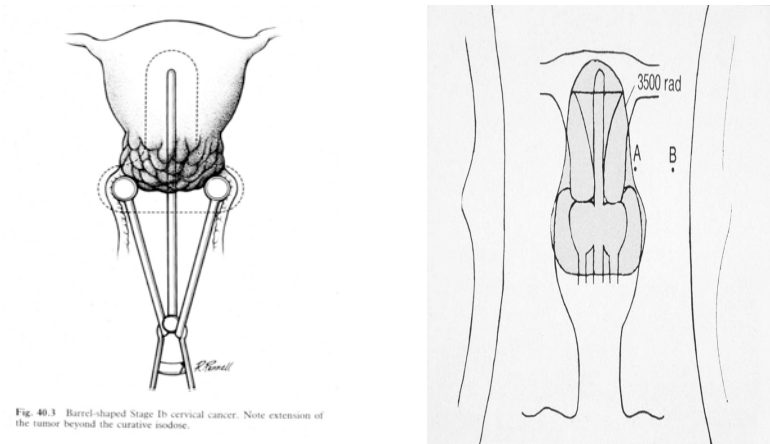
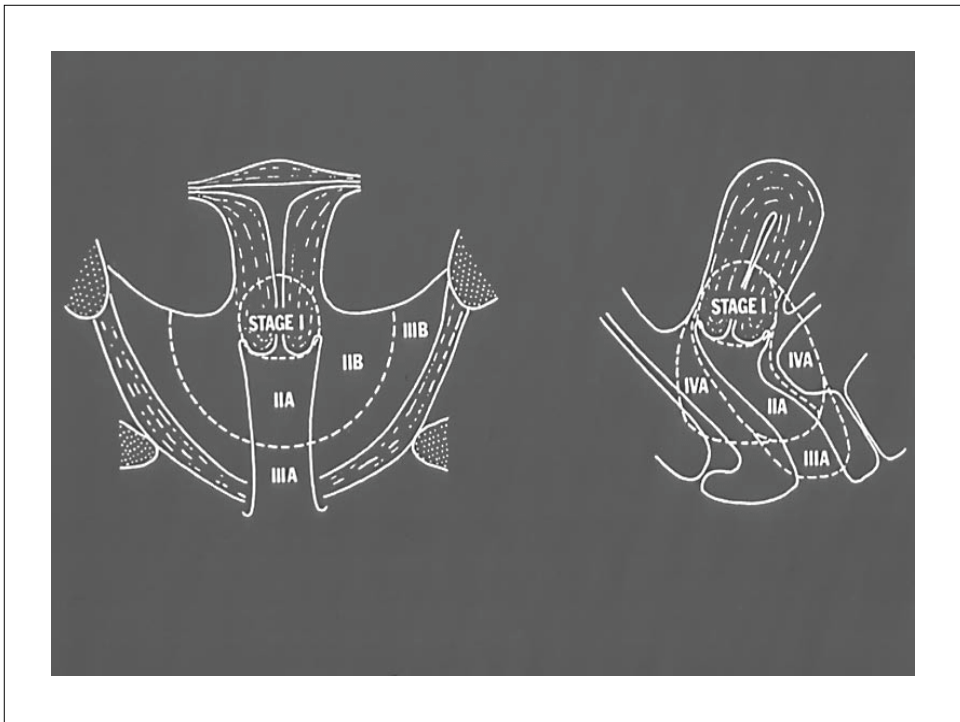
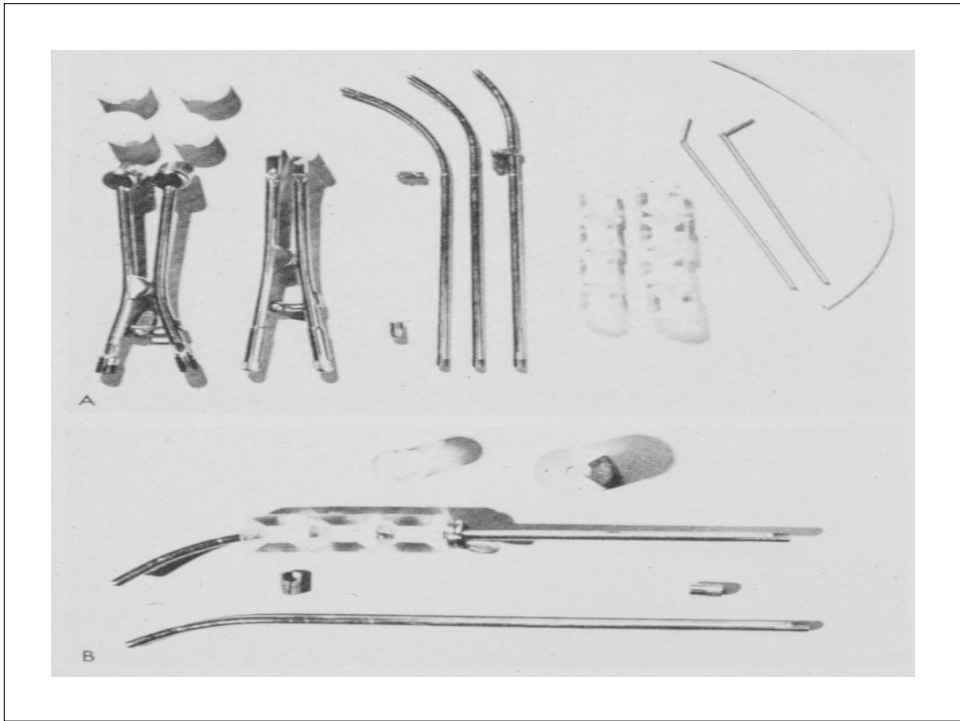


Fig. 40.3 Barrel-shaped Stage Ib cervical cancer. Note extension of the tumor beyond the curative nodose.

A = 2cm above os & 2 cm lateral, B = 3 cm lateral to A



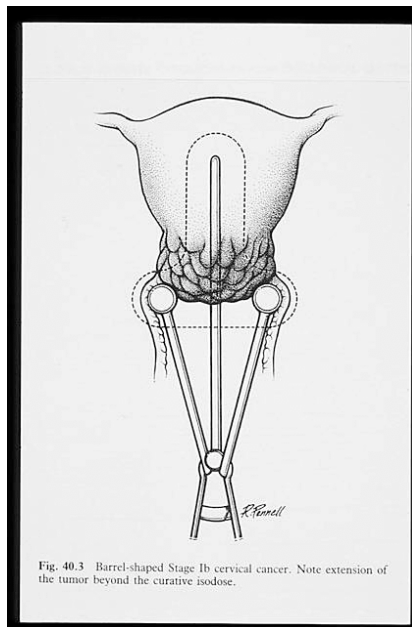
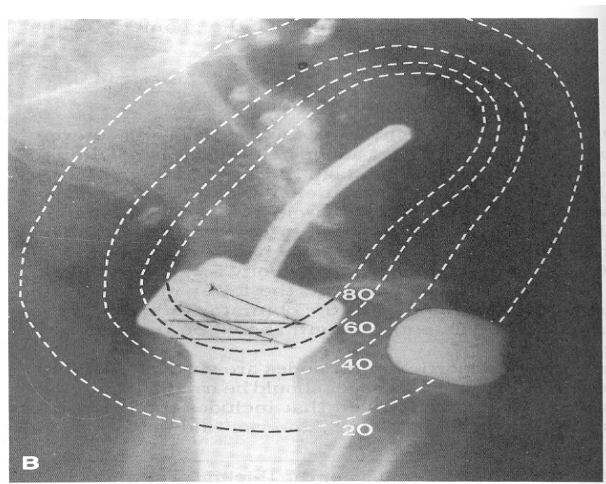
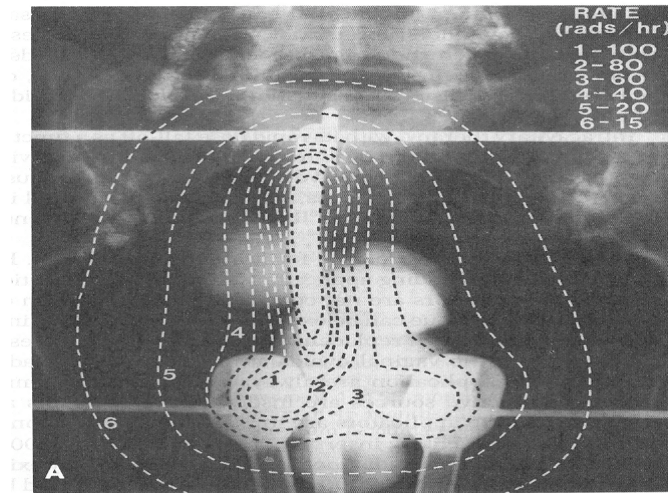


Fig. 40.3 Barrel-shaped Stage Ib cervical cancer. Note extension of the tumor beyond the curative isodose.

Rectal / Bladder Points



Dose Distribution



Future Programs:

Manage Your Stress

Before It Manages You

Thursday, October 23, 2008

2:00-4:00 p.m. Central Time

HIV Serology Update 2008

Tuesday, October 28, 2008

9:00-11:00 a.m. Central Time