THE SIGNIFICANCE OF PERITONEAL CYTOLOGY IN ENDOMETRIAL CANCER

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subspec.

Kosovo

Uterus:

- At first sight common organ, small as such for the individual, but so important for humanity.
  - Author

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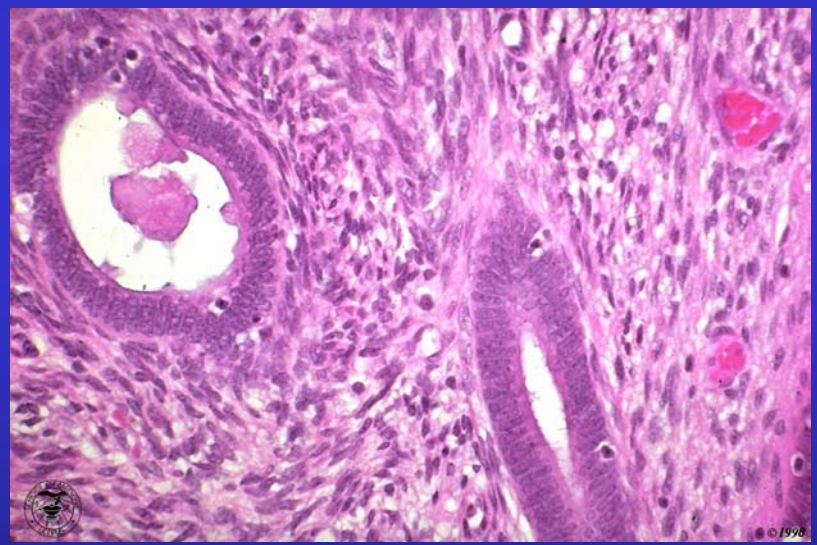
Endometrium



- The endometrium is the lining of the uterus.

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INTRODUCTION

- Endometrial carcinoma represents one of the most common malignancies in the female genital tract all over the world. Its occurrence has increased worldwide, due to increasing longevity in women.

- The International Federation of Gynecology and Obstetrics (FIGO) in 1988 adopted the surgical staging system for patients with this invasive, very serious disease .

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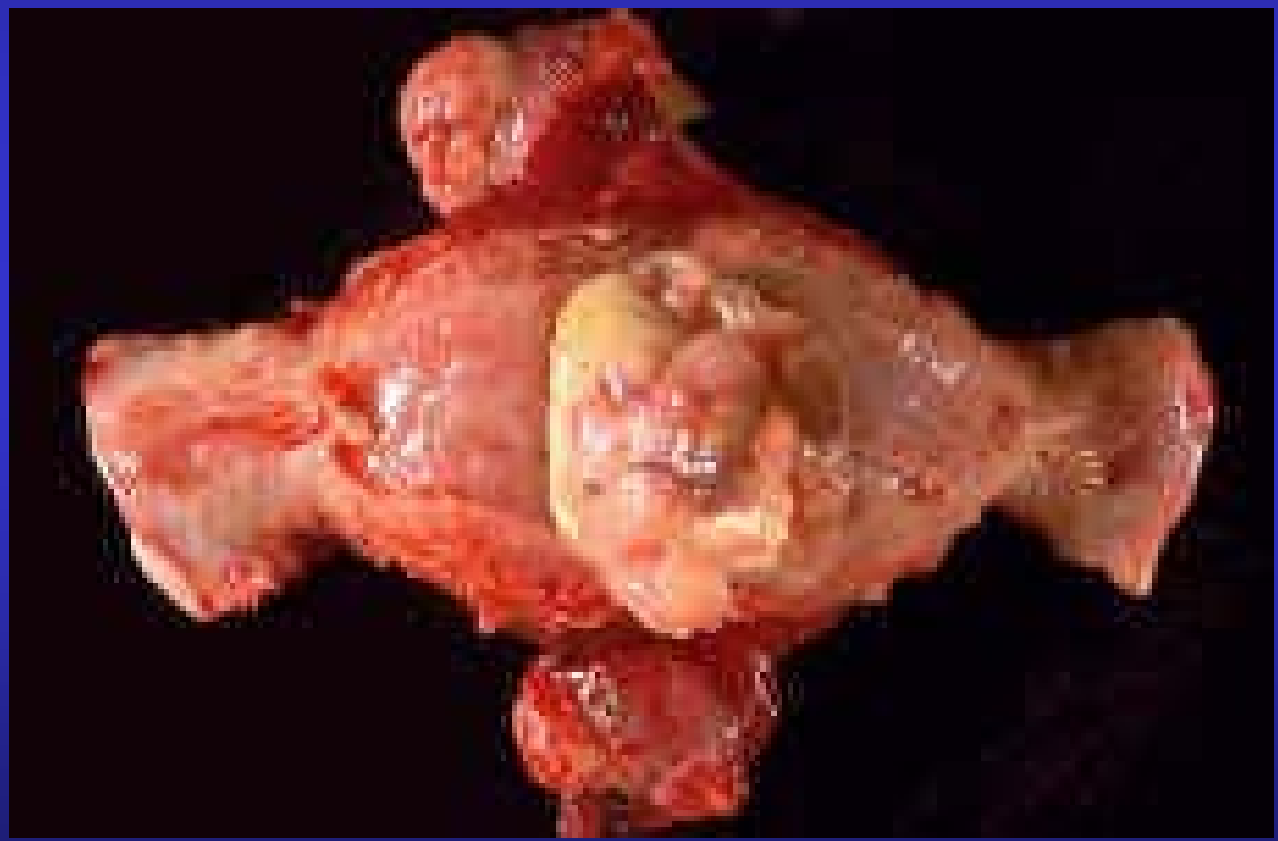
Endometrial cancer



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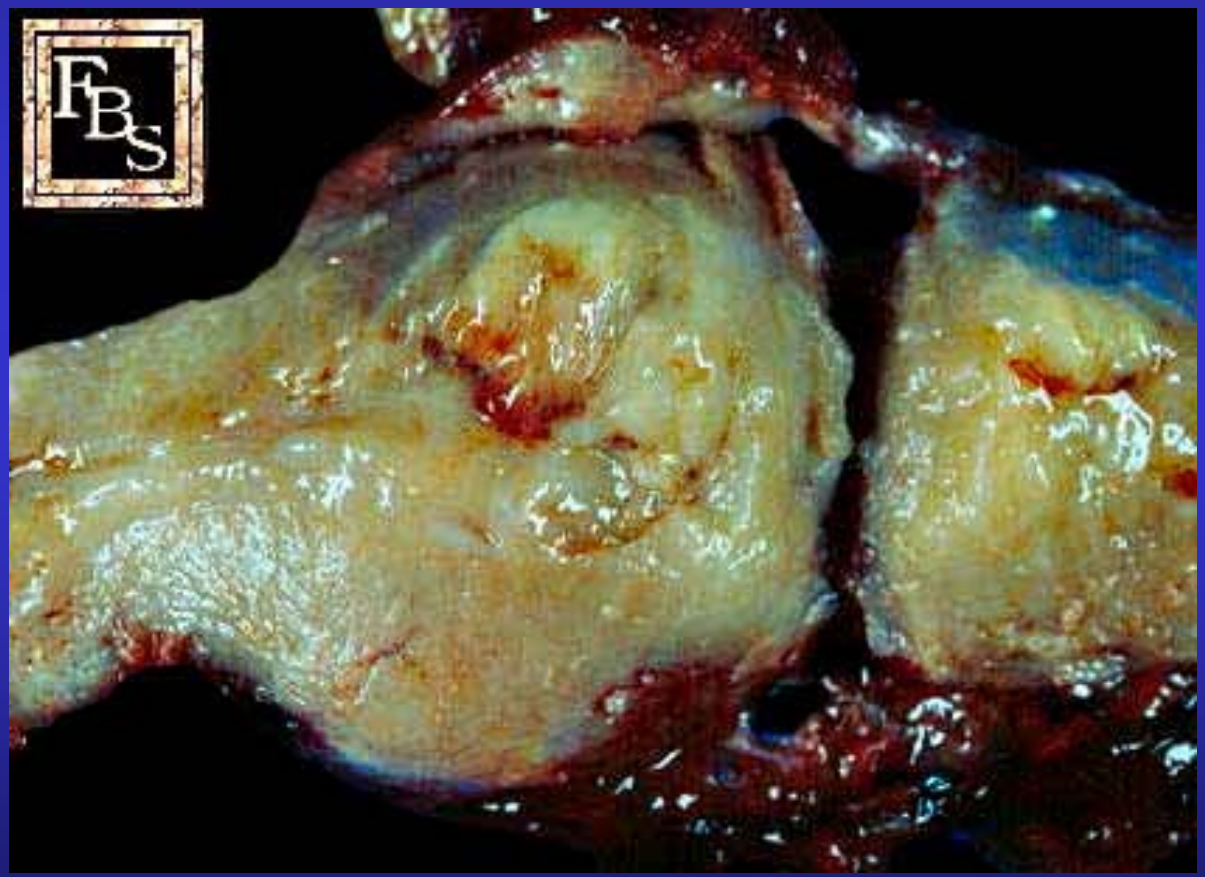
Endometrial cancer



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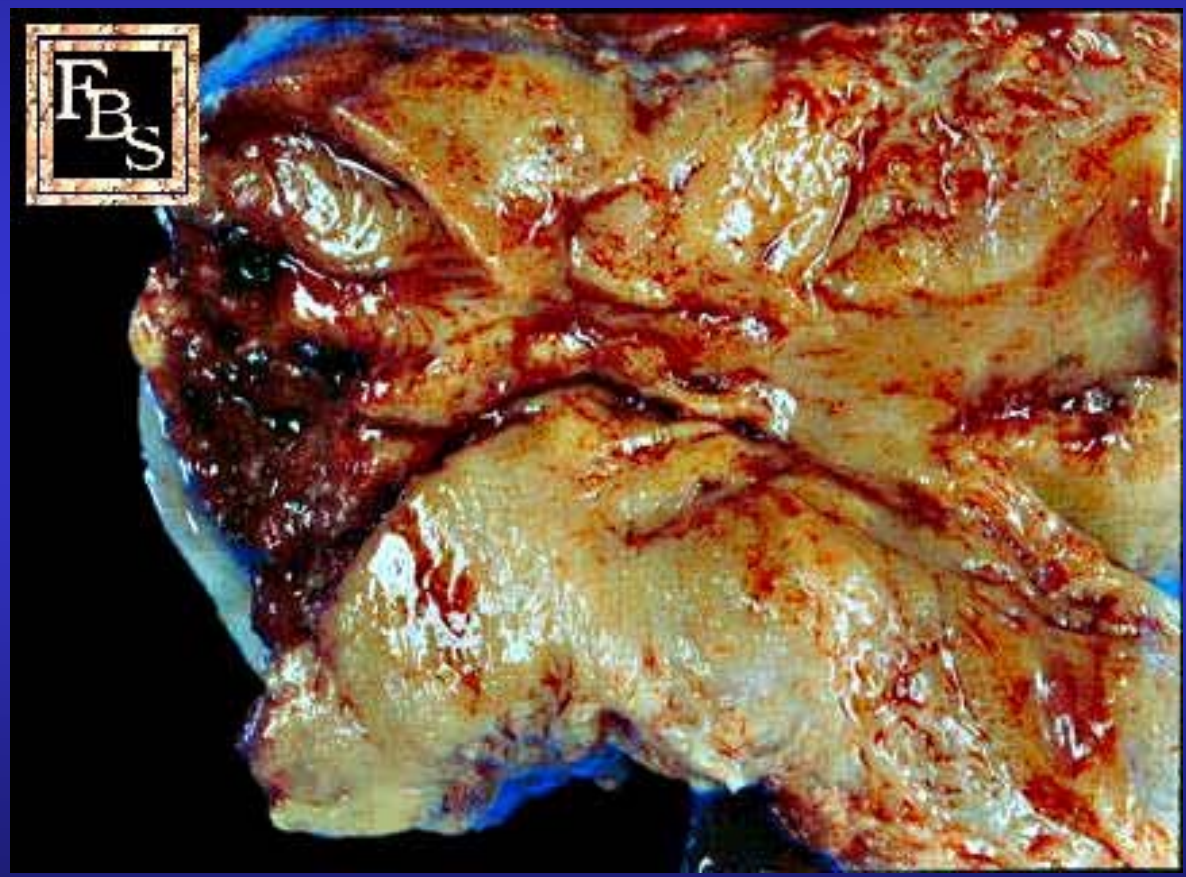

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INTRODUCTION

Peritoneal cytology was introduced first in 1956 by Keetle and Elkins to assess the spread of ovarian carcinoma.

However, malignant cells were first identified in the ascites of patients with gynecologic neoplasm in 1882.

First reports of the presence of malignant cells in the peritoneal washings in patients with endometrial cancer can be dated from 1961 by Morton et all.

Today, obtaining peritoneal washings is an accepted part of the evaluation of patients with endometrial carcinoma.

OBJECTIVE

- To review the literature on the prognostic significance of peritoneal cytology in endometrial cancer

MATERIALS

- Studies included women with endometrial cancer of all stages.

- Peritoneal cytology was correlated with the staging classification and with the prognosis of endometrial carcinoma.

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METHODS

- Literature search using a computerized Medline search to identify relevant literature
- The search was restricted to literature published between 1980-2001

Table 1 Incidence of positive peritoneal cytology in stage I

Author	Year	No. of patients	Incidence % (+cyto)
Keettel and Pixley	1958	39	5 (12.8)
Creasman et al.	1981	342	49 (14.3)
Szpak et al.	1981	54	12 (22.2)
Burell et al	1982	172	5 (2.9)
Yazigi et al.	1983	93	10 (10.7)
Boronow et al.	1984	171	26 (15.2)
Ide	1984	94	28 (29.8)
Hernandez et al.	1985	73	8 (11.0)
Kennedy et al	1987	144	8 (5.9)
Creasman et al.	1987	621	76 (12.0)
Harouny et al	1987	276	47 (17.1)
Mazurka et al	1988	253	16 (6.3)
Lurain et al.	1988	157	30 (19.0)
Imachi et al.	1988	35	5 (14.0)
Konski	1988	127	14 (11.0)
Turner et al.	1989	567	28 (4.9)
Total		3218	367 (11.4)

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Table 2.The incidence of positive peritoneal cytology in patients with endometrial cancer(all stages)

Author	Year of publ.	No of patien.	Incidence (+ cyto)	Stage I	Stage II	Stage III	Stage IV
Turner et al.	1989	565	28 (4.9)	a, b			
Zuna et al.	1996	135	17 (12.6)	+			
Grimshaw et al.	1990	381	24 (6.3)	+			
Jones et al.	1991	48	3 (6.0)	+	+	+	
Fung Kee et al.	1991	44	12 (27.3)	+		+	
Kadar et al.	1992	254	19 (7.5)				
Kadar et al.	1992	269	34 (12.6)	+	+		
Eltabbakh et al.	1997	332	29 (8.7)	+			
Kashimura et al.	1997	303	44 (15.0)	+	+	+	+
Connell et al.	1999	40	16 (40.0)			+	
Fukuda et al.	1999	99	8 (8.1)	+	+	+	+
Gu et al.	2000	284	27 (9.5)	+	+	+	+
Obermar et al.	2000	113	10 (8.8)	a, b			
Benevolo et al.	2000	182	27 (14.8)				
Luo et al.	2001	115	18 (15.7)				
Zerbe et al.	2000	222	21 (9.5)				
Takeshima et al.	2001	534	119 (22.3)				
Sonda et al.	2001	377	21 (5.57)				
Total		4297	477 (11.1)				

Table 3 Correlation of histologic grade and malignant cytology

Author	Year of publ.	Grade 1	Grade 2	Grade 3	Significance (p value)
Creasman et al.	1981	8 / 74	15 / 63	3 / 30	NS
Szpak et al.	1981	5 / 30	5/ 18	2/ 6	NS
Yazigi et al.	1983	7/66	1/ 15	2/ 12	NS
Hernandez et al	1985	4/ 32	1/13	3/11	NS
Creasman et al.	1987	13/ 23	5/ 23	5/23	NS
Kennedy et al.	1987	1/56	3/62	4/26	$P < 0.05$
Harouny et al.	1988	10/104	18/103	13/41	$P < 0.01$
Imachi et al.	1988	4 / 28	8 / 22	2 / 11	NS
Konski et al.	1988	6 / 70	10 /54	3 / 10	NS
Mazurka et al.	1988	6/ 119	6/ 98	4/ 31	NS
Lurain et al.	1988	11/ 83	7/ 36	11/32	$P < 0.05$
Turner et al.	1989	7/ 169	14/ 255	6/ 81	NS
Kadar et al.	1992	11/34	9/34	14/34	$P < 0.05$
Zerbe et al.	2000	6/21	8/21	7/21	$P = 0.05$
Total		99 / 909	110 / 817	79 / 369	
		(11%)	(13.5%)	(21.4%)	

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Correlation of histologic grade and malignant cytology

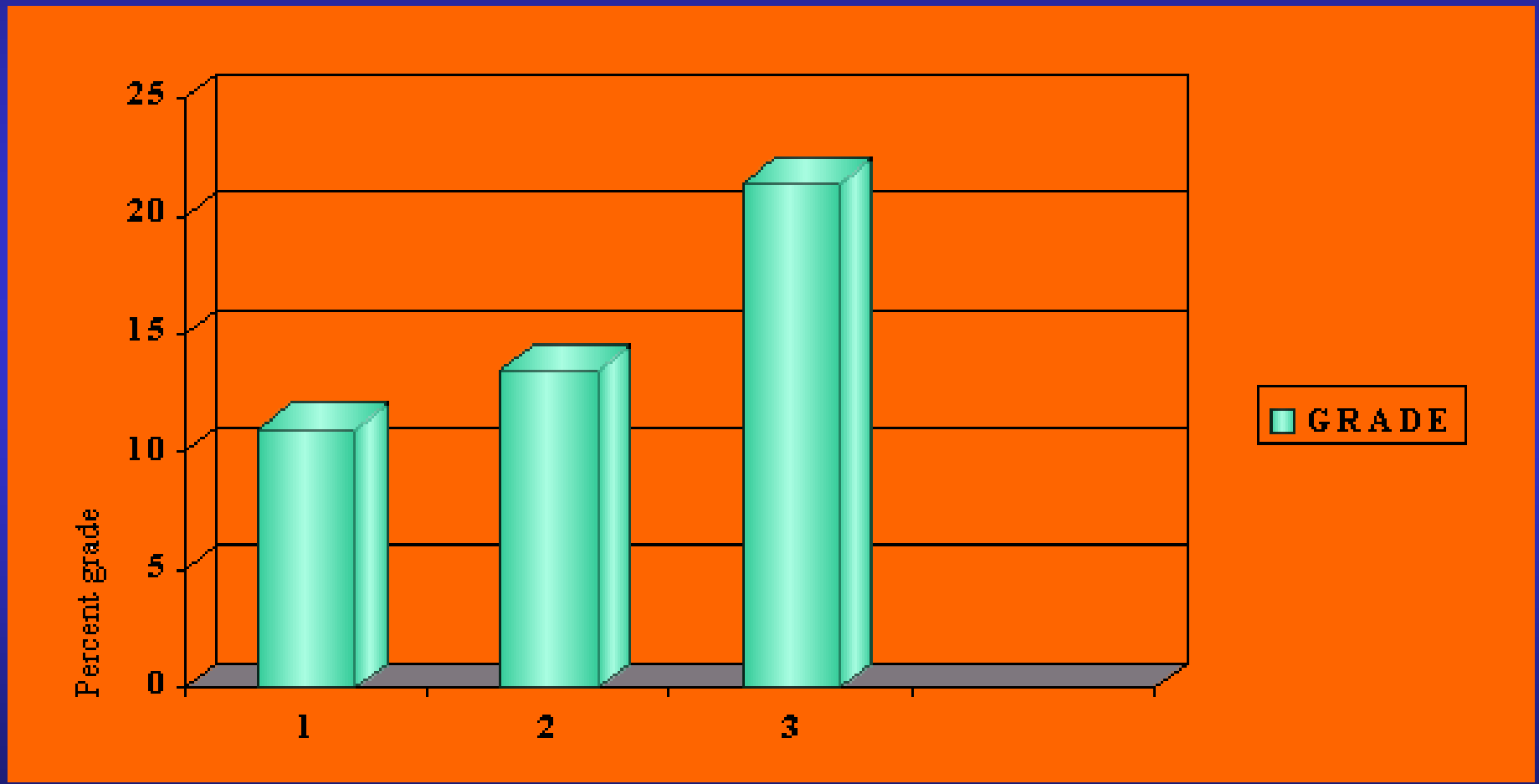

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Table 4 Correlation of myometrial invasion and malignant cytology

Author	Year of publ.	No invasion	< 50	> 50	Significance (p value)
Creasman et al.	1981	6/ 72	9/ 60	8/ 25	P < 0.05
Szpak et al.	1981	6/ 27	3/ 21	3/ 6	NS
Yazigi et al.	1983	6 / 16	1/ 35	3/ 14	NS
Ide	1984		6/ 63	18/ 27	P < 0.05
Hernandez et al.	1985	2/ 17	4/ 35	2/ 20	NS
Kennedy et al..	1987	2/63	4/60	2/21	NS
Harouny et al.	1988		24/185	12/ 35	P < 0.05
Mazurka et al.	1988	1/ 37	7/ 21	7/77	NS
Lurain et al.	1988		19/ 125	10/ 26	P <0.05
Turner et al.	1989		24/ 529	4/ 6	NS
Kashimura et al.	1997	4/ 80	13/ 106	20/ 100	P < 0.02
Zerbe et al.	2000	2/ 21	10/ 21	9/ 21	P = 0.60
Total		29/ 333	124/ 1361	98/ 408	
		(8.7 %)	(9.1 %)	(24.0 %)	P <0.01

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Correlation of myometrial invasion and malignant cytology

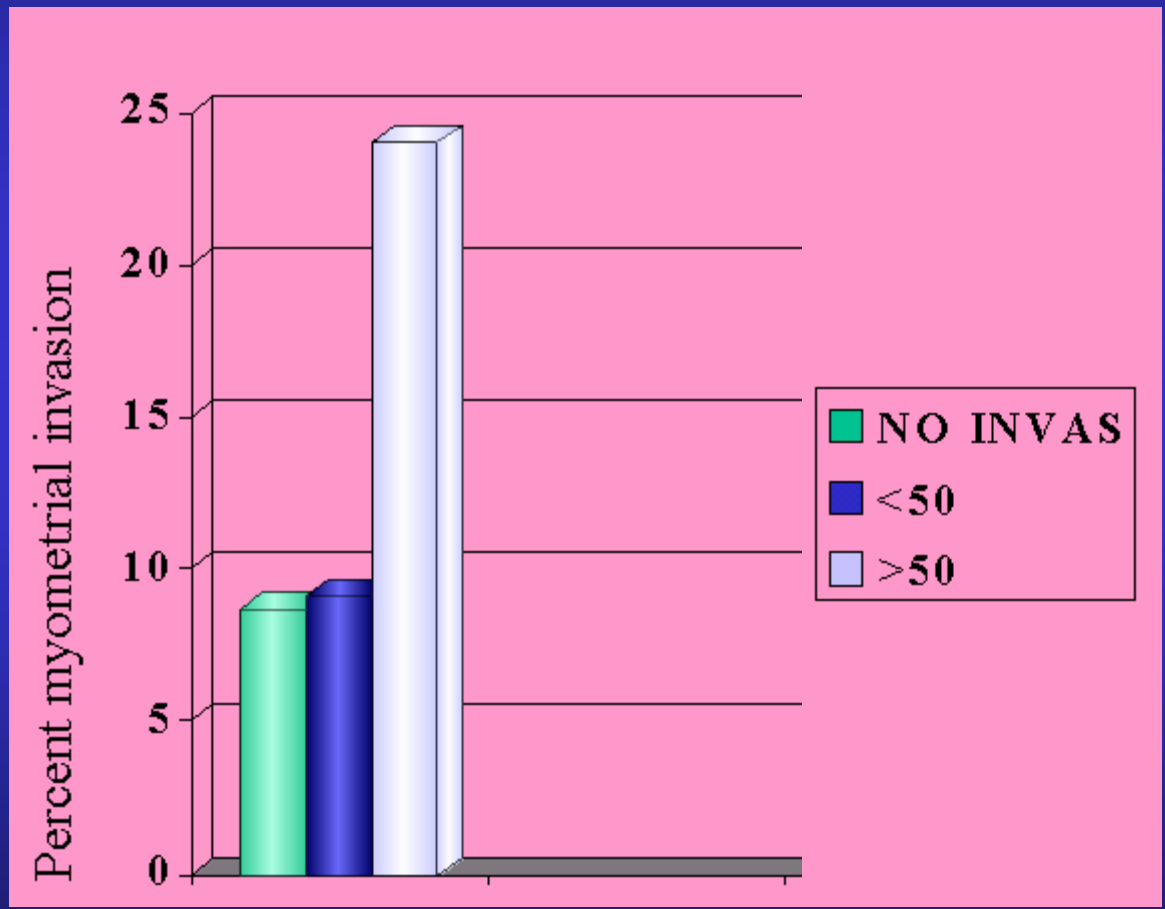

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Table 5 Correlation between lymph node metastases and peritoneal cytology

Author	Year of public.	+ cyto	- cyto	Significance (p value)
Creasman et al.	1981	11/17	15/ 150	P < 0.001
Hernandez et al.	1985	1/ 1	2/ 22	NS
Creasman et al.	1987	19/ 75	38/ 537	
Harouny et al.	1988	3/ 4	12/ 74	NS
Kadar et al.	1992	10/ 34	18/ 235	P < 0.001
Zerbe et al.	2000	8/ 21	20/ 201	P < 0.01
Takeshima et al.	2001	28/ 119	45/ 415	
Imachi et al.	1988	2 / 9	7 / 44	NS
Total		82 / 280	157 / 1678	P < 0.01
		(29.3%)	(9.4%)	

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Correlation between lymph node metastases and peritoneal cytology

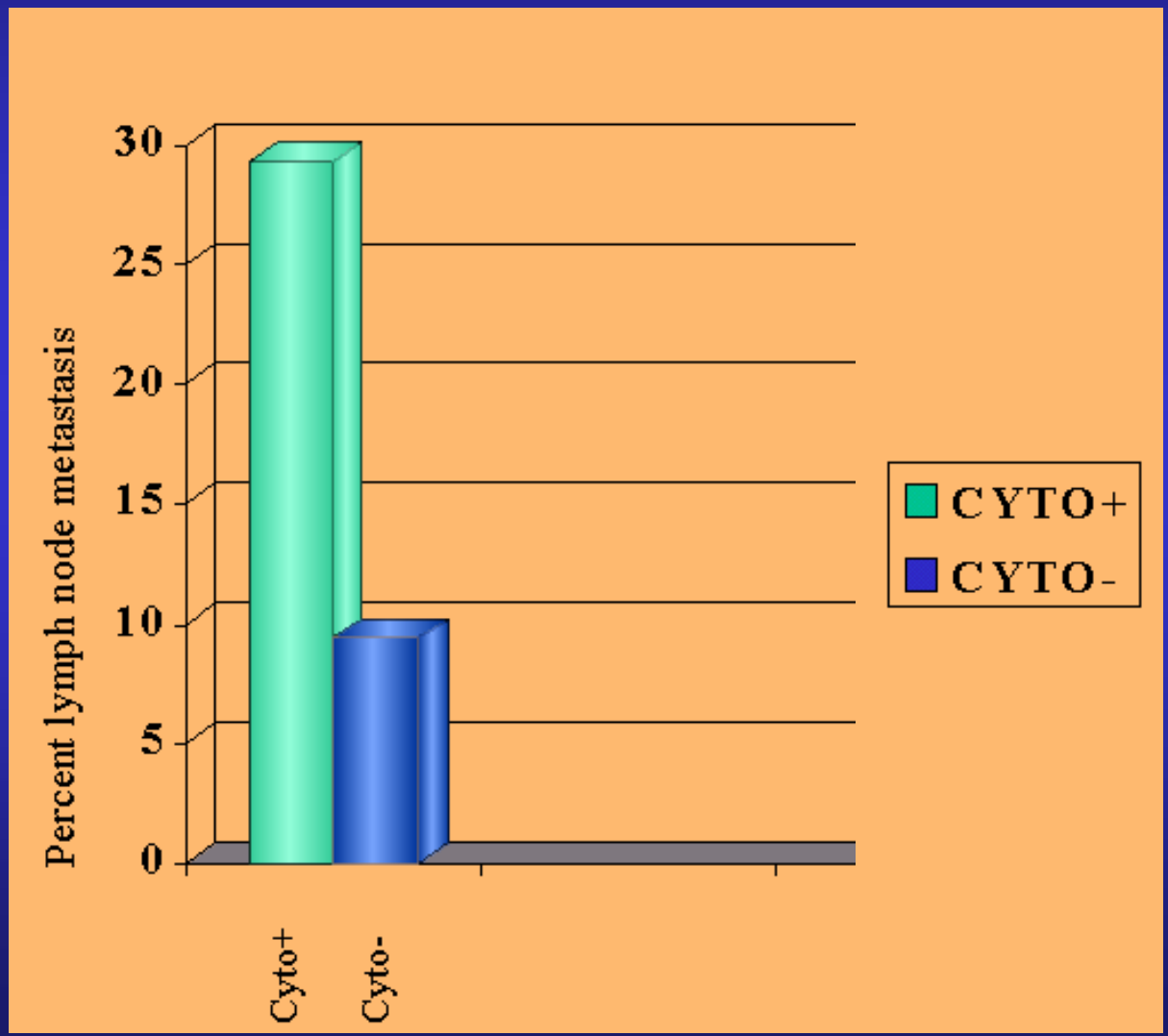

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Table 6 The recurrence according to cytologic findings

Author	Year of publ.	+ cyto	- cyto	Significance (p value)
Creasman et al.	1981	13/ 26	14/ 141	P < 0.001
Szpak et al.	1981	6/ 12	0/ 42	P < 0.0001
Yazigi et all	1983	1/ 10	4/ 136	NS
Ide	1984	13/ 28	7/ 66	NS
Ravinsky et al.	1986	2/ 5	4/ 47	NS
Harouny et al.	1988	12/ 41	6/ 207	P < 0.001
Kennedy et al.	1987	3/ 8	4/ 136	P < 0.05
Mazurka et al.	1988	4/ 16	13/ 237	P < 0.01
Lurain et al.	1988	4/ 29	8/ 122	NS
Turner et al.	1989	9/ 28	38/539	NS
Lurain et al.	1991	10/ 38	18/192	P <0.01
Kadar et al.	1992	16/ 34	25/ 210	P < 0.001
Morrow et al.	1991	25 / 86	64 / 611	P < 0.01
Total		115 / 353	199 / 2497	
		(32.6 %)	(8 %)	P < 0.01

Recurrence according to cytologic findings

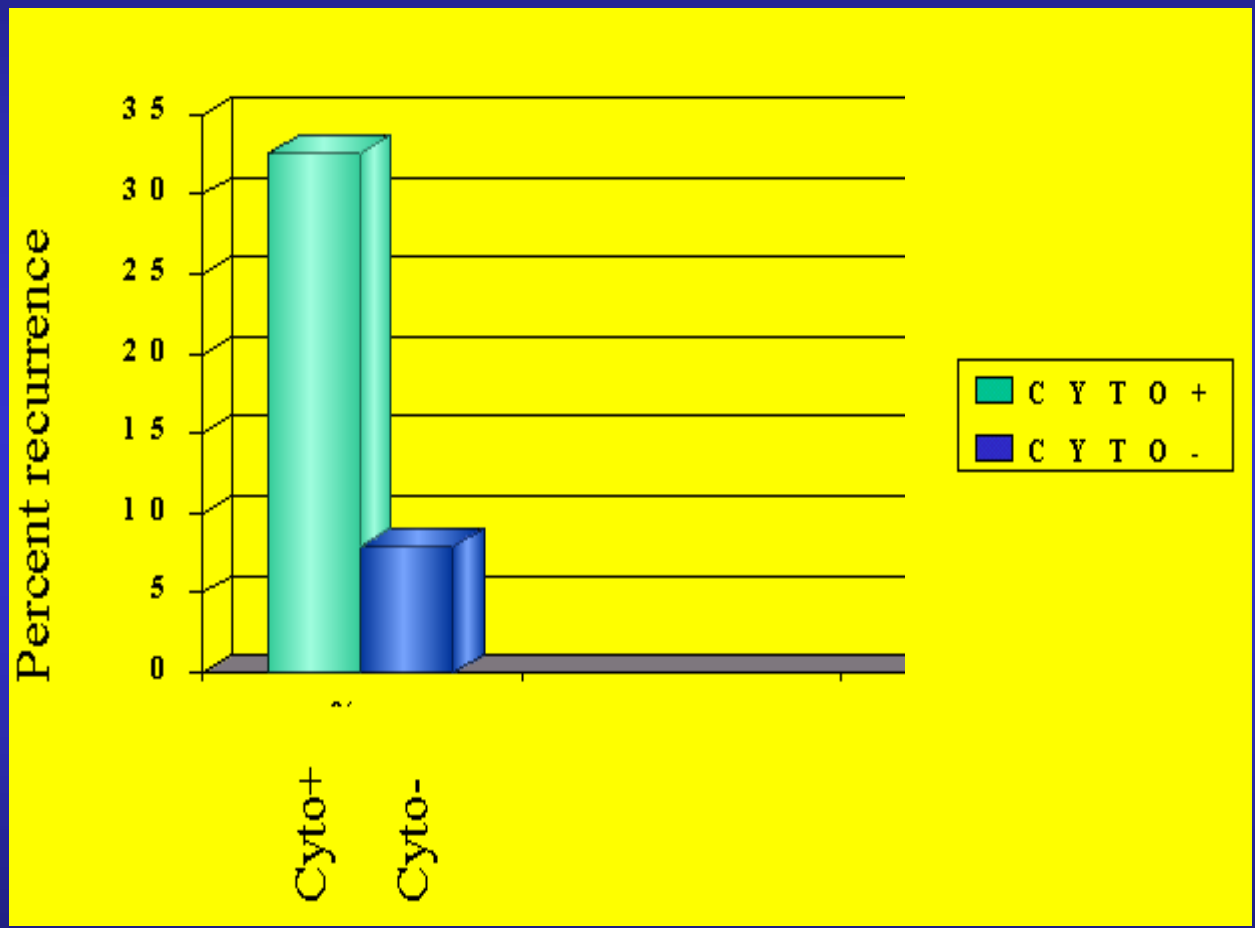

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Table 7 Prognostic significance of peritoneal cytology in Stage I

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Author	Year	No of patients	+ cyto (%)	Significance (pos vs neg)
Creasman	1981	167	16	SN (Rr = 34 % vs 9.9 %)
Szpak	1981	54	22	SN (Rr = 42 % vs 0 %
Yazigi et al.	1983	93	11	NS (5 y SR = 88 % vs 94 %)
Ide	1984	94	30	SN (5 y SR = 54 % vs 88 %)
Heath	1988	190	13	SN (3 y SR = 56 % vs 91 %)
Imachi et al.	1988	35	14.3	NS (2 y SR = 75 % vs 92 %)
Hirai et al.	1989	173	15	NS (10 y SR = 90 % vs 90 %)
Turner et al.	1989	28	4.9	SN (5 y SR = 84 % vs 96 %)
Grimshaw et al.	1990	16	5	NS (5 y SR = 80 % vs 86 %
Sutton	1990	276	17	SN (5 y SR = 71 % vs 97 %)
Lurain et al.	1991	230	17	NS (Rr = 26 % vs 9 %)
Gal et al.	1991	93	19	SN (5 y SR = 55 % vs 97 %)
Kashimura et al.	1997	199	9	SN (5 y SR = 92 % vs 80 %)
Obermair et al.	2001	13	3.5	SN (DFS = 67 % vs 96 %)

Note. SN = significant ; NS = non significant ;Rr = recurrence rate ; ySR = year survival rate ; yDFS = year disease – free survival

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Table 8 Survival by cytologic finginds in Stage III endometrial cancer

Author	Year	No of patients	DFS (5 year)	SV (5 year)
Milton et al.	1972	17[1]	80.5%	81.8 %
Frick et al.	1973	22[1]		55 %
Antoniades et al.	1976	6[1]	67 %	
Danoff et al.	1980	7[1]	80 %	60 %
Bruckman et al.	1980	15[1]	80 %	
Mackillop et al.	1985	18[1]		82.3 %
Grigsby et al.	1987	13[1]		76.9 %
Sall et al.	1987	11[2]		64 %
Greven et al.	1989	42[1]		60 %
Potish	1989	11[2]	83 %	
Morrow et al.	1991	7[1]	85.7 %	
Gal et al.	1992	90[2]		60 %
Greven et al.	1993	45[1]	64 %	
Kadar et al.	1994	13[2]		25 %
Ebina et al.	1997	40[2]		82.8 %
Connell et al.	1999	12[1]	70.9 %	
Mulvany et al.	2000	81[2]	82 %	
Veighted average			77 %	65 %

Note : DFS = disease free survival ; SV = survival ;1- solitary adnexal involvement ; 2 – « metastatic sites « (includes adnexa, regional nodes, and other gross findings)

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Discussion

- Utilization of the literature review to evaluate peritoneal cytology as a test for the detection of malignant cells in the peritoneal cavity is limited by many factors:

- varied used of preoperative radiation therapy by different centers;
- inherent subjectivity of cytologic interpretation;
- authors used varying parameters of myometrial depth

DISCUSSION

- Published opinions are mixed about the significance of positive peritoneal washings in the absence of extrauterine spread:

- several studies show malignant peritoneal cytology to be a poor prognostic factor,

- whereas other studies show no prognostic significance for malignant peritoneal cytology by itself.

DISCUSSION

Various *incidence* of positive peritoneal cytology were shown in the past literature, from 4.9 % to 40 %.

This variety in the incidence was found probably due to the use of different diagnostic criteria for cytology and different philosophy of cytodiagnosis in each paper.

DISCUSSION

The manner by which malignant cells appear in the peritoneal cavity in the absence of peritoneal disease has long been a subject of discussion and still represents one of the most controversial dilemma about significance of the peritoneal cytology in patients with endometrial cancer.

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DISCUSSION

RECURRENCE:

- was found to be affected by positive peritoneal cytology;
- was higher in cases with positive cytology

DISCUSSION

Survival:

- was found to be affected by positive cytology;
- was better in cases with negative cytology

Discussion

Positive peritoneal cytology is associated with known poor prognostic factors such as:

- grade 3 histology,
- deep myometrial invasion,
- lymph node metastasis and
- other extrauterine spread of disease.

This fact suggests that positive peritoneal cytology associated with other demonstrable disease outside the uterus is a marker for an aggressive type of metastasizing tumor and indicates worse prognosis.

Discussion

- The significance of positive washings in the absence of other high – risk factors is debateable.

- The questions of whether and how to treat patients with positive peritoneal cytology only are still unanswered.

Conclusions

• Endometrial carcinoma is one of the most common gynecologic malignancies with many thousands of fatalities every year.

• The best way to protect from this serious disease is preventive and early detection which substantially decreased the recurrence rate and prolonged the survival rate.

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Conclusions

- One of the most common tests to diagnose and evaluate a disease spread is the peritoneal cytology.

- Because of its unreliability, the peritoneal cytology is often a subject of tempestuous controversies between different investigators.

- However, the significance of positive peritoneal cytology in patients with endometrial cancer remains still unclear. Further studies are needed for final conclusions.

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PREVENTION

Live sensibly, among a thousand people , only one dies a natural death, the rest succumb to irrational modes of living.

Maimoniades
1135- 1204

CONCLUSIONS

- Everyone expects of woman to be a exellent mother, exellent wife and, exellent worker. But, do we take enough care of her? This is a question we should ask everyday, in order to make the woman` s life easier and more comfortable, thus enabling her to face all her assignments and difficulties.

Author

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- Can you imagine the world without woman?
- Can you imagine the pregnant man?

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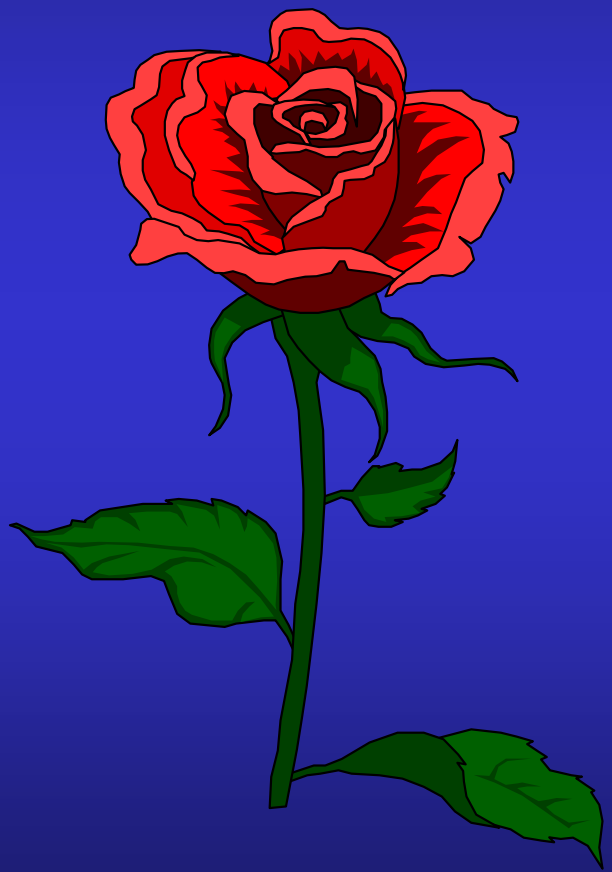
About a woman



- Every day one flower for a woman, because she merits it

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I want to live
happily,
without disease.

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