

ATLAS OF CANCER CYTOPATHOLOGY Volume 2
O.A.N. Husain, M.D.

THE CYTOPATHOLOGY OF BREAST CANCER

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in association with

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6 Languages: English German French
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**COLOR ATLAS
THE CYTOPATHOLOGY
OF BREAST CANCER**

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PREFACE

This is the second volume from the series "Color Atlas of Cancer Cytopathology" focusing on the cytological interpretation with histological correlation of breast tumours. It is a comprehensive book encompassing all aspects for accurate diagnosis of Fine Needle Aspiration of the Breast.

Breast cancer remains one of the most frequent malignancies of women and much advancement in the treatment and diagnosis has been made. In the role of cytology, FNAB is considered an excellent technique as a diagnostic and pre-operative aid. This book describes in detail; breast cysts, tumour-like lesions, atypical hyperplasias, benign epithelium, mixed connective tissue, the male breast, sarcomas, primary lymphomas and metastatic malignant tumours, with major emphasis on malignant criteria and difficult differential diagnosis. A separate chapter has been entirely designated to nipple secretion. We have included detailed histological presentation in conjunction with each cytological case in order to compare and correlate, thus allowing one to further enhance one's expertise in diagnosis.

Fifty years of reference have been reviewed and carefully selected. This book could not have been produced without the substantial contribution of 25,000 cases submitted to us from four main sources; Institute of Pathology, Kantonsspital St. Gallen, Cancer Society of Switzerland St. Gallen, Centre Regional Francois Baclesse Cancer Hospital, France, and the Peking Cancer Institute, China. Also special cases from India and various other hospitals in China were gratefully accepted.

Although the main text is in English, due to the success of the last book which included five languages, the legends are once again in 6 languages in order to reach professionals worldwide. We have tried to maintain a consistent excellence in the quality of the colour illustrations. In general, the Papanicolou stain has been used for cytology, with Haematoxylin and Eosin for histological sections. Special stains have been mentioned where necessary.

We wish to express our heartfelt thanks to all the people who kindly assisted us namely: Dr. Pyousuke Kondo, Dr. Yoshiro Okamura and Dr. Shinji Urakawa for their time and effort in translation of the Japanese text. Also, we wish to thank members of our staff both of the Cancer Society of Switzerland (Krebsliga) and Institute of Pathology, Kantonsspital St. Gallen; Ann Schmidt MSc CT (ASCP), Magreth Hell CT, Mayumi Yoshida CT (IAC), and Lynette Ostrom CT (CSLT), for their assistance. Special thanks to Bao-lan Zhang for preparing manuscripts, Monika Würth and Noriko Sugie for typing. Also we wish to acknowledge our thanks to Dr. Xiao-Jing Peng, Dr. Bo-Wen Ma and Dr. Chandralekha P. Shroff for submitting rare material.

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FOREWORD

THE CYTOPATHOLOGY OF BREAST CANCER by Yi-Jing Shu, M.D. and Peter Spieler, M.D. in association with Friedrich J. Gloor M.D. and Franz A. Ikle M.D.

I write with some praise of the quality of this volume on Breast Cytology. The authors, Dr. Yi-Jing Shu and Dr. Peter Spieler in association with Dr. F.J. Gloor and Dr. F.A. Ikle and their 10 distinguished contributors from all over the world are to be congratulated on a substantial treatise on breast cytopathology and histopathology. The photomicrographs are of high quality and give much instructional detail at high magnification. The Authors have endeavoured by considerable reference to the literature to give it the nature of a text book with the quality and extent of a substantial descriptive text and references to a number of seminal works.

Much extensive editing has gone into this volume and the fact that it is presented in 6 languages will make it much more universally attractive.

The use of only the Papanicolaou stain for cytology could be considered a drawback to those who use the Romanosky stain, but the latter is not so essential for this organ's analysis except when studying the lymphoreticular lesions.

It acts as a substantial reference monograph by virtue of its wide range of illustrations of the various lesions and I recommend it to all cytopathologists as a valuable addition to their library and as a day to day reference manual.

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INTRODUCTION

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| 1. INCIDENCE AND MORTALITY | A. Histological classification of breast tumours by WHO |
| 2. DIAGNOSTIC ACCURACY | B. Sensitivity rate in histological typing of breast carcinoma |
| 3. PROBLEM OF INADEQUATE SMEARS | 7. COMPARISON OF CARCINOMA DETECTION RATES WITH VARIOUS METHODS |
| 4. FALSE NEGATIVE RATE | 8. TECHNICAL NOTES: TECHNIQUE, INDICATION, COMPLICATIONS |
| 5. FALSE POSITIVE RATE | |
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INTRODUCTION

1. INCIDENCE AND MORTALITY

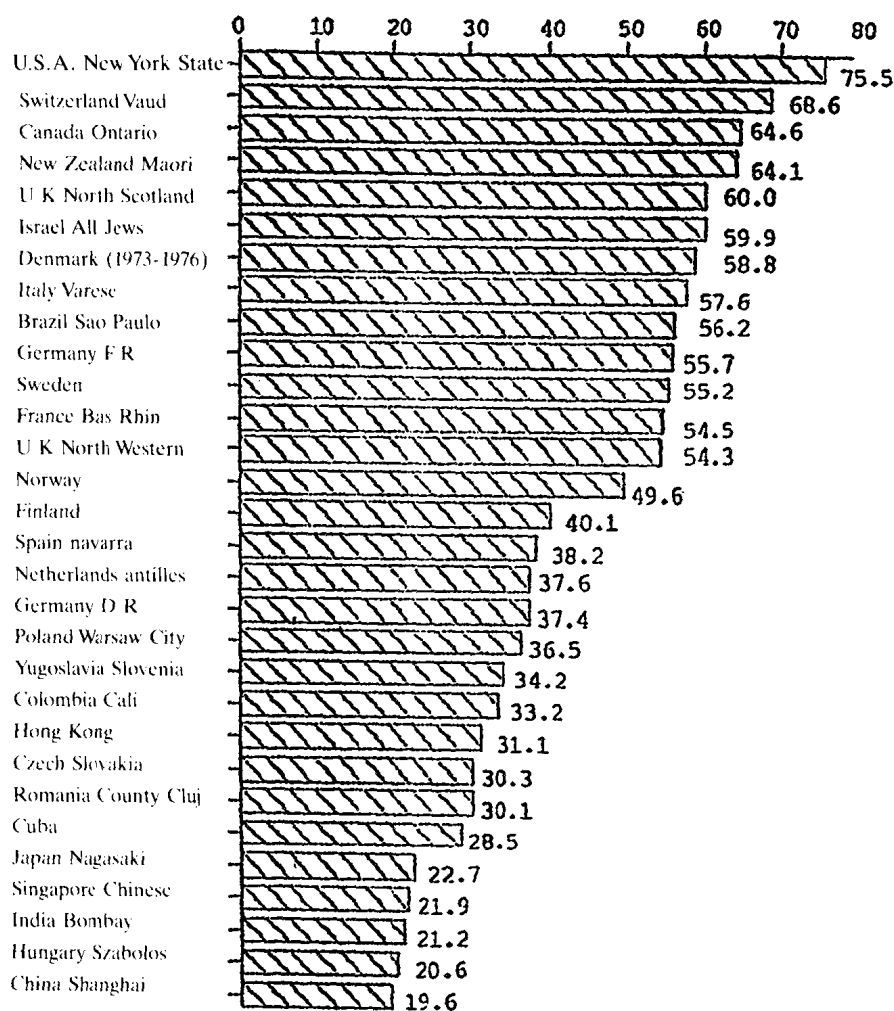
The breast is the site of one of the most common malignant tumours in women. There is a sharp contrast between the relatively high incidence and mortality rate in North America and the relatively low incidence in Asia.

In most of the countries in Europe, breast cancer is still the most common site of malignant tumours in woman, but the mortality rate in comparison to that of North America remains low. (Fig. 1-1)

The mortality rate of breast cancer per 100,000 women is higher in most European countries and in the United States than in Asia and South America. (Fig. 1-2)

Fig. 1-1 INCIDENCE OF BREAST CANCER IN DIFFERENT COUNTRIES.

THE INCIDENCE OF BREAST CANCER IN FIVE CONTINENTS

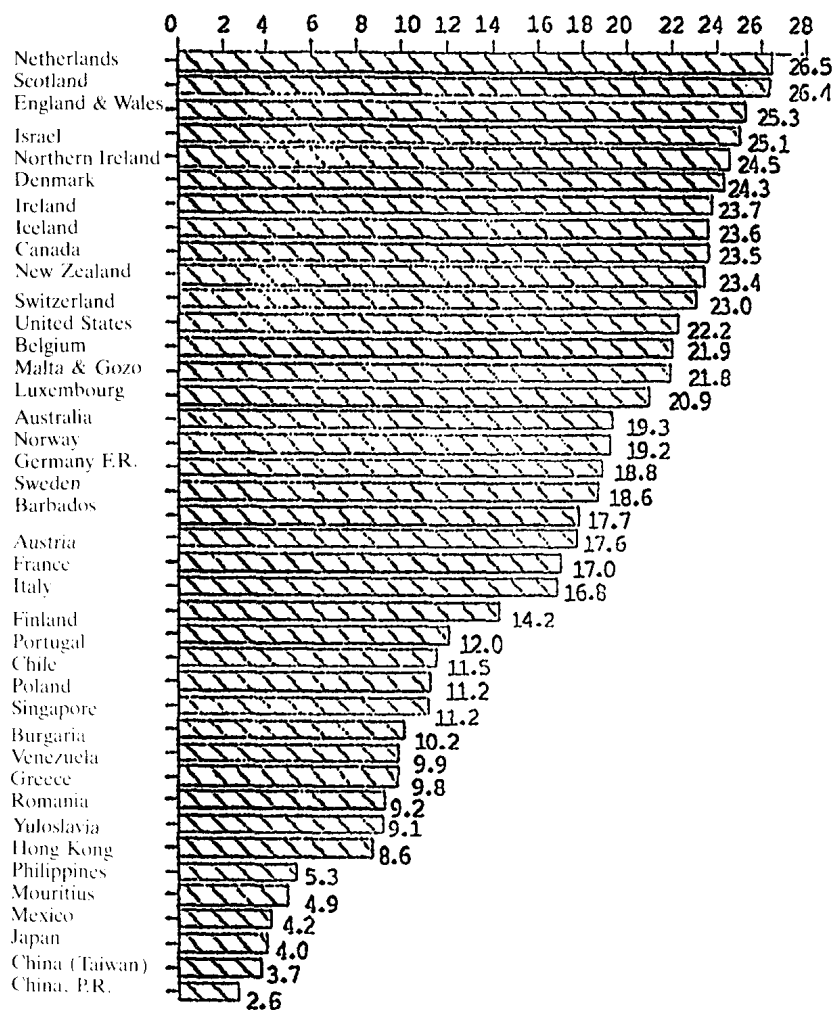


WHO: CANCER INCIDENCE IN FIVE CONTINENTS 1982.

World age-standardized in female per 100,000 population for 30 countries.

Fig. 1-2 THE MORTALITY RATE OF BREAST CANCER AROUND THE WORLD

THE MORTALITY RATE OF BREAST CANCER AROUND THE WORLD



Age adjusted death rates per 100,000 population for 39 countries, 1968-1969, China P.R. 1977
 Masukawa T. compendium on diagnostic cytology. p497, 1976. (2)

2. DIAGNOSTIC ACCURACY

In 1930, the pioneering work of Martin and Ellis at the Memorial Hospital for Cancer and Allied Diseases (Memorial Sloan-Kettering Cancer Hospital) in New York, involved the aspiration biopsy technique in 6 cases of breast tumours. By 1934, they had expanded their experience to the diagnosis of 280 cases of breast cancer by aspiration biopsy.

Saphir and Godevin (USA) in the early 1950's recommended the use of fine needle aspiration (FNAB) for breast lesions and by 1967, Zajicek and Franzen (Sweden) were reporting 2,200 cases of mammary tumours diagnosed by FNAB.

In the last 35 years, FNAB has become widely used throughout the world and remains a powerful tool for the diagnosis of breast cancer. Because of this simple, rapid and accurate technique, thousands of cases were diagnosed by FNAB with a minimum of discomfort to the patient.

In general, a high accuracy rate is reported with FNAB. In 1959, Smith (Canada); 1968, Franzen (Sweden); 1975, Zajicek (Sweden); 1975, Geier (Germany); 1978, Schondorf (Germany); 1985, Feldman (USA); 1986, Gantenbein Spieler (Switz) in group A achieved a sensitivity rate of 90% or above, for breast cancer. The diagnostic accuracy or specificity for benign lesions is also approximately 90%.

Tables 1-1 and 1-2 show aspiration cytology having a sensitivity rate (positive and suspicious) of 77% to 98% for the presence of carcinoma and a specificity rate of 97.6% - 100% for the absence of carcinoma. This gives evidence of the diagnostic value of aspiration biopsy in preoperative diagnosis.

Table 1-1 ACCURACY OF DIAGNOSIS BY FNAB OF BREAST CANCER

Authors	Area	Year	Total cases reported	Histological diagnosis malignant	Cytological Diagnosis					
					Pos. No. %	Sus. No.	Neg. No.	Unsatisf. No.	Sensitivity (POS. + SUS.) No. %	
Adair	England	1949	1579	1579	1343 (85)	—	236	—	1343	85
Smith	Canada	1959	294	100	92 (92)				92	92
Franzen	Sweden	1968	3479	873	662 (76)	117	(-- 94 ----)		779	89
Laumonier	France	1968	1000	456	335 (73)	21	51	49	356	78
Zajicek	Sweden	1970	4700	1068	823 (77)	139	(-- 106 ----)		962	90
Cornillot	France	1971	2267	1335	1173 (88)	—	62	100	1173	88
Zajdela	France	1975	2772	1745	1539 (88)	54	63	89	1593	91
Geier	Germany	1975	974	72	57 (79)	10	5	—	67	93
Takeda	Japan	1976	860	71	56 (79)	—	15	—	56	79
Schondorf	Germany	1978	2778	307	283 (92)	18	6	—	301	98
Kline	USA	1979	3545	341	213 (62)	89	35	4	301	88
Garadicki	U.K.	1980	233	129	96 (74)	16	6	11	112	87
Kudoh	Japan	1983	167	40	35 (88)	—	5	—	35	88
Feldman	USA	1983	300	100	80 (80)	15	—	5	95	95
Eisenberg	USA	1986	1874	1480	984 (66)	152	173	171	1136	77
Spieler*	Switz	1986	1768	80	65 (81)	7	8	—	72	90
Kan	China	1986	8129	1012	772 (76)	60	173	7	832	82

Table 1-2 ACCURACY OF DIAGNOSIS BY FNAB OF BENIGN BREAST LESIONS

Authors	Area	Year	Total cases reported	Histolog. or follow up Diag. benign	Cytological Diagnosis				
					Unsatisf.	Neg.	Sus.	Pos.	Spe* %
Franzen	Sweden	1968	3479	807	(— 783 —)	23	1		> 99.0
Laumonier	France	1968	1000	544	(84 424)	23	13		97.6
Zajicek	Sweden	1970	4700	1009	— 980 —	28	1		> 99.0
Cornillot	France	1971	2267	932	86 831)	—	15		98.4
Zajdela	France	1975	2772	1027	66 916	42	3		> 99.0
Kreuzer	German	1976	602	355		305	46	4	98.9
Kline	USA	1979	3545	3177	— 3188	59	—		100.0
Feldman	USA	1985	300	200	35 160	5	—		100.0
Spieler*	Switz	1986	1768	146		142	4		100.0
Kan	China	1986	8129	635	9 595	30	1		> 99.0

*Specificity

*Gantenbein and Spieler.

3. PROBLEM OF INADEQUATE SMEARS

Reviewed literature revealed a rate of inadequate smears ranging from 0.7% to 11.4%. (average 6.6%) Inexperience in technique and practice remain an important reason for this.

Table 1-3 INADEQUATE SMEAR IN MALIGNANT CASES

Authors	Area	Year	Histological diagnosis malignancy	Cytological diagnosis					
				Sensitivity rate		False negative (specificity)		Inadequate smears	
				No.	%	No.	%	No.	%
Laumonier	France	(1968)	456	356	78.0	51	11.2	49	10.8
Cornillot	France	(1971)	1335	1173	88.0	62	4.6	100	7.4
Zajdela	France	(1975)	1745	1593	91.0	63	3.6	89	5.4
Kline	USA	(1979)	341	302	88.0	35	10.3	4	1.7
Gardicki	U.K.	(1980)	129	112	87.0	6	4.6	11	8.4
Feldman	USA	(1985)	100	95	95.0	0	0	5	5.0
Eisenberg	USA	(1986)	1480	1136	77.0	173	11.6	171	11.4
Kan	China	(1986)	1012	832	82.0	173	17.1	7	0.7
Total			6598	5598	84.8	563	8.6	436	6.5

Gantenbein and Spieler (1986) reported 1768 cases by fine needle aspiration biopsies (FNAB) of the breast. The sensitivity and specificity of the method were calculated on the basis of two groups (A and B). In group A the FNAB was performed by a cytopathologist and in group B by general practitioners and specialists or hospital doctors. Sensitivity of 90.0% was calculated in group A and 79.0% in group B. The specificity in the evaluated material was 100% for both groups. In group A, 5% of all carcinoma showed a false negative cytologic diagnosis, because of inadequate smears, while in 9% of all FNAB the aspirated material was not representative, but in group B, 19.1% of the carcinomas were missed because of inadequate material. (Table 1-4)

Table 1-4 COMPARISON OF THE RESULTS BETWEEN GROUP A AND B

Cytological finding	Histological diagnosis carcinoma			
	Group A (N=80)		Group B (N=214)	
	No.	%	No.	%
Malignant	65	81.25	154	72.00
Susp./malignant	7	8.75	15	7.00
Benign (false negative)	4	5.00	4	1.90
Inadequate	4	5.00	41	19.10
Total	80	100.00	214	100.00

SENSITIVITY RATE: 90% IN GROUP A AND 79% IN GROUP B.

In conclusion, FNAB performed by a cytopathologist yielded a higher accurate diagnostic rate. In view of this, we suggest if possible, patients should be referred to the Cytology Laboratory for specimen collection or at least to a doctor being familiar with the technique. (Table 1-5.)

Table 1-5 ACCURACY OF CYTODIAGNOSIS OF BREAST CARCINOMA
IN CASES OF FNAB PERFORMED BY CYTOPATHOLOGISTS

Author		Histology confirmed No. of carcinoma	Accurate diagnosis	Carcinoma suspected	Sensitivity rate incl. suspected cases
Zajdela	1975	1745	1539 (88.0%)	54 (3.0%)	91.0%
Zajicek	{1970	1068	823 (77.0%)	139 (13.0%)	90.0%
Cornillot	1977	1335	1173 (87.9%)	—	87.9%
Geier	1975	72	57 (79.2%)	11 (15.2%)	94.4%
Gantenbein & Spieler	1986	80	65 (81.2%)	7 (8.7%)	90.0%

4. FALSE NEGATIVE RATE

A review of the literature has shown a false negative rate ranging from 5.0% to 23.4%.

Table 1-6 FALSE NEGATIVE RATE OF MALIGNANT LESIONS BY FNAB

Authors	Area	Year	Total cases reported	Histological diagnosis malignant	False negative			
					Cytodiag. Neg. No.	Inadeq. Smear No.	%	
Franzen	Sweden	1968	3479	873	—	94	—	10.8
Laumonier	France	1968	1000	456	51	—	49	21.9
Zajicek	Sweden	1970	4700	1068	—	106	—	9.9
Cornillot	France	1977	2267	1335	62	—	100	12.1
Zajdela	France	1975	2772	1745	63	—	89	8.7
Kreuzer	Germany	1976	602	247	—	33	—	13.4
Kline	USA	1979	3545	341	35	—	4	11.4
Garadicki	U.K.	1980	233	129	6	—	11	13.2
Feldman	USA	1985	300	100	0	—	5	5.0
Eisenberg	USA	1986	1874	1480	173	—	171	16.4
Spieler*	Switz	1986	1768	80	8	—	0	10.0
Kan	China	1986	8129	1012	173	—	7	17.8
Total	1968 —	1986	30642	8866	804	—	436	14.0

From our own experience and reviewing these false negative results, several facts have to be pointed out:

1. The size of tumour: A lower rate of cytologically positive diagnosis is apparent when the lesion is less than 1 cm in diameter, usually due to difficulty in palpation. Kline et al., (1979) reported 35 false negative cases in 368 malignancies. In 19 cases the needle tract did not extend into the tumour and in 11 of these, the tumour was not greater than 0.8 cm in diameter. Zajdela et al., (1975) also mentioned 23 false negative cases from 46 tumours all less than 1 cm in diameter. However very large tumours may not yield more positive results perhaps due to excessive necrosis, hemorrhage and inflammation. Eidenberg et al., (1986) and Zajdela et al., (1975) report a positive diagnosis obtainable more frequently in tumours of moderate size between 1 cm to 5 cm.
2. Zajdela et al., (1975) analysed the stages of cancer, 39 cases (3.9%) were reported as false negative in 982 malignancies. A false negative cytologic examination was encountered in 6%, 2.7%, 3.2% and 2%. T1 tumours, T2, T3, and T4 tumours respectively.

3. Screening inexperience.
4. Unsatisfactory aspirates as well as bad performance of FNAB were important factors, as already mentioned.
5. Histological type and differentiation of the tumour: Difficulty in the interpretation of well differentiated carcinomas such as tubular, lobular types, and scirrhous carcinoma.

It thus follows that cases presenting diagnostic difficulties or unsatisfactory smears must be repeated or biopsied.

Gantenbein and Spieler (1986) presented a paper of 948 aspirations from patients without carcinoma, 146 lesions had histologic control. In 89% of these lesions the cytologic and histologic diagnoses were in accordance. Most difficulties arose in differentiation between fibroadenoma and fibrocystic mastopathy with epithelial proliferation. (Table 1-7)

Table 1-7 BENIGN CYTOLOGIC DIAGNOSES AND THEIR DIAGNOSTIC ACCURACY

Diagnosis	Cytology		Histology				MALIGNANCY (FALSE NEGATIVE)
	Total cases	Performed No.	%	Concordance No.	%	Other benign lesions	
Proliferative mastopathy without atypia	324	53	16.4	47	88.7	2	4
Cyst/cystic mastopathy	293	38	13.0	37	94.4	0	1
Proliferation	9	0	0	0	0	0	
Fibroadenoma / papilloma	105	29	27.6	24	82.8	3	2
Mastitis	29	9	31.0	9	100.0	0	0
Gynecomastia in male	16	2	12.5	2	100.0	0	0
Lipomatous lesion	22	0	0	0	0	0	0
Other benign change	25	2		2		0	0
Cellular elements of normal breast	125	13	10.4	8	61.5	4	1
Total	948	146	15.6	129	88.3	9 (6.2%)	8 (5.5%)
Total benign concordant diagnoses 94.5% false negative rate 5.5%							

Gantenbein and Spieler, Schweiz Med. Wschr. 116/1986

5. FALSE-POSITIVE RATE

In a survey of the literature, false positive rates range from 0% to 2.4%.