

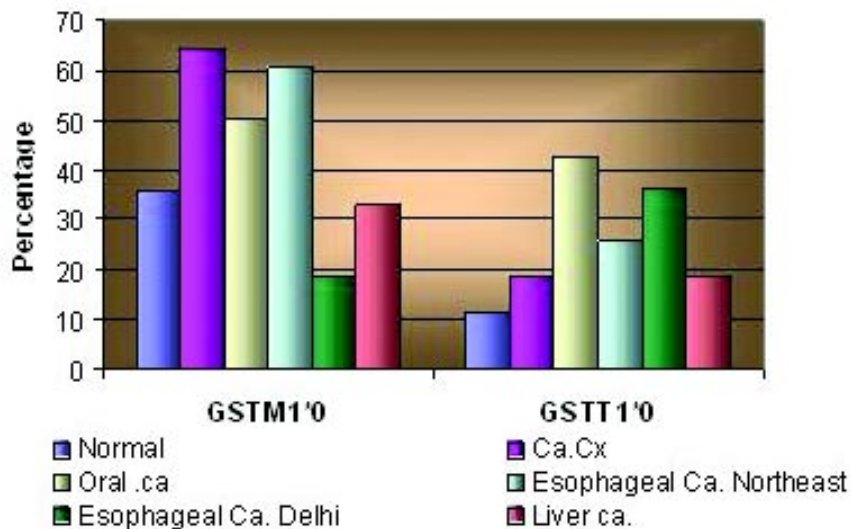
# **Miscellaneous Scientific Activities**

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## Genetic Polymorphisms and Susceptibility to Various Cancers

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**G**LUTATHIONE S-transferases (GST's) constitute a super family of ubiquitous, multifunctional enzymes, which play a key role in cellular detoxification. The GSTs catalyze the conjugation of the tripeptide glutathione (GSH) to a wide variety of exogenous and endogenous chemicals with electrophilic functional group (e.g., products of oxidative stress, environmental pollutants, and carcinogens), thereby neutralizing their electrophilic sites rendering the products more water-soluble. On the bases of sequence homology and immunologic cross reactivity, human cytosolic GSTs have been grouped into seven families, designated GST- $\alpha$ ,  $\mu$ ,  $\pi$ ,  $\sigma$ ,  $\omega$ ,  $\theta$ , and  $\zeta$ . One major reason of individual variation of GST activity is due to existence of polymorphism in these genes. The GST- $\mu$  family is encoded



GSTM1 and GSTT1 null polymorphism in various cancers

by a 100kb gene cluster at 1p13.3 arranged as 5'-*GSTM4*-*GSTM2*-*GSTM1*-*GSTM5*-*GSTM3*-3'. Deletion of *GSTM1* gene, *GSTM1*\*0, results in null allele. Individual homozygous for null allele are frequent in most of the populations studied and it as high as 100% in some tribal populations. A meta analysis has shown *GSTM1* null genotype in 53% Caucasians, with a 42–62% range.

We have shown that in Indian population 35% of individual are having null genotype. Similarly *GSTT1* also has null allele and the gene is located on long arm of chromosome 22. *GSTP1* also shows 4 polymorphic forms and the one reported by us still has to be characterized. There are several other polymorphisms reported which are being studied but not to that extent as *GSTM1*, *GSTT1* null and *GSTP1* polymorphisms. Other reason for differential activity of GSTs may be due to their expression factors that may range from nutrition, mutation in promoter regions or methylation of these genes. We have taken up several case control studies to look for the polymorphisms in *GSTM1*, *GSTT1* and *GSTP1* genes and susceptibility to various cancers.

We have conducted case control studies in cervical cancer (n=150), esophageal cancer (50 cases from Northeast India, 31 cases from Delhi), oral cancer (n=40), liver cancer (n=23), CML (n=50) and breast cancer (n=50) and found one or the other *GST* gene is associated with the susceptibility to these cancers. *GSTM1* gene is associated with cervical and esophageal cancer, *GSTT1* gene is involved in oral cancer and *GSTP1* gene with CML. Though the increased risk to individual with defective allele is small but the population impact is significantly higher as the proportion of population with these genotype are much higher as compared to high penetrance gene mutations like *BRCA1* and *p53*.

# Detection of Ovarian Malignancies among Women with Adnexal Masses and Their Genetic Characterization—A Multimodal Approach

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<i>Collaborators</i>	: <b>Swaraj Bhatra</b> , MAMC & LNJP Hospital, New Delhi <b>Sudha Salhan</b> , Safdarjung Hospital, New Delhi <b>S.K. Kochar</b> , Dharamshila Cancer Hospital, Delhi <b>M.S. Upadhyay</b> , District Hospital, Noida

OF all gynecological malignancies, ovarian cancer continues to cause the highest mortality with a least possibility of diagnosing it at an early stage. Only about 25% of women with newly diagnosed ovarian cancer present with stage I disease while 75% present in the advanced stages. The main reasons for this dismal picture are the absence of symptoms in early-stage disease, lack of readily recognizable and detectable precursor lesions and absence of specific and sensitive screening tests. Approximately, 4 to 24% of ovarian masses discovered before menopause and between 39% and 63% of those found after menopause are malignant.

Early detection of ovarian cancer would increase long term survival, since effective treatment modalities are available for early onset disease. Screening with trans-vaginal ultrasound and serum CA125 suggest promising results. In India, neither reliable statistics nor published reports are available regarding modalities to predict ovarian malignancy.

With the aim of developing modalities for early detection of ovarian cancer the following objective were formulated:

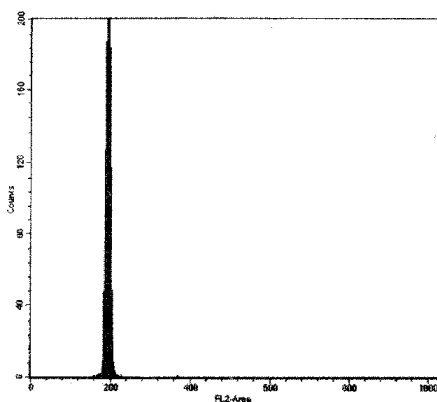
- To determine the ability of internal pelvic examination for detection of ovarian enlargement/adnexal masses.
- To study the ability of tumour marker test CA-125 and ultrasonography to predict malignancy in adnexal masses.
- To examine use of Doppler Ultrasonography in predicting ovarian malignancy.
- To study the genetic aspects like BRCA gene, p53 and Her-2/neu status in ovarian cancer.

# Flowcytometric DNA Analysis and Cytological Diagnosis of Pleural Effusions

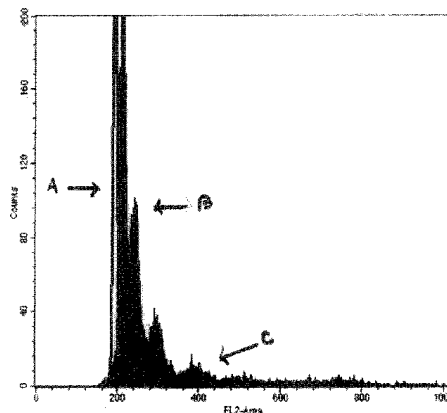
*Team Leader* : **Veena Kashyap**  
*Co-Investigator* : **Suresh Bhambhani**  
*Staff* : **Pushpa Bhadola**  
**Vijay Ali Khan**  
*Investigator* : **Saurabh Verma**, Institute of Pathology, New Delhi

**T**HE cytomorphological evaluation of effusion is a challenging aspect of non-gynecology cytology. The definite diagnosis of malignant effusion is often complicated by the presence of inflammation, exuberant mesothelial hyperplasia or a paucity of malignant cells. Flowcytometry offers the pathologist/cytologist methods to measure DNA content of a large population of cells in solid tumors and in dispersed cells as found in cytologic specimen. It can also be used as an adjuvant technique in the assessment of effusions.

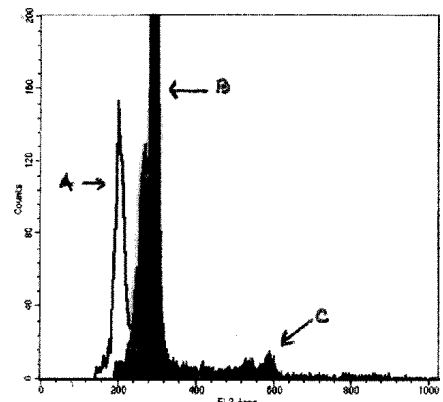
For this study fifty samples of pleural effusions were simultaneously evaluated by cytology and flowcytometry. After the acquisition of data on flowcytometry (FCM) the cytological diagnosis of the samples were correlated with diploid and aneuploid DNA histogram and it was observed that by flowcytometry, it is possible to detect more number of abnormal cases than by cytology alone. Flowcytometric DNA analysis can precisely differentiate diploid and aneuploid cell population which strengthens the concept that FCM DNA analysis can be considered as an adjunct with cytological diagnosis of pleural effusions.



DNA histogram of human peripheral blood lymphocytes at channel 200  $\pm 5$  with main peak at 2n



DNA histogram of case diagnosed as atypical mesothelial cells revealed G0/G1 hyper diploid (B) population of cells with a small peak at G2+M (C). Peak A represent control



DNA analysis of malignant pleural effusion showing peak A of control, peak B (G0/G1) of aneuploid cells with peak C (G2+M)

## Exploration of National Cancer Registry Programme Data and its Statistical Modeling

*Team Leader* : **L. Satyanarayana**

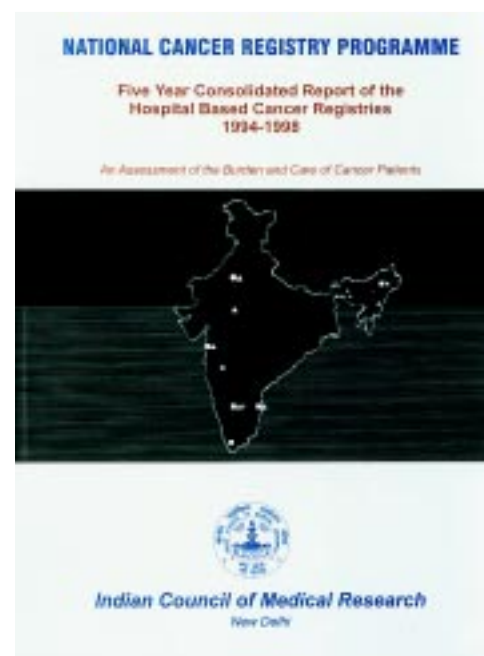
*Investigators* : **Smita Asthana**

*Staff* : **K.C. Sharma**

**C**ANCER registries provide data in different areas of the country through National cancer registry programme (NCRP) reports. Data on incidence rates, mortality rates and various other details of cancers of various sites are available from different population based cancer registries (PBCRs) since the year 1982. There appears to be a lot of scope for exploration and statistical modeling of these secondary data. This project aims (i) to explore the data to recognize any pattern or structure that requires explanation, and (ii) to attempt statistical modeling of data to understand the significant hidden trends.

One such scope to meet the objective is to compute cumulative rates and risks for all years and attempt their temporal study as these site-specific rates and risks (0–64 years) were reported by NCRP for recent years only. This present exercise aims to compute the site, sex region specific cumulative rates and risks (0–64) years of commonest cancers and observe the trends between the years 1982 and 2000.

Age and sex specific incidence rates of 10 major cancers data available from NCRP reports from the year 1982 to 2000 were used to compute the cumulative rates and risks. The method computation adopted by NCRP was used for similarity of estimates in different years. Trends were studied using linear regression method. The computed risk estimates were converted into one in number of persons develop cancer. Computations are done for 3 to 6 population based cancer registries in the years 1982 to 2000. The Mumbai cancer registry showed an increase in breast cancer risk from 1.65 to 2.2 for 0–65 years and from 2.21 to 3.56 for 0–75 years of age. There was significant declining trend in cervical cancer and increasing trend in breast cancer in Mumbai, Bangalore, Chennai and Delhi. The significant temporal changes observed were shown in Table overleaf for other registries for various cancer sites in either sex.



Commenced under the ICMR in 1981, National Cancer Registry Programme networks the cancer registries across the country and provides the most useful raw-data for statistical modeling

Significant trends (1982-2000) of cancer life time (0-64 years) risk in different cancer registries

Cancer Registries	Sex	Site	Trend	p-value	R-square	
Bangalore	Female	Breast	0.036	0.01	53	
		Cervix	-0.065	0.009	55	
		Mouth	-0.023	0.02	45	
		Oth lymph node	0.006	0.013	50	
	Male	Mouth	-0.009	0.024	43	
Barshi	Female	Stomach	-0.008	0.089	56	
	Male	Larynx	-0.008	0.08	59	
Bhopal	Female	Oesophagus	-0.03	0.067	63	
	Male	Stomach	-0.01	0.022	82	
		Oth lymph node	0.02	0.052	69	
Chennai	Female	Breast	0.032	0.01	53	
		Cervix	-0.098	<0.001	89	
		Mouth	-0.015	<0.001	87	
		Stomach	-0.007	0.01	54	
		Oth lymph node	0.006	<0.001	87	
	Male	Oesophagus	0.009	0.013	50	
		Prostate	0.003	0.085	24	
		Oth lymph node	0.01	0.001	72	
Delhi	Female	Cervix	-0.066	0.034	76	
		Oesophagus	-0.009	0.034	76	
		Stomach	-0.007	0.025	81	
		Gall blader	0.018	0.082	58	
		Oth lymph node	0.003	0.092	56	
		Thyroid gl	0.005	0.054	68	
	Male	Liver	-0.004	0.013	88	
		Mouth	0.003	0.089	56	
	Mumbai	Female	Breast	0.028	0.001	75
			Cervix	-0.018	0.004	63
Oesophagus			-0.011	0.004	62	
Ovary			0.006	0.051	32	
Stomach			-0.008	0.009	55	
Gall bl			0.004	0.02	45	
Oth lymph node			0.007	0.001	74	
Tongue			-0.002	0.055	31	
Male		Hypophaynx	-0.017	0.015	49	
		Oesophagus	-0.015	0.001	76	
		Stomach	-0.006	0.009	55	
		Larynx	-0.008	0.013	51	
		Oth lymph node	0.01	<0.001	80	
		Tongue	-0.008	<0.001	90	

## Referral, Diagnostic and Consultation Services

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<i>Staff</i>	: <b>Vijay Khan</b> <b>Kaushik Halder</b> <b>K.L. Chachra</b> <b>Pushpa Bhadola</b> <b>Thankamma James</b> <b>Sham Sunder</b> <b>Dinesh Kumar</b> <b>Ram Bhajan</b> <b>Daniel Das</b>

**T**HE Division of Cytopathology of the institute offers referral diagnostic services in the field of cytology and pathology. Patients are referred from Maulana Azad Medical College & LNJP Hospital, Delhi and associated hospitals. Patients referred from ESI Hospital, C.G.H.S. Dispensary & Government District Hospital, Noida are also examined. Consultation is being rendered to Northern Railway Central Hospital, New Delhi for diagnostic cytology. Specialized diagnostic services of fine needle aspiration, Pap smear, effusion cytology, C.S.F. cytology, urinary cytology, sputum cytology, histopathology etc. are being rendered free of cost.

Cervical smears	: 13,019
Effusions	: 392
FNAC	: 833
Histopathology	: 162

### Screening and diagnosis of Pap smears as per Bethesda System of classification

Under this service Pap smears from symptomatic patients, received from Gynae OPD of hospitals are being screened for cytological diagnosis of inflammatory changes, lower genital tract infections, HPV infection, atypical squamous cells for undetermined significance (ASCUS), Atypical Glandular cells of undetermined significance (AGUS) and for precancerous and cancerous lesions of the cervix.



Cytology screening being performed at ICPO



Fine needle aspirations and cytology are performed routinely for referred patients at ICPO Noida campus