Cytological characteristics of gynaecological specimens referred to Cytology Division, I.M.R. in 1970

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CENTRAL LABORATORIES which routinely process a large number of samples can often make an additional health science contribution by summarising and communicating the results of studies based on materials from many different sources. This may be particularly true in the case of a new procedure or newly-established laboratory such as the IMR Department of Cytology and Cytogenetics, established in June 1968. The purpose of this paper is to summarise the cytological variations observed in the different age and racial groups with reference to contraceptive usage in Malaysia and to discuss briefly some sociological and biological considerations raised by these variations.

Source of specimens

The 1970 specimens were chosen as the basis for this first report because of more complete information available on each of more specimens than for earlier years.

Although the majority of these specimens came from the state of Selangor which includes the Federal capital, Kuala Lumpur, the major urban area of the country, other less urban areas are also represented, particularly by the family planning clinics (Table I). From Table 1 it can be computed that approximately 69% of these specimens were from family planning clinics, with 24% of the specimens coming from government hospitals and the remaining 7% from private clinics. From Table 2 it can be computed that 74% of the specimens from the family planning group were oral contraceptive (pill) users, with 35% and 24% being the respective analogous values for the government hospital and private clinic groups. Due to the rather small numbers, we have omitted from subsequent consideration in this report the 558 specimens from those women using some form of contraceptive other than the pill (Table 2).

The racial origins and contraceptive usage of those Malaysians from whom the specimens were obtained are given in Table 3, with 61 specimens being excluded from subsequent consideration in this report because of unsatisfactory smears, and 776 specimens being excluded because the patient's age and/or race was unspecified or other than

Table 1

Number of specimens by type and location of medical facility

State	Type of Medical Facility			
	Family Planning Clinic	Government Hospital	Private Clinic	Total
Selangor	6201	1621	843	8665
Pahang	664	1060	3	1727
Malacca	650	105	2	757
Johore	355	140	4	499
N. Sembilan	297	33	12	342
Kelantan	6	130	0	136
Trengganu	0	31	0	31
Perak	605	29	20	654
Penang	196	4	26	226
Kedah	0	2	2	4
Total	8974	3155	912	13041

Table 2

Number of specimens of contraceptive usage and type of medical facility

Contraceptive	Type of Medical Facility			
	Family Planning Clinic	Government Hospital	Private Clinic	Total
"Pill"	6610	1096	215	7921
None	2-12	1871	680	4563
IUCD	252	108	14	374
Other	100	80	3	183
Total	8974	3155	912	13041

Table 3

Number of specimens, by contraceptive usage and race of patients

Contraceptive	Chinese	Indian	Malay	Total
None	2651	1042	281	394
Pill	4454	2948	274	7676
Total	7105	3990	555	11650

In addition, 61 specimens were unclassifiable due to technical causes, and 776 specimens were from patients whose age or race was unspecified or "other".

Chinese, Malay or Indian, the three major racial groups in Malaysia. As can be computed from Table 3, the percentages of specimens from Chinese, Malays and Indians were 69, 34, and 5, respectively. The estimated relative proportions of the three racial groups in West Malaysian females are 0.37, 0.52 and 0.10 respectively (Chander, personal communication).

As the incidence of cytological variations may differ among age, racial, and contraceptive usage groups, in Table 4 are given the number of specimens examined from the three major racial groups reporting either none or pill contraceptive, by 10-year age groupings. From Table 4, it can be seen that the percentage reporting no contraceptive usage increases in each older age group, with the exception of the Malay 21-30 age group. Also, the percentage reporting no contraceptive usage is least in Malays and greatest in Indians, with the Chinese always intermediate.

Although we have examined the records for those 396 specimens from which malignancy cannot be excluded (i.e. Class III, IV, and V) by searching for multiple specimens from a single individual, we have no practical way of checking all 13,045 records, at present. However, we feel that the remaining possible bias is very unlikely to be of such magnitude as to alter substantially conclusions which might arise from the data.

The optimum statistical inference strategy to follow in analysing these data were not apparent to us, because of two reasons. Firstly, the total number of statistical tests possible is so large that presentation of the results of all possible statistical hypothesis testing would be rather cum-

Table 4

Number of specimens by age and racial groups for patients using either pill or no contraceptive.

Age	Chinese			Malay			Indian			Total	
	Pill	None	% None	Pill	None	% None	Pill	None	% None	Pill	None
< 20	133	47	26	162	63	28	16	4	20	311	114
21 — 30	2121	929	30	1626	503	24	170	130	43	3917	1562
31 — 40	1856	1146	38	1056	386	27	77	103	57	2989	1635
41 — 50	340	423	55	103	74	42	11	32	74	454	529
> 50	4	106	96	1	16	94	0	12	100	5	134
Total	4454	2651	37	2948	1042	26	274	281	51	7676	3974

bersome; and secondly, as will be briefly discussed later, the precise population to which inferences would be made is not completely defined.

On the other hand, it seems desirable to utilise the power of statistical inference whenever possible. Therefore, our strategy was to provide in Table 8 the minimum differences required for significance (two standard errors which provides a significant level of 4.55% to be exact) in comparisons of two groups obtained by simple random sampling. For example, the difference between the per cent Chinese and per cent Malay age 21-30 reporting none contraceptive, 6 per cent (i.e., the difference between 30% and 24%, Table 4), is greater than two standard errors (i.e. 3.6%) for subgroups of size 1,000 for percentages around 20 (Table 8), and thus as these two groups, the Chinese and the Malay age 21-30, are also at least size 1,000 we conclude these two groups are significantly different from each other at least at the 4.55% level. Further comparisons of interest to the reader can then be made by using Table 8 as a quick approximation to the difference necessary for statistical significance between percentages computed from any two groups of the various respective sizes given.

Cytological classification

The specimens were processed and stained according to the Papanicolaou method. They were screened by primary screeners, checked by a senior cytotechnician, and finally by the cytopathologist. They were then classified essentially according to the International Standard (Seybolt, 1968) as follows:

Class I — Negative, with no abnormal cells detected;

Class II — Negative, abnormal cells present but considered to be of a non-malignant mature;

Class III — Inconclusive, abnormal cells present but malignancy cannot be excluded;

Class IV — Inconclusive, abnormal cells strongly suggestive of malignancy are present;

Class V — Positive, presence of abnormal cells which provide conclusive evidence of a malignant neoplasm.

Results and Discussion

In Tables 5, 6, and 7 are given the incidence of Class II, III and Class IV + V combined specimens, respectively, per 1,000 gynaecological specimens for the age, racial, and contraceptive groupings shown in Table 4. Alternatively, incidence rates per 1,000 can be considered as a percentage to the nearest tenth. If desired, the actual numbers of Class II, III, IV + V specimens observed are obtained upon multiplying the total numbers examined given in Table 4 by the various rates in Table 5, 6, and 7 respectively.

The observed Class II, III and IV + V incidences show a trend of increasing cytological abnormalities with age in all three races in both the pill and the none contraceptive groups (Table 5, 6, and 7). The incidnce of Class II specimens is greater in the Chinese than in the Malays in all age groups except the pill users under 21 (Table 5), while the incidence among the Indians fluc-

Table 5

Incidence of Class II (slightly abnormal) specimens per 1000 gynaecological specimens, by age and racial groups for patients using either "pill" or no contraceptive.

Age	Chinese		Malay		Indian	
	Pill	None	Pill	None	Pill	None
< 20	75	149	117	95	63	250
21 — 30	116	166	111	141	118	140
31 — 40	162	205	146	163	260	243
41 — 50	188	270	175	243	455	188
>50	250	340	0	125	—	500

Table 6

Incidence of Class III (definitely abnormal with malignancy not excluded) specimens per 1000 gynaecological specimens examined.

Age	Chinese		Malay		Indian	
	Pill	None	Pill	None	Pill	None
< 20	0	0	0	0	0	0
21 — 30	1	3	0	0	0	8
31 — 40	3	2	1	3	0	10
41 — 50	6	10	0	0	0	63
>50	0	28	0	125	0	0

Table 7

Incidence of Class IV + V (suspected or definitely malignant) specimens per 1000 gynaecological specimens examined.

Age	Chinese		Malay		Indian	
	Pill	None	Pill	None	Pill	None
< 20	0	0	0	0	0	0
21 — 30	0	1	0	0	0	0
31 — 40	1	4	0	0	0	0
41 — 50	6	0	0	0	0	31
>50	0	1	0	0	0	0

tuates both above and below the incidences of the other two racial groups. Although a few of these groups are too small to reach statistical significance by themselves, the near unanimity of the Chinese-Malay comparisons provide a rather clear indication of a real racial difference in the incidence of cytological abnormalities.

Although the causes of these observed racial differences in cytological variations are not yet clear, the importance of their elucidation is emphasised by the finding of Stern and Neely (1964) that 85% of cervical carcinomas had progressed through dysplasia of the cervix. Classification of high risk groups may include cultural, genetic, and sampling factors. For example, a higher risk of cervical cancer in the United States was associated with several factors, including lower socio-economic class, non-circumcision of sexual partners, and early first intercourse (Hammond, 1969). While socio-economic data are not generally available for the individuals in this study, we feel that the majority of both the Chinese and the Malays examined are of lower socio-economic class. Malay males are circumcised, while practically none of the Chinese are. On the other hand, more Malays than Chinese get married under age 21.

For another factor, Petrakis (1971) and Wallace et al. (1971) have recently suggested the existence of a genetic basis for two types of cancer, and we cannot exclude hereditary factors as being important in the racial variation of cytological abnormalities found in this study.

Differences among the races also occur with respect to the incidence of cytological abnormalities in the pill users as compared to the no contraceptive group. Within the Chinese, the no contraceptive groups clearly have an increased incidence of Class II specimens over the pill groups within each of the five age classes, and the same trend prevails among the Malays, with the exception of the youngest age group. Again, within the Indians, the trends are not so clear although in three of the five age groups the pill users suffer greater incidence of cytological abnormalities, and in a fourth group, there is no comparison possible because of zero observations. These observed racial differences could again be due to a number of causes, including both differences in the actual incidence in the populations as well as differences in diagnostic coverage. For example, Stern et al., (1971) found differences in the prevalences of dysplasia in a homogenous population even prior to use of the contraceptives.

A further point emerges from these data which is quite clear statistically but interpretationally seems rather obscure. Regardless of the racial and

Table 8

Two Standard Errors 1, 2 for Comparisons of Percentages from Two Groups of Various Sizes.

First Group Sizes	Second Group Sizes								
	4000	1000	300	100	80	50	30	20	10
	For Percentages around 1								
4000	0.4	0.6	1.2	2.0	2.2	2.2	3.6	4.4	6.4
1000		0.3	1.2	2.0	2.2	2.8	3.6	4.4	6.4
300			1.6	2.2	2.6	3.0	3.8	4.6	6.4
100				2.8	3.0	3.4	4.2	4.8	6.6
80					3.2	3.6	4.2	5.0	6.6
50						5.0	4.6	5.2	6.8
30							5.2	5.8	7.2
20								6.2	7.8
10									8.8
	For Percentages around 20								
4000	1.8	2.8	4.8	8.0	9.0	11.4	14.6	18.0	23.4
1000		3.6	5.2	8.4	9.2	11.6	14.8	18.0	25.4
300			6.2	9.2	10.0	12.2	14.4	18.4	25.9
100				11.4	11.8	13.8	16.6	19.6	26.6
80					12.6	14.4	17.0	20.0	26.8
50						16.0	18.1	21.2	27.8
30							20.6	23.0	29.2
20								25.2	31.0
10									35.8

First Group Sizes	Second Group Sizes								
	4000	1000	300	100	80	50	30	20	10
	For Percentages around 10								
4000	1.4	2.0	3.6	6.0	6.8	8.6	11.0	13.4	19.0
1000		2.6	4.0	6.2	7.0	8.6	11.2	13.6	19.0
300			4.6	7.0	7.6	9.2	11.4	13.8	18.2
100				8.4	8.6	10.4	12.4	14.6	19.8
80					9.4	10.8	12.8	15.0	20.0
50						12.0	13.8	15.8	20.8
30							15.4	17.2	21.8
20								19.0	23.2
10									26.8
	For Percentages around 50								
4000	2.2	3.4	6.0	10.2	11.2	14.2	18.2	22.4	31.6
1000		4.4	6.6	10.4	11.6	14.4	18.6	22.6	31.8
300			7.8	11.6	12.6	13.2	19.2	23.0	32.2
100				14.2	15.0	17.4	20.8	24.4	33.2
80					15.8	17.8	21.2	24.8	33.4
50						20.0	23.0	26.4	34.6
30							25.6	28.8	36.4
20								31.8	38.8
10									44.8

1 Equivalent to 4.55% significance level.
2 The standard errors were computed as $se = PQ\,(1/n + 1/n')^{\frac{1}{2}}$, where P = proportion "successes" in a population, Q = 1-P, n = sample size for one group and n' = sample size for the other groups.

age differences present, there is a lower incidence of cytological abnormalities in the pill users than in the no contraceptive group. However, we believe that such observed results should be treated with extreme caution because of the possibility that the pill and the no contraceptive groups are initially different. For example, Stern et al. (1971) found 45.2% of those choosing the pill had dysplasia prior to contraceptive usage, compared to 36.2% of the intra-uterine contraceptive device group with prior dysplasia.

To obtain evidence on this point, we examined 3,622 records that came to IMR in five randomly selected 2-week periods for some indication of gynaecological abnormalities or complaints prior to the clinic visit. The results were that 27.5% of the 2,613 specimens from contraceptive users (largely pill) had prior complaints, compared to 28.8% of the 1,009 no contraceptive group with prior complaints. Thus, these data provide little indication that a larger proportion of the no contraceptive group specimens resulted from individuals with a realised need for health care, as compared to the pill user group. However, we speculate that the family planning program may be providing generally better cancer and pre-cancer detection services to those whom it reaches, in addition to the other services the program provides and in similarity to the Barbados Island Family Planning Program (Cummins, 1969).

Summary and Conclusions

Based on 11,650 gynaecological specimens examined by the IMR Cytology Unit in 1970, the incidence of slightly abnormal specimens is greater in

1) 22 of 24 successively older, race by contraceptive groups;
2) 9 of 10 Chinese as compared to Malay age by contraceptive groups, with the Indians being generally intermediate but based on rather smaller numbers; and
3) 11 of 14 no contraceptive as compared to pill user age by racial groups.

Further, although the incidence of the more serious cytological variations are much lower and therefore show greater statistical fluctuation, the data available are generally consistent with the foregoing pattern of slightly abnormal specimens described above. Although some discussion regarding the causal factors of these observed cytological variations has been offered, much further work remains before any definitive conclusions can be reached.

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