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The Aetiology and Pathology of Uterine Cancer in Ceylon*

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In a previous paper based on the study of 2,295 biopsies of malignant tumours it was pointed out (Cooray, 1944) that carcinoma of the uterus ranked highest in biopsy material received from various parts of Ceylon. It was therefore considered appropriate to make a more extensive study of this condition which is known to cause a high morbidity and mortality amongst women in this country.

Material and Methods

Nine hundred and thirty-two consecutive biopsy specimens of carcinoma of the uterine cervix and body sent to the Department of Pathology, University of Ceylon, by the Gynaecological Surgeons of the General Hospital, Colombo, during the fifteen year period 1936-1950, were carefully examined. All these specimens were graded according to the degree of differentiation. The cervical carcinomata were further classified into three morphological groups viz. spinal cell, spindle cell and transitional cell groups according to the type cell that predominated in a section (Novak, 1940). The histological material was also made use of to study the genesis of the carcinomatous process in the cervix. Unusual histological patterns were noted and the mode of extension of the growth, as far as could be ascertained from sections, was also studied. Particular attention was paid to stromal reactions and vascular changes in cervical carcinoma because it was thought that certain anomalous features in the behaviour of cervical growths could be explained on the basis of stromal changes.

Case records were available in 539 cases of cervical carcinomata. These were carefully analysed, particular attention being paid to the observations recorded at the time of admission of the patient to hospital, regarding the extent of the growth. The information so obtained was made use of to ascertain whether or not a relationship existed between invasiveness and the degree of malignancy revealed in the biopsy specimen. An attempt was also made to find out whether parity plays an aetiological role in carcinoma of the cervix. Other useful information obtained from the case records were, the age, racial incidence and social status of the sufferers, duration of the growth prior to seeking treatment and the geographical distribution of the disease.

In order to gain a rough idea regarding the prevalence of uterine carcinoma in Ceylon, the total number of admissions to the Gynaecological wards of the General Hospital, Colombo and the total number of uterine carcinomata during the period under review were estimated.

*Paper read before the medical section of the Ceylon Association for the Advancement of Science in December 1951.

Results

The results obtained are given below in the following tables.

TABLE 1

Incidence of uterine carcinoma amongst admissions to Gynaecological wards of the General Hospital, Colombo (1936-1950).

Total admissions (all gynaecological complaints) 30,199.

	No. of biopsies	
Carcinoma of the cervix 3,426 (11%)	885	26%
Carcinoma of the body 75 (0·2%)	47	63%
	932	

TABLE 2

Site distribution of carcinoma in biopsy material (1936-50).

Total number of biopsies—uterine cervix and body 932.

	No. of biopsies	
Epidermoid carcinoma (Portio vaginalis)	856	92%
Adenocarcinoma (cervical canal)	27	3%
Mixture of adenocarcinoma and epidermoid carcinoma	2	
Endometrial carcinoma (uterine body)	47	5%
Total	932	100

TABLE 3

Cellular types in 856 *epidermoid carcinomas.*

	Number	%
Spinal cell type	375	44
Transitional cell type	416	49
Spindle cell type	44	5
Unclassified	21	2
	856	100

TABLE 4

Histological grading.

	Portio Vaginalis		*Cervical Canal Adeno-Carcinoma*		*Mixture of Adeno and Squamous Carcinoma*		*Uterine Body*	
	No.	%	*No.*	%	*No.*	%	*No.*	%
Grade I—75% Differentiation (no anaplasia) ..	49	6	14	52	—	—	28	60
Grade II—50% Differentiation..	68	8	6	22	—	—	7	15
Grade III—25% Differentiation..	179	21	4	15	—	—	5	11
Grade IV—No Differentiation (most anaplastic)..	544	64	3	11	—	—	4	9
Unclassified ..	16	1	—	—	—	—	3	5
Total	856		27		2		47	
GRAND TOTAL			932					

TABLE 5

Invasiveness in 534 cases of cervical carcinoma as estimated clinically.

	Portio Vaginalis	*Cervical Canal*	*Total*	%
Stage 1. Carcinoma confined to the cervix ..	100	5	105	20
Stage 2. Parametrium infiltrated but no invasion of pelvic wall. Upper 1/3 of vagina also infiltrated ..	198	8	206	39
Stage 3. Invasion of parametrium and pelvic wall—Lower 1/3 of vagina involved ..	178	3	181	34
Stage 4. Involves bladder—Recto vaginal fistula Distant metastases ..	32	—	32	6
Not staged for lack of data..	10	—	10	1
	518	16	534	100

TABLE 6

Distribution of 534 cases of cervical carcinoma in each grade according to clinical stage.

Grade	Stage	*Portio Vaginalis* Number	%	*Cervical Canal* Number	%
I	1 & 2	19	76	10	90
	3 & 4	5	20	1	10
	Unstaged	1	4	—	—
II	1 & 2	24	54	1	50
	3 & 4	20	46	1	50
	Unstaged	—	—	—	—
III	1 & 2	54	51	—	—
	3 & 4	51	48	1	100
	Unstaged	2	1	—	—
IV	1 & 2	193	59	1	50
	3 & 4	129	39	1	50
	Unstaged	7	2	—	—
Not Graded	1 & 2	8			
	3 & 4	5			
	Unstaged	—			
Total		518		16	
GRAND TOTAL		534			

Tables 7, 8 and 9 have been prepared with a view to ascertaining whether any relationship exists between (1) invasiveness of cervical growths as established clinically and ages of patients and duration of symptoms prior to seeking medical advice (2) age and the degree of malignancy as estimated histologically.

TABLE 7

Invasiveness (Stage) and age—(498 cases of cervical carcinoma).

	Stage 1 No.	%	*Stage* 2 No.	%	*Stage* 3 No.	%	*Stage* 4 No.	%
Under 44 years	55	51	95	46	81	51	12	43
Over 44 years	52	49	112	54	75	49	16	57
	107		207		156		28	

TABLE 8

Invasiveness (Stage) and duration of symptoms. (526 *cases of cervical carcinoma*).

	Stage 1		*Stage* 2		*Stage* 3 & 4	
	No.	%	No.	%	No.	%
Under 3 months	39	36	70	34	60	28
3-6 months	27	25	62	29	68	32
Over 6 months	40	37	67	32	81	40
Period unknown	2	2	8	4	2	—
Total	108		207		211	

TABLE 9

Degree of malignancy (grade) and age. (856 *cases of cervical carcinoma*).*

	Grade I		*Grade II*		*Grade III*		*Grade IV*	
	No.	%	No.	%	No.	%	No.	%
Under 44 years	14	29	27	40	68	38	228	42
Over 44 years	24	49	38	56	96	54	261	48
Age unknown	11	22	3	4	15	8	55	10
	49		68		179		544	

*In 16 cases the grade could not be ascertaind.

TABLE 10

Interval between first symptom to first consultation. (*Carcinoma of cervix*).

2 weeks	2%
2 weeks-1 month	8%
1-3 months	23%
3-6 months	29%
6 months-1 year	26%
1-2 years	7%
Over 2 years	3%
Not stated	2%

TABLE 11

Age distribution of carcinoma of portio vaginalis, cervical canal, and uterine body.

Age groups in years	*Portio Vaginalis*		*Cervical Canal*		*Uterine Body*	
	No.	%	No.	%	No.	%
15-24	4	1	1	4	1	2
25-34	77	9	3	12	—	—
35-44	266	31	6	24	10	21
45-54	246	29	13	44	7	15
55-64	133	16	3	12	14	30
65-74	32	4	—	—	6	13
75-84	10	1	—	—	2	4
85-94	1	—	—	—	—	—
Not stated	87	9	1	4	7	15
Total	856		27		47	

TABLE 12

Racial Distribution

	Cervix		*Body*	
	No. of Cases	%	*No. of Cases*	%
Sinhalese	742	84	35	74
Ceylon Tamils	83	9	1	
Indian Tamils	13	1	—	
Burghers	31	3	4	
Muslims	7		1	26
Malays	5	2	—	
Europeans	1		1	
Race unknown	3		5	
Total	885		47	

The localities from which patients with uterine cancer were admitted to the Gynaecological wards of the General Hospital, Colombo, are shown in Table 13.

TABLE 13

	% *of Cases*
Colombo Municipality	20
Western Province	44
Southern Province	10
North-Western	9
Sabaragamuwa	6
Central	4
Northern	4
North-Central	1
Eastern	1
Uva	1

Marital State. There were only two unmarried women in the whole series. Table 14 shows the relationship between parity and incidence of cervical carcinoma and Table 15 the percentage of pregnancies in each age group.

TABLE 14

Parity and incidence of cervical carcinoma.

Number of pregnancies	*% of cases of cervical carcinoma*
0	2
1	5
2	9
3	8
4	10
5	15
6	14
7	10
8	7
9	9
10	5
11	2
12	3
13	1

TABLE 15

Percentage of pregnancies in different age groups.

Age group in years	*% of pregnancies*
15-24	2
25-34	9
35-44	38
45-54	35
55-64	15
65-74	1

Discussion

Incidence of uterine cancer. Mortality and morbidity records which are sometimes helpful in estimating the incidence of uterine carcinoma are not of much value in this country for several reasons. On account of inaccuracies in death registration mortality figures of the Registrar General show only 1,021 cases of deaths in the whole island due to uterine cancer during the 13 year period 1937-1949. The unreliability of this figure as an indication of incidence of uterine carcinoma is seen by the fact that carcinoma admissions during this same period into one single hospital in the island (viz. General Hospital, Colombo) were 2,966. It is therefore quite apparent that a large number of uterine cancers fail to be entered in death certificates.

Statistics of the medical department based on hospital returns are also unreliable. In the first place, owing to the absence of a separate column for uterine cancer in the forms used by hospitals, carcinoma of the uterus is included under the general heading ' cancer of the female genital organs '. Secondly, as no special effort to

diagnose uterine carcinoma such as vaginal examination, biopsy and curettage is made, excepting in the larger provincial hospitals, several such cases are undetected and are therefore not included in the hospital returns of the island.

Uterine cancer, however, ranks very high in biopsy material received from various parts of Ceylon. One of us (Cooray, loc. cit.) has shown in a previous study that 348 out of 1,815 carcinoma biopsies were from the uterine cervix and body (316 from the cervix and 32 from the body). There is also evidence that its incidence amongst gynaecological admissions is extremely high. The gynaecological wards of the general hospital, where a high standard of accuracy in diagnosis is maintained, receive patients from all parts of the island. Table 1 shows that amongst 30,199 admissions for gynaecological complaints which also include abortions, there have been 3,426 (11 per cent.) cases diagnosed clinically as carcinoma of the cervix and 75 (0·2 per cent.) as of the uterine body. If 'abortions' are excluded from the series, the incidence of uterine carcinoma amongst purely gynaecological admissions will be found to be even much higher. If to these cancer admissions is added the number of cases that are directed to other institutions, such as 'homes for the incurables', the incidence will be found to be still higher. It would therefore appear that Ceylon is in no way different from other tropical countries where this form of malignant disease has been reported to occur with great frequency. (Willis, 1948 and Khanolkar, 1950).

It is seen (Table 1) that the large number of uterine carcinomas is made up chiefly of cervical cancers, there being only a few cases (viz. 0·2 per cent.) of corporeal cancers. According to the statement of Willis (loc. cit.) that cervical cancer is only 3 or 4 times as common as body cancer, there appears to be a marked disproportion in this country between the two. This marked difference of cancer incidence in the two different sites is probably due to two causes ; (1) on account of the lower expectation of life in tropical countries only a few live up to the age period when corporeal carcinoma commences. (2) On account of early marriage and child bearing the proportion of unmarried and nulliparous women in the population who are more likely to develop uterine body cancer is low in a country like Ceylon. Diagnostic failures too may account for a number of unrecognised cancers of the uterine body. Whereas in an exposed site such as the cervix the diagnosis of carcinoma is relatively easy, in the uterine body, carcinomata are liable to be missed unless more elaborate methods such as curettage followed by microscopy are employed in diagnosis. Only a few hospitals in Ceylon employ such methods. It is therefore difficult to state whether the low incidence of corporeal carcinoma is apparent or real. Possibly it is far less common than cervical cancer, but the figure 0·2 per cent. appears to be a very low estimate.

Geographical Distribution. A study of table 13 shows that uterine cancer is islandwide in prevalence. Only 20 per cent. of the patients resided within the municipal limits of Colombo and 43 per cent. came from urban as well as rural areas in the Western Province. The remaining 37 per cent. were from larger towns as well as remote villages in distant parts of the island. These figures do not give any indication whatsoever as to the incidence of uterine cancer in the different provinces of Ceylon, but they do indicate that 80 per cent. of women outside Colombo affected with uterine cancer are put to considerable hardship, as their limited incomes are

spent in seeking treatment in Colombo. Is it not highly probable that those who are even poorer do not go to any hospital at all till the disease is far too advanced, when they are compelled to seek treatment only for the relief of symptoms ?

Economic Status, Parity and Uterine Cancer. Almost all these cases were admitted to the non-paying section of the General Hospital, Colombo, which is intended mainly for the poor. Some of these women were wage earners—particularly the Indian Tamils (Table 12), employed in estates—while others had no definite occupations excepting housework, the bread winners being employed as daily paid labourers, motor car drivers, mechanics, carpenters, and clerks. The incomes of these people probably did not exceed Rs. 50/- to 150/- per mensem. It is well known that cancer of the cervix occurs more often in the poorer classes. Clemmesen and Nielsen (1951), in a very careful study, found this to be so in Copenhagen. No reliable statistics regarding the incidence of cervical cancer in higher economic strata in Ceylon are available. However, if the number of admissions of cervical cancer to the paying wards of the hospital, where only the richer classes could afford treatment is compared with that of non-paying wards, such admissions amongst women of the higher income groups will be found to be very low. It is also well known that poorer classes have larger families. In this series nearly 50 per cent. of the women with cervical cancer had gone through 4 to 7 pregnancies (Table 14). Poverty no doubt, influences the course of the pregnancy and more particularly that of the labour and the puerperium. In most instances the labour is conducted in poor homes under unfavourable hygienic conditions. Injuries to the cervix sustained during parturition are more liable to be undetected in such circumstances and on account of unclean habits and improper attention during the puerperium cervical lesions are likely to progress without healing. These factors predispose to chronic cervicitis and cervical erosions, which behave as precancerous lesions (vide pp. 12 and 13). That the incidence of cervical cancer bears a close relationship to the number of pregnancies is shown in Table 14. Only 2 per cent. of the cases occurred in nulliparae, while nearly 50 per cent. occurred in women with 4 to 7 pregnancies. Table 15 shows also that the largest number of pregnancies, viz. 38 per cent. and 35 per cent. occurred in the two age groups 35 to 44 and 45 to 54 in which the cervical cancer incidence was also highest. These facts, viz. that a woman is most liable to develop cervical cancer during the period of greatest fertility and the increase in carcinoma incidence with parity, show that the act of child bearing plays a definite aetiological role in the onset of carcinoma. From the earlier discussion on economic status and carcinoma incidence, it would appear that both child bearing and unfavourable economic conditions do operate in the causation of cervical carcinoma. Women among our poor classes get more children—in other words repeated traumatisation of the cervical tissue results, and lack of attention during the puerperium and unclean habits also due to poverty, lead to failure of healing of the cervical lesions. It is probably a combination of these two aetiological factors which is responsible for the high incidence of cervical cancer in this country. We are not in a position to state whether hormonal changes associated with pregnancy exert an additive effect on the local lesions of the cervix caused during parturition.

Age Incidence. In Table 11 the age incidence of carcinoma of portio vaginalis, cervical canal and uterine body is tabulated separately. In the case of the portio vaginalis, there is no significant difference in the number of women in the two age

groups 35-44 and 45-54 who are likely to develop carcinoma. The largest number of cases are thus seen in the twenty year period 35-54. The maximum incidence in cervical canal carcinoma is between 45-54 years. If both these sites are considered together in studying the age incidence of cervical carcinoma as was done previously Cooray (loc. cit.) it will be found that the maximum incidence lies in the age group 45-54 years. It is not possible to draw any definite conclusions regarding age incidence of corporeal carcinoma as in 15 per cent. of the cases the age had not been recorded. The available figures (Table 11) however suggest that cancer of the body occurs at a later period of life, viz. 55 to 64 years.

The age incidence of cervical carcinoma as recorded by Truelsen (1949) in Copenhagen is in close agreement with our findings. In a series of 1,633 cases he noted that 28·9 per cent. and 28·7 per cent. were found in the age groups 35-44 and 45-54 respectively. As in our series the morbidity was highest in the age group 45-54 years and fell slowly after this age. These figures are at slight variance from those recorded in voluntary and L.C.C. hospitals in London by Harnett (1949). He found that the largest number of cases were seen in the age groups 45-54 and 55-64. In the former age group there were 285 cases (33 per cent.) and in the latter 252 (29 per cent.). In the younger age group 35-44 there were only 140 cases (16 per cent.) (cf. 31 per cent. in our series). It would therefore appear that a greater proportion of younger women both in Ceylon and Denmark are more liable to develop cervical cancer than in London. The evidence which has been adduced earlier strongly suggest an aetiological relationship between cervical carcinoma in Ceylon and parturition.

Duration of cervical cancer prior to treatment. A fair indication of the awareness of a community to cancer can be judged by the time interval between the onset of the first symptom and the first consultation (Table 10). Twenty-nine per cent. of the sufferers sought medical advice between 3-6 months of the onset of symptoms, 10 per cent. within a month, 31 per cent. within 3 months, but 26 per cent. did not consult a doctor for one year. Conditions are not much different amongst other communities which are acknowledged to be more enlightened about cancer. In Harnett's (loc. cit.) series of hospital class patients 45·5 per cent. consulted a doctor within 3 months (cf. 33 per cent. in our series) 20·7 per cent. within the next 3 months and in 25·6 per cent. the symptoms were of more than 6 months duration. It would therefore appear that women as a class are reluctant to seek medical advice early. More often vaginal bleeding or a watery discharge is apt to be considered as being some menstrual disorder associated with the ' change in life '. During this period when no notice is being taken of the symptoms, the cancer starts to spread. It is seen (Table 8) that a larger proportion of cervical growths remained confined to the cervix as long as the symptoms were less than 3 months in duration. The percentage of cases in stages 3 and 4 increased with the duration of symptoms. Delay in seeking treatment is thus conducive to the spread of carcinoma, which in turn, interferes adversely with therapeutic procedures. A reasonable chance of therapeutic success is afforded to those who seek treatment within 3 months and from our figures it would appear that only 33 per cent. are benefited by early treatment. However, the fact that a fairly large proportion of stage 1 and 2 carcinoma were seen in women whose symptoms had lasted as long as six months suggest a tendency of the carcinoma to remain confined to the cervix or its immediate vicinity, the parametrium, for a considerable

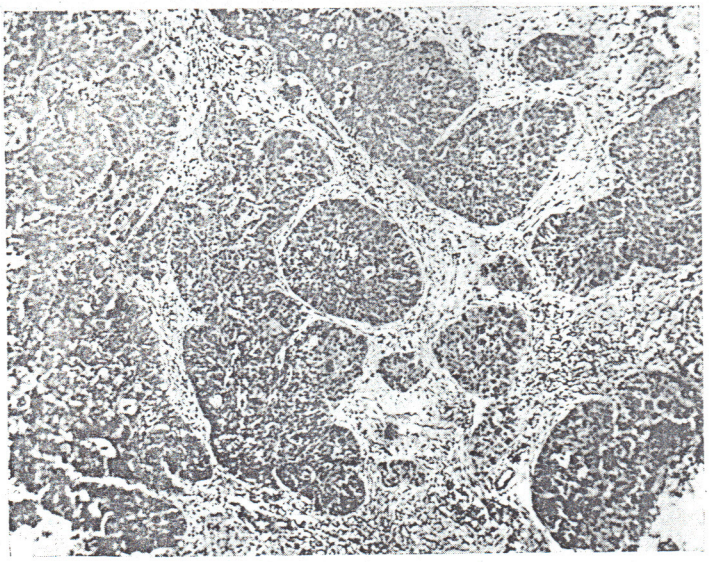

Fig. 1
A fairly common type of cervical carcinoma, composed of undifferentiated cell masses
H & E × 70

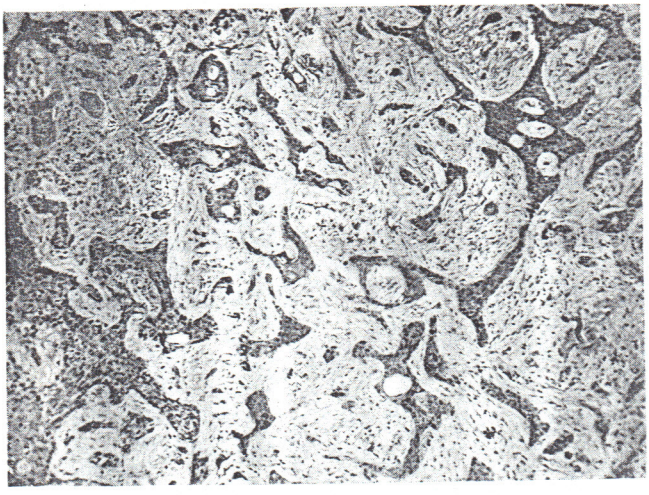

Fig. 2
A fairly well differentiated type of cervical carcinoma with abundant stroma
H & E × 70

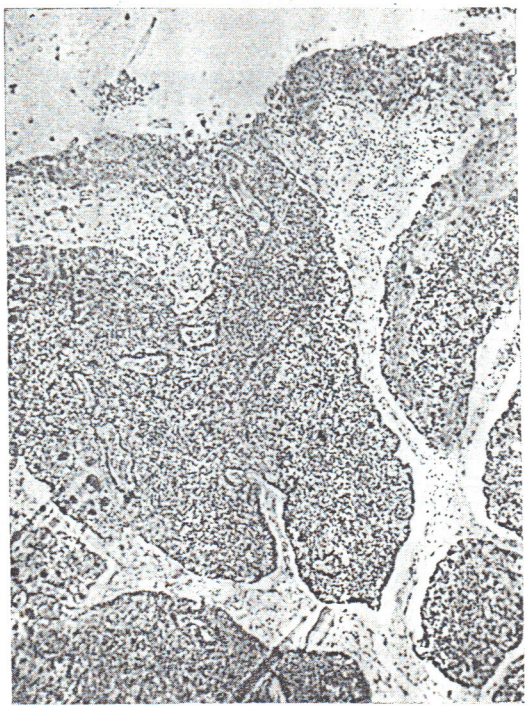

Fig. 3

Carcinoma of the cervix. Note resemblance to rodent ulcer. (Lining epithelium on top)
H & E × 70

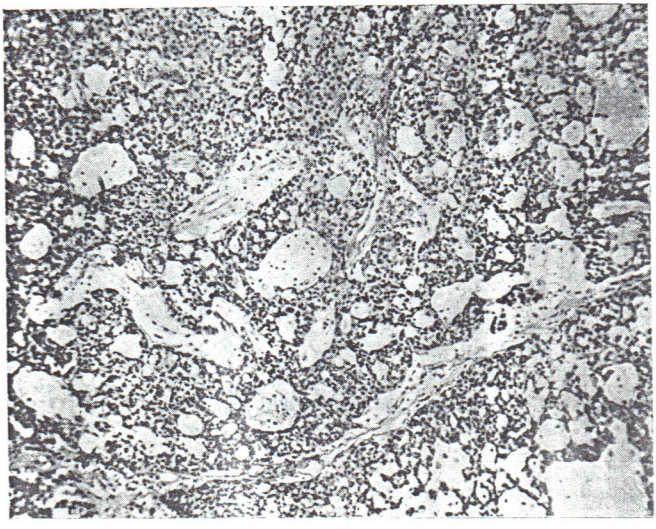

Fig. 4

Carcinoma of the cervix. Note resemblance to cystic type of basal cell carcinoma
H & E × 70

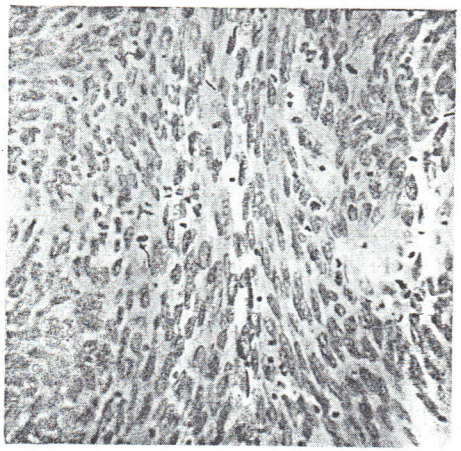

Fig. 5
Spindle cell carcinoma of the cervix
H & E × 200

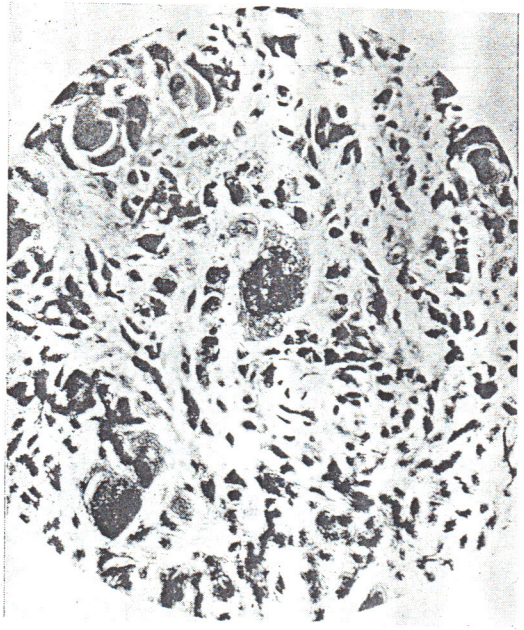

Fig. 6
A markedly anaplastic type of cervical carcinoma.
Note conspicuous tumour giant cells
H & E × 200

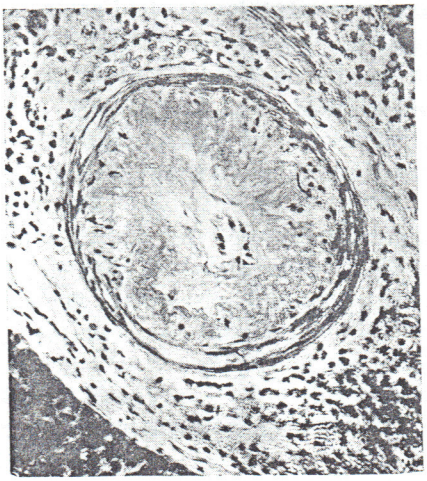

Fig. 7
Blood vessel in a carcinomatous growth, showing marked narrowing of lumen with fibrinoid necrosis of vessel wall
H & E × 200

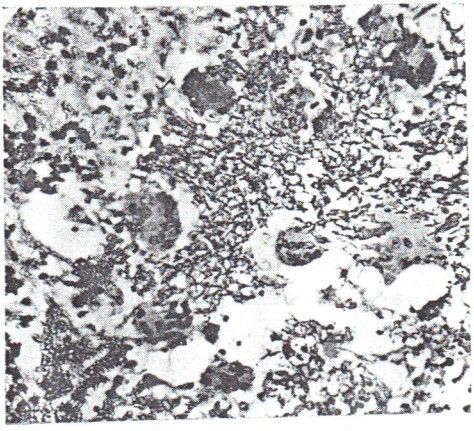

Fig. 8
Giant cell reaction around keratinised material in a squamous carcinoma
H & E × 200

period of time. As we will point out later, on account of retrogressive changes taking place in the neoplasm itself, the rate of its growth is temporarily retarded. The lack of strict correlation between duration of the growth and its invasiveness. (Table 8) is to be explained by these retrogressive changes (*vide infra*).

Histology. Carcinomas of the uterine body and cervical canal were in most cases fully differentiated growths (vide Table 4) conforming to the well recognised picture of 'adenocarcinoma'. Histological differentiation between growths occurring at these two sites was often difficult, excepting in a few cases where there was metaplastic epithelium in corporeal carcinomas (adenoacanthoma). Carcinomas of the portio vaginalis, on the other hand consisted of undifferentiated growths, 64 per cent. being grade IV carcinomata and only 6 per cent. being grade I (Table 4). As regards cell type, 49 per cent. were of the transitional type, 44 per cent. of the spinal cell type, only 5 being of the spindle cell variety (Table 3). Classification of growths according to cell type does not appear to be of much practical value, for it only indicates the type of cell that predominates in a particular section without indicating the degree to which the growth is differentiated. For this reason we have considered grading based on epidermoid differentiation of greater value in the study of carcinoma of the portio vaginalis.

There is so much structural variation in different tumours that several complicated histological patterns are seen. A fairly common type (Fig. 1) consists of masses of undifferentiated cells separated from each other by scanty stroma. Some tumours are completely devoid of stroma and consist only of cells ('encephaloid type') whereas in others abundant stroma is found between smaller masses of differentiated epithelium (Fig. 2). An unusual pattern seen at times is that which resembles a basal cell carcinoma consisting of epithelial masses with a peripheral layer of hyperchromatic columnar cells (Fig. 3). Sometimes the growth resembles the cystic type of basal cell carcinoma (Fig. 4). Occasionally the tumour is composed almost entirely of spindle shaped cells simulating a spindle cell sarcoma (Fig. 5) and in not a few cases anaplasia is so marked that giant cells form a conspicuous feature (Fig. 6). This diversity of structure in cervical carcinoma has been commented on by Willis (loc. cit.).

Retrogressive changes in cervical carcinomata. In a number of cases we have noted certain histological changes which are likely to bring about a temporary arrest or retardation of growth. A considerable reduction in the blood flow to the tumour is brought about by sub-endothelial proliferation of the intimal connective tissue with marked narrowing of the lumen. Fibrinoid necrosis of the intima has been noted in some vessels (Fig. 7). As the result of these vascular changes the tumour parenchyma undergoes necrosis. Unusual histiocytic reactions also bring about destruction of tumour elements. In some, giant cells aggregate around keratinised material (Fig. 8) ingesting fragments of keratin. Secondary infection of cervical growths lead to the accumulation of polymorphonuclear leucocytes which result in the dissolution of large tumour masses (Fig. 9). The effect of these changes is to cause a temporary arrest or retardation of the growth. These retrogressive changes in the neoplasm probably limit its capacity to invade and thus afford an explanation for the lack of strict correlation between invasiveness, as estimated clinically and the duration (Table 8). We also believe that these changes deprive cervical neoplasms

which are histologically of a very high grade of malignancy of their invasive properties. Thus in stages 1 and 2 there were 51 per cent. of grade III carcinomata and 59 per cent. of grade IV carcinomata (Table 6). If strict correlation existed between invasiveness as estimated clinically by staging and the degree of malignancy estimated histologically, such a large proportion of grades III and IV carcinomas would not have been found in stages 1 and 2. This lack of strict correlation is once again probably caused by retrogressive changes. The practical importance of this observation is that histological grading is not always helpful in predicting the behaviour of a cervical carcinoma. The evidence presented in Table 6 suggests that grade I growths, i.e. highly differentiated carcinomata, are the least likely to invade and tend to be confined to the cervix or its immediate vicinity, but with the onset of de-differentiation prediction of behaviour on the basis of a histological examination becomes impossible.

The mode of origin of cervical carcinoma. Hyperplasia of the epithelium lining the portio vaginalis is met with in a large number of benign cervical lesions. A careful study of the histological material has shown that the initial stages of the carcinomatous process commence in this hyperplastic epithelium. The epithelial cells in the deeper parts undergo a transformation. They become altered in their morphological appearances so as to be distinguishable from the non-malignant cells, assume a polarity (Fig. 10) and divide rapidly by mitosis. These changes may be regarded as a malignant change occurring *in situ* before the acquisition of invasive properties by the growth and may be looked upon as constituting pre-invasive carcinoma. The recognition of this condition is of the utmost practical importance as, undoubtedly, the pre-invasive carcinomata could be most effectively treated and cured by simple conservative measures. Moreover according to Novak (loc. cit.) there may apparently be a very definite and perhaps long pause or lag between the pre-invasive and invasive phase of the cancer process. The invasive phase commences by growth downwards into the stroma of slender tongue like epithelial processes (Fig. 11) at multifocal points. The various stages of the cancer process, viz. the simple hyperplasia, carcinoma *in situ* or pre-invasive cancer and the early invasion by slender epithelial processes can sometimes be visualised in single sections as shown in Fig. 12.

Another mode of origin is from metaplastic epithelium lining dilated cervical glands which are the seat of adenomatous proliferation (Figs. 13 and 14). Both these changes, viz. hyperplastic squamous epithelium and adenomatous proliferation of glands which have been shown to be the precursors of cervical carcinoma are frequently seen in the condition known to gynaecologists as chronic cervicitis. The presumption that a causal relationship exists between chronic cervicitis and carcinoma appears to be justified, although it is not yet possible to express a definite opinion on the question. However, it is advisable to regard those cases of cervicitis exhibiting a gross degree of epithelial hyperplasia and glandular proliferation as precancerous. Such cases would require periodic examination. We have already drawn attention to the possible relationship between parturition and chronic cervicitis (p. 9) and the evidence which has now been adduced, regarding the aetiological role of chronic cervicitis in the causation of cervical carcinoma, is sufficient to justify the conclusion that, in the prophylaxis of uterine cancer, periodic post-natal examination should be conducted with the utmost care. Failure to inspect the cervix with the aid of a

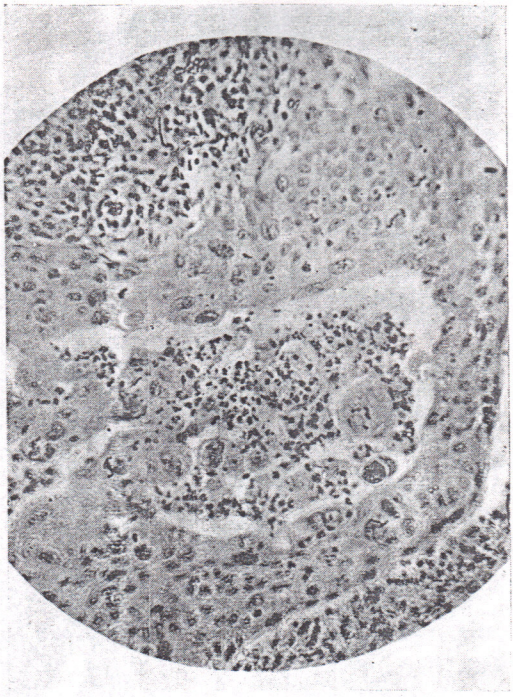

Fig. 9
A large epithelial mass invaded by polymorpho-nuclear leucocytes (centre) H & E × 200

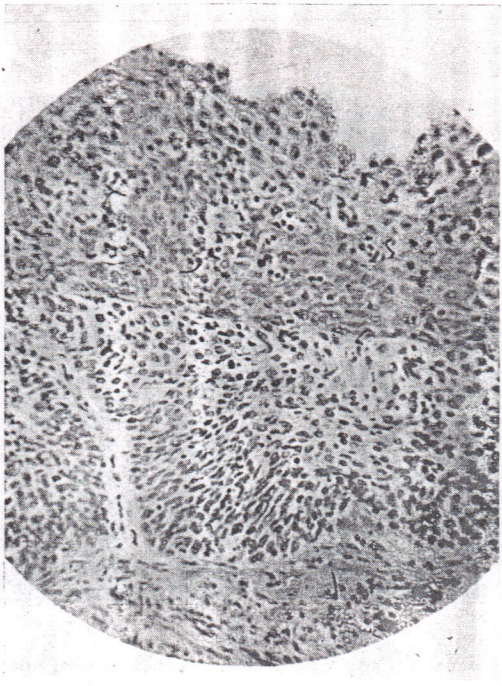

Fig. 10
Pre-invasive carcinoma. Marked epithelial hyper-plasia with malignant transformation of the epithelial cells in the b ottom half of the picture H & E × 200

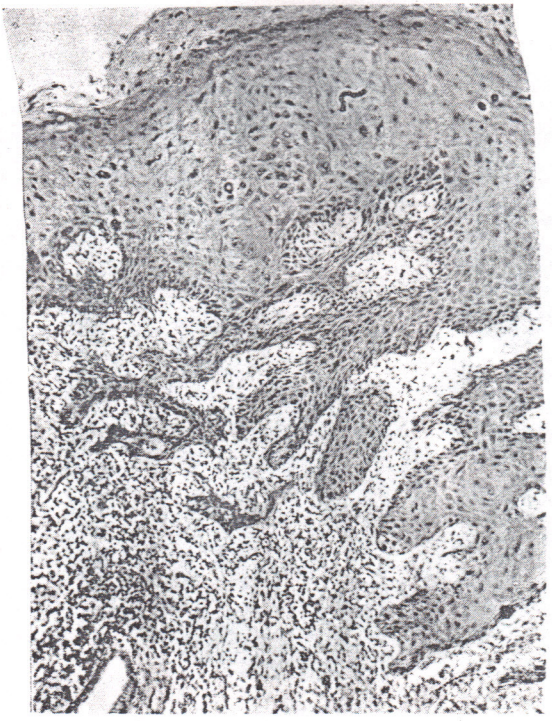

Fig. 11
Early invasive carcinoma. Tongue-like epithelial processes growing into the deeper tissue
H & E × 70

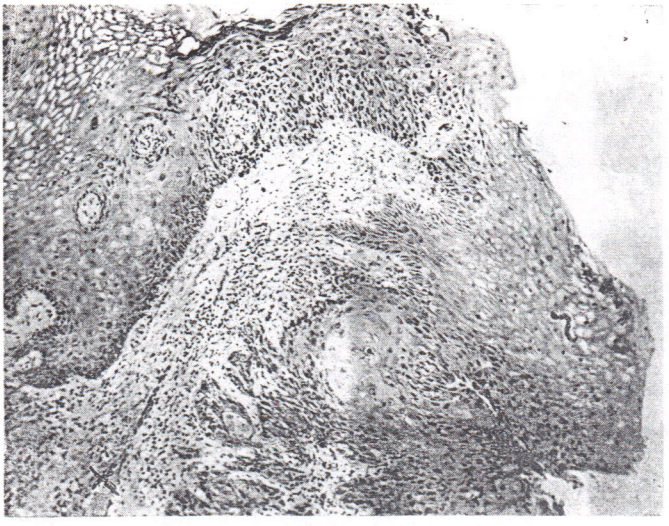

Fig. 12
Composite picture of the different stages of the carcinomatous process. Hyperplastic epithelium on left, pre-invasive carcinoma on top and invasive carcinoma with cell nests bottom right
H & E × 70

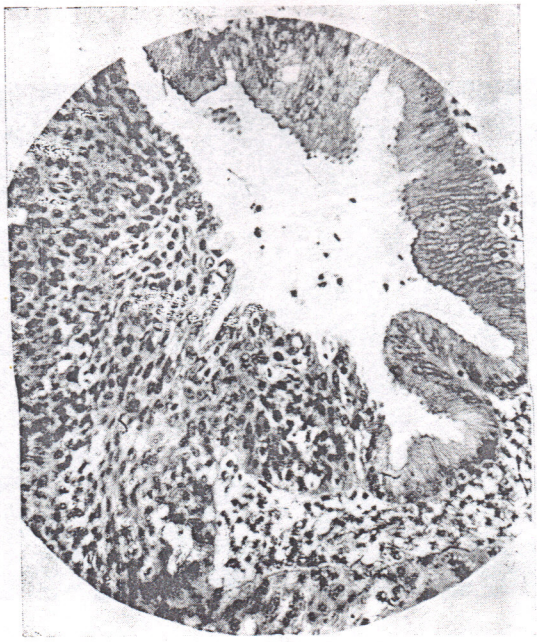

Fig. 13

Carcinoma arising from metaplastic epithelium of a dilated cervical gland. Rest of the gland lined by tall columnar epithelium

H & E × 200

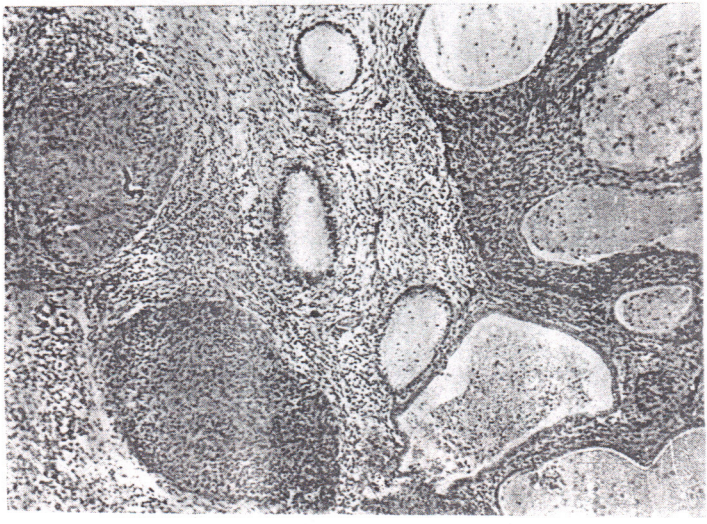

Fig. 14

Multicentric origin of cervical cancer from dilated cervical glands

H & E × 70

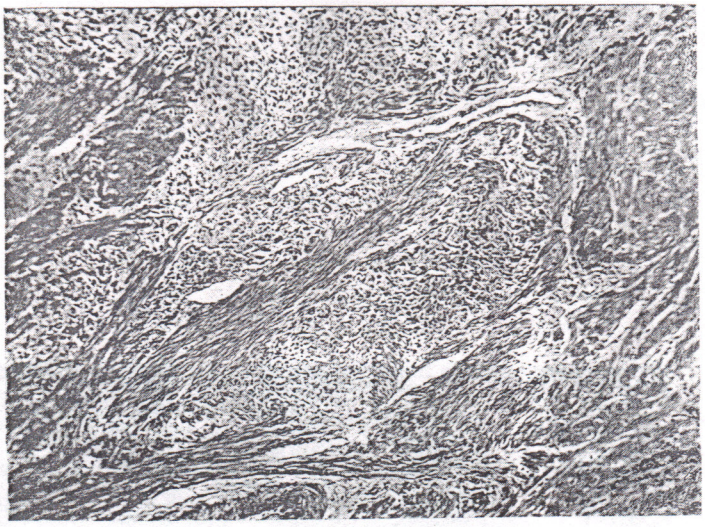

Fig. 15
Spread of carcinoma along tissue planes. Cervical muscle is widely separated by the proliferating cancer cells
H & E × 70

Fig. 16
Lymphatic spread of cervical carcinoma. Masses of cancer cells are seen in lymphatics
H & E × 70

Fig. 17
Growth of cancer cells in thrombosed blood vessels
H & E × 70

speculum will lead to failure in the diagnosis of not only chronic cervicitis but also early pre-invasive or grade I carcinoma which can be treated effectively.

Spread of carcinoma of portio vaginalis. Local spread take place by invasion along tissue planes (Fig. 15). In this way the underlying smooth muscle of the cervix is invaded. Metastases result from entry of tumour cells into lymphatics (Fig. 16) and blood vessels. In the later case the tumour cells coming into contact with the flowing blood become covered by a layer of thrombus (Fig. 17). Subsequently they infiltrate the thrombus along its interstices until they reach larger vascular trunks, when they are carried to distant parts as emboli.

Summary and Conclusions

1. Eleven out of 100 women admitted for gynaecological complaints suffer from cancer of the cervix ; a very much smaller number suffer from body cancer. The markedly low incidence of body cancer may be due to (i) the smaller numbers reaching the age when such cancers are known to arise (ii) the smaller proportion of nulliparous and single females in our population as compared with other countries (iii) possible diagnostic failures resulting from lack of facilities for the thorough investigation of post menopausal bleeding.

2. Uterine cancer is islandwide in distribution. Eighty per cent. of the cancer admissions are from all over the island outside the Colombo municipal limits. It is therefore imperative to provide diagnostic centres and facilities for treatment in all the larger hospitals. Such measures would make the detection of early cases possible.

3. Carcinoma of the portio vaginalis appears to show maximum incidence a decade earlier than that of the cervical canal, and corporeal carcinoma, a decade later.

4. Parturition *per se* is probably not an aetiological factor in cervical carcinoma, but in a poverty stricken population child bearing is not unattended by certain risks. Lack of proper attention during the puerperium and unhygienic conditions in the case of the poorer classes lead to progressive changes in the traumatised cervix which probably predispose to carcinoma.

5. Sixty-four per cent. of cervical cancers belong to the undifferentiated (grade IV) type. Grade I type form only 6 per cent. and these are the least invasive. The behaviour of the carcinoma as regards invasiveness cannot be predicted in the case of grades II, III and IV, on account of certain intrinsic changes that take place in the growth. For the same reason the rate of growth is temporarily retarded. Delay in seeking treatment increases the chances of spread once the carcinoma extends beyond the territory of the cervix. There is no relationship between age and the degree of malignancy and invasiveness.

6. The retrogressive changes in the neoplasm which retard the continued growth even of anaplastic and undifferentiated types are (*a*) histiocytic and polymorphonuclear reactions which destroy cancer cells and (*b*) occlusive changes in blood vessels which interfere with their nutrition.

7. Correct histological diagnoses depend on the recognition of the different types of cervical cancer which show a marked variability.

8. Epithelial hyperplasia precedes neoplasia. The neoplastic epithelium at first is not invasive. It is urged that due recognition be given to this stage as

appropriate treatment before the acquisition of invasive properties is the only hope of a radical cure and lowering of mortality.

Acknowledgements

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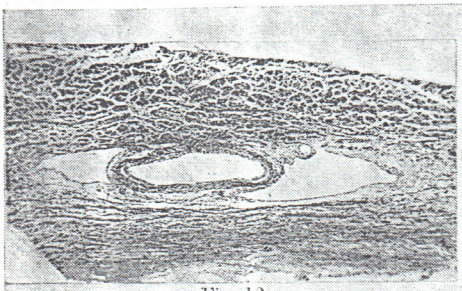


Fig. 12

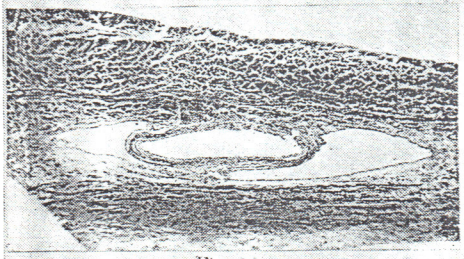
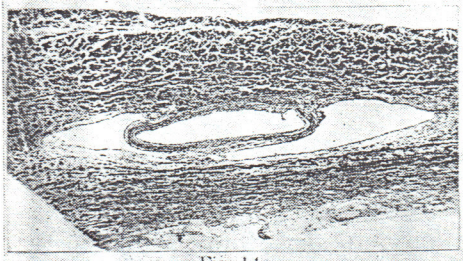


Fig. 13



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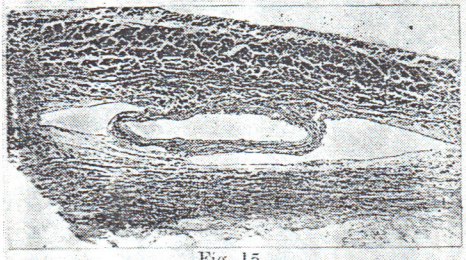

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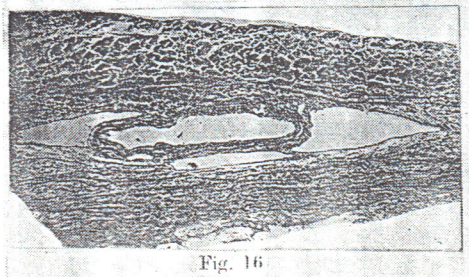


Fig. 16

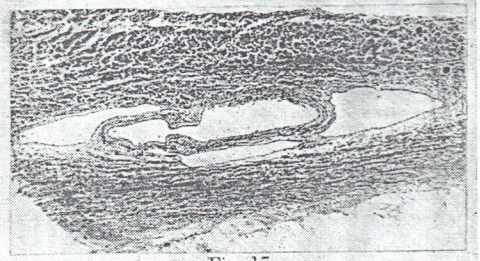
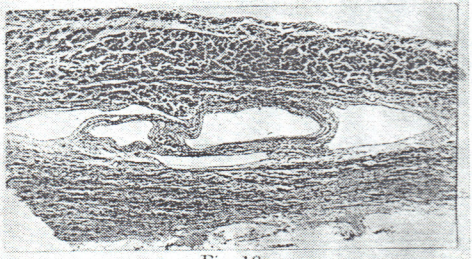


Fig. 17



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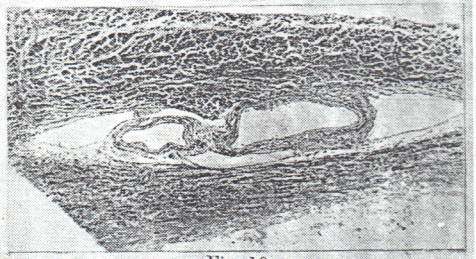

Fig. 19

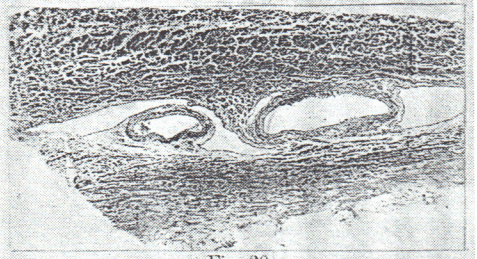

Fig. 20

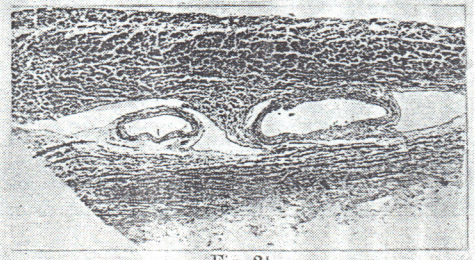

Fig. 21

PLATE IV

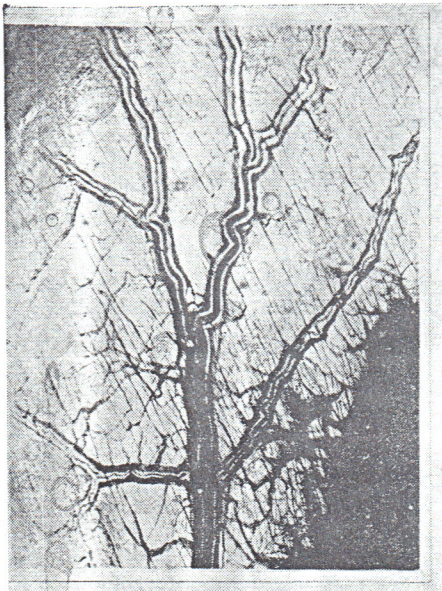

Fig. 8

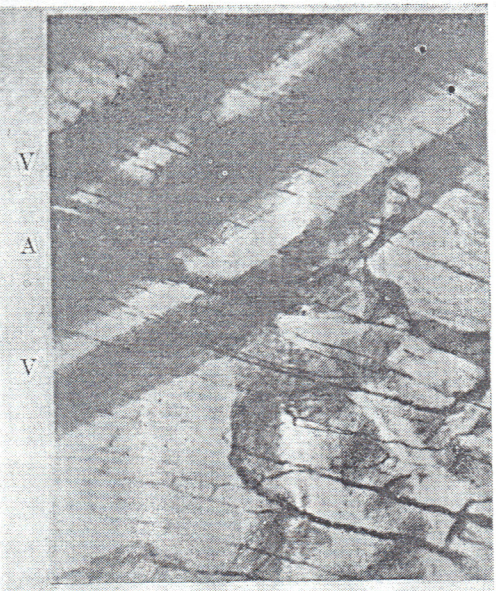

Fig. 9

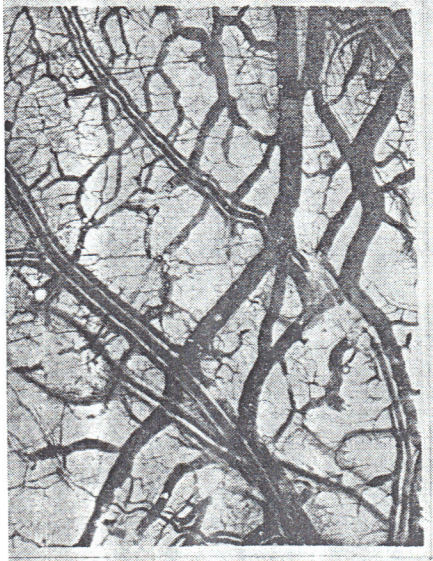

Fig. 10

Fig. 11

PLATE III

PLATE IV

Figures 12-21—Serial sections of the dura mater parallel to the superior sagittal sinus.

The branching of the venae comites prior to the division of the artery and the subsequent communication between the daughter veins after the arterial bifurcation could be followed in these sections. Any section in the region of this venous communication (figs. 20, 21) gives the appearance of an artery embedded in a venous channel.

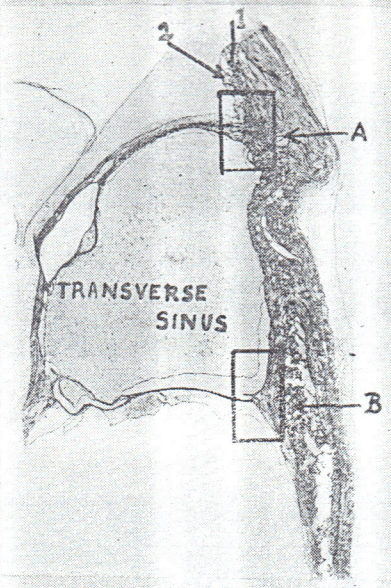

Fig. 5

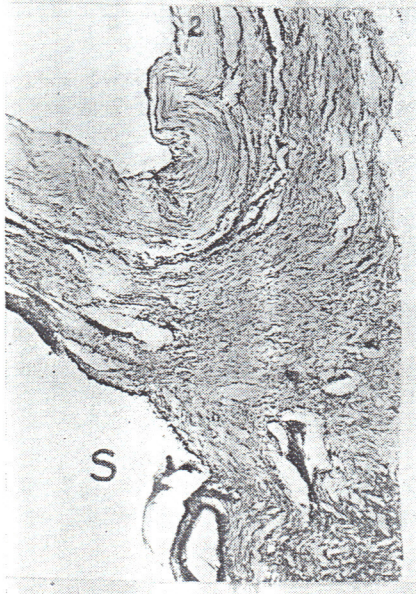

Fig. 6

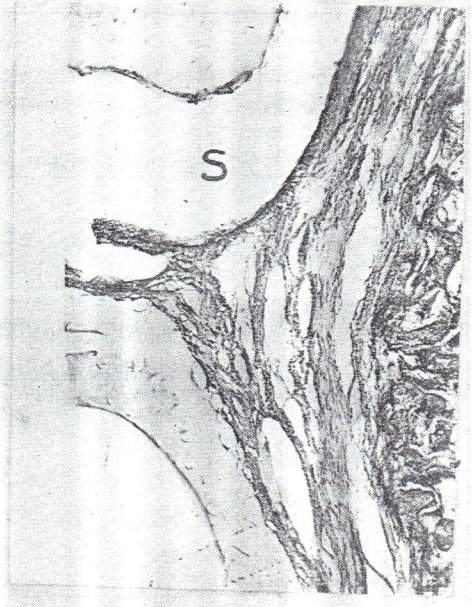

Fig. 7

PLATE III

Figure 8.—Photomicrograph of the dura mater ×5.

This shows the branches of the middle meningeal artery, with the constant venae comites.

Figure 9.—Photomicrograph of the dura mater ×12.

A—Artery. V—Venae comites.

This illustrates the fine plexus of veins lying superficial to the meningeal vascular bundle.

Figure 10.—Photomicrograph of dura mater ×5.

This illustrates the large veins of the deep plexus lying deep to the meningeal vascular bundle.

Figure 11.—Photomicrograph of dura mater ×102.

This shows obliquely running vessels which connect the superficial and deep plexuses of veins.

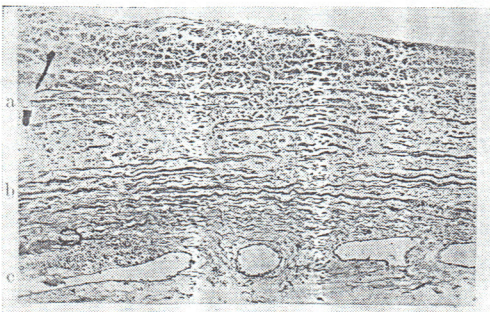

Fig. 1

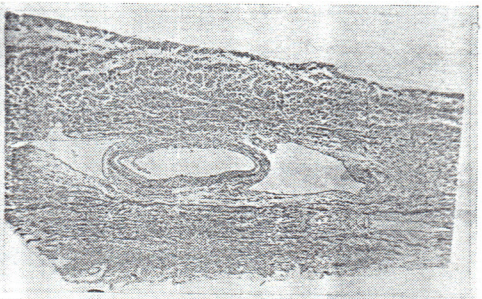

Fig. 2

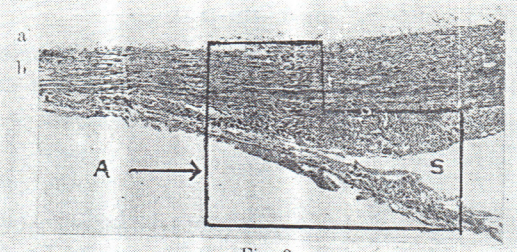

Fig. 3

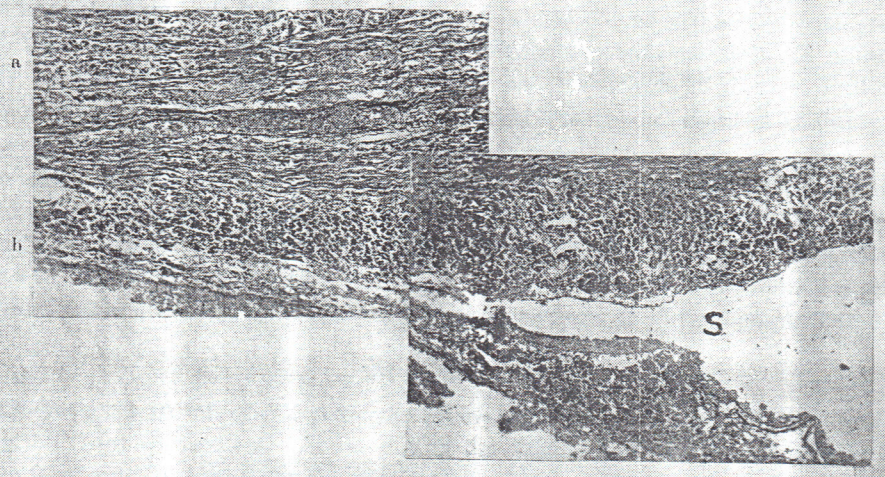

Fig. 4

PLATE I

Plate II

Figure 5.—Transverse section of the Transverse Sinus ×5.

1. outer layer of the dura mater,
2. inner layer of the dura mater.

Figure 6.—Area A in fig. 5 ×42.

This shows the whole set of inner fibres (2) passing inwards to form a superficial layer of the tentorium cerebelli, while the outer layer (1) separates to enclose the transverse sinus—S.

Figure 7.—Area B in fig. 5 ×42.

This shows the complete absence of the inner layer of the dura mater below the level of the sinus—S.