Epidemiological features of choriocarcinoma

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By means of hospital records and death certificates, 91 cases of choriocarcinoma were identified in the cities of Manila, Quezon, Pasay, and Caloocan in the Philippines during the 5 years 1970–74. The overall incidence was 17.4 per 100 000 live births. The other principal findings in this population-based study concerned maternal age, history of fetal wastage, and number of pregnancies. Very high incidence rates for choriocarcinoma were registered for mothers aged 40 years and over and there was a slightly higher than average risk for women under 20 years of age. Risk increased with the number of fetal losses. The effect of number of pregnancies was evident only for very old and very young mothers. A case–control study was also conducted on 28 patients with choriocarcinoma and on 187 age-matched controls; for all of these women, the disease had been diganosed (cases) or children had been born (controls) between 1970 and 1975. Compared with the control group, a higher proportion of the case group had a history of pulmonary tuberculosis and had previously used contraceptive pills. Because of the low and unequal levels of cooperation among patients and controls, these findings need further confirmation.

Choriocarcinoma, a rare neoplasm in western countries, occurs with strikingly high frequency in the Far East. It is a very malignant neoplasm and usually originates from the chorionic epithelium of the fetus; it is believed to develop in the mother some time after the termination of gestation. Alternatively, it may develop from the germinal epithelium of the gonads of either sex or, rarely, from embryonal rest cells in extragonadal sites. Choriocarcinomas of different origins are similar in their histological and clinical behaviour. They are rapidly metastasizing tumours and patients with metastasis, if untreated, usually die within a year. Only gestational choriocarcinoma responds to chemotherapy (9) and has been known as the first chemotherapeutically " curable " human cancer. Very rarely, spontaneous regression occurs " even after they are labelled as fatally malignant " (24).

Despite a markedly improved prognosis because of chemotherapy, a substantial proportion of patients with choriocarcinoma continue to succumb to the disease. Between 1960 and 1970, about 30% of those suffering from choriocarcinoma in Singapore died of the disease (29). In Manila, the use of methotrexate has produced an overall " cure " rate of 64% (14). The malignant and non-malignant forms of trophoblastic disease have been the subject of numerous reports in different countries. Studies have dealt with the clinical, pathological, epidemiological, and immunological aspects of the condition. The etiology of the disease remains unknown. Some investigators have suggested dietary deficiency or racial factors to explain its high prevalence in certain groups.

Choriocarcinoma has been shown to be associated with hydatidiform mole, both in geographical distribution and in individuals. Both forms of trophoblastic disease are more prevalent among Asians and Mexicans (13) than among Caucasians. An appreciable number of choriocarcinoma cases follow molar pregnancies. Hydatidiform mole increases a woman's risk of developing malignant trophoblastic disease, the reported risk ranging from 2% to 19% (15). Because of this relationship, it may be worth while investigating whether factors that are associated with hydatidiform mole are also associated with choriocarcinoma.

Some of the previous studies, including those conducted in the Philippines, were limited to cases in selected hospitals. The present study was undertaken to estimate the incidence of choriocarcinoma in a total population and to study other epidemiological characteristics of the disease.

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MATERIALS AND METHODS

An attempt was made to identify all cases of gestational choriocarcinoma first diagnosed within the 5-year period 1970–74 among residents of the four cities in the metropolitan area, namely, Manila, Caloocan, Pasay, and Quezon. The investigation was undertaken for 1 year, starting in February 1975. The records and pathology files of 32 general and gynaecological hospitals in the metropolitan area were examined, as were death certificates in the four cities. Cases with a clinical diagnosis of choriocarcinoma, with or without pathological confirmation, were included in this series. To estimate disease rates, the cases were related to registered live births in the study area. The distribution of live births, according to specific variables, was based on analysis of a 1% sample of the total number of births.

Variables other than those available in the existing records were investigated by the case–control approach. The case series included incident cases between 1970 and 1975 in residents of the above-mentioned cities and in some towns of the neighbouring province of Rizal (also part of the metropolitan area), and who were not shown as dead in hospital records. The control group, which included mothers who had given birth to live babies, was drawn from the files of live-birth certificates; for each case five controls, matched for maternal age, were chosen at random. The sampling frame was the list of children whose indicated place of residence was the same as the patient and who had been born on the same day that the case had been diagnosed. For some cases, however, the number of control subjects who satisfied the selection criteria was less than five, especially when the patient was 40 years of age or more. Personal interviews were conducted in the homes of the women with choriocarcinoma and control subjects by trained, non-medical interviewers. The interview related to past illnesses, usual body weight, reproductive history including the use of contraceptive pills, personal habits, other cases of choriocarcinoma in the family, and socioeconomic status.

In the population-based study, disease rates were computed and chi-square analysis was used to test the null hypothesis of no association between the disease and the specific variable. The risk ratio (RR) was used in the case–control study to quantify the strength of the association between the disease and a specific factor. Interval estimates of the risk ratios were likewise obtained.

The risk ratio (RR) was the ratio of the two products obtained by multiplying diagonally across a four-fold table and it represents the risk of disease for individuals who had a characteristic of interest relative to that for individuals who did not. The interval estimate of RR for large samples was based on the assumption that the logarithm of the estimated risk ratio (log $\hat{RR}$) has approximately a normal distribution and was computed by Gart's method (18), except for the one-half corrections, as follows:

$$RR_L, RR_U = \exp [\ln \hat{RR} \mp Z_{1-\alpha/2} \text{ SE } \hat{RR}]$$

$$\text{and SE } \hat{RR} = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

where RR_L, RR_U = the lower and upper bounds, respectively, of the interval estimate;

exp = " exponential of ";

ln = the natural logarithm;

$Z_{1-\alpha/2}$ = the 100 $(1 - \alpha/2)$ percentile of the standard normal distribution;

SE $\hat{RR}$ = the standard error of $\hat{RR}$; and

a, b, c, and d = the cell frequencies of a four-fold table.

RESULTS

One hundred and seventy-three cases of malignant trophoblastic disease were identified, of which 162 were choriocarcinoma, 3 malignant mole, 4 chorioadenoma destruens, and 4 unspecified trophoblastic malignancy.

Of the choriocarcinoma cases, 146 were identified from hospital records and 16 from death certificates. Histological confirmation of the clinical diagnosis was made for 82 cases (51%).

Incidence study

Of the 162 women with choriocarcinoma, 61 were residents of the provinces and in 10 others the disease was diagnosed in 1975. Therefore, only 91

Table 1. Incidence of choriocarcinoma per 100 000 registered live births in selected cities, 1970-1974. $\chi^2 = 3.43$; d.f. $= 3$; $P > 0.30$

City	No. of cases	Rate
Manila	47	17.9
Caloocan	11	20.2
Quezon City	29	18.9
Pasay City	4	7.5
Total	91	17.4

could be related to the 523 536 live births registered in the four cities during the 5-year period 1970–74. The overall incidence was 17.4 per 100 000 live births (Table 1) or 1 in 5753 live births. The variation in incidence by city was not statistically significant.

The denominator used to express incidence was the number of registered live births. It is recognized that this is not ideal in as much as the number of live births does not represent all pregnancies. Nevertheless, it is the only measure available in the study area that can be used with reasonable accuracy. The registration of births in the metropolitan area is quite satisfactory, whereas a proportion of pregnancies are terminated outside the hospital and fetal losses are very poorly registered.

To convert the denominator from live births to pregnancies, the recent figure on fetal wastage from the National Demographic Survey (unpublished data, 1973) for the whole country was used. This survey estimated fetal wastage at 10% of all pregnancies. Hence, with 523 536 live births, the estimated number of pregnancies was 581 707, giving an incidence of choriocarcinoma of 15.6 per 100 000 pregnancies or 1 in 6392 pregnancies.

Estimates of the incidence of the disease according to maternal age and number of pregnancies are given in Table 2. The ages of women with choriocarcinoma ranged from 17 to 51 years. One salient feature is the very high rate among mothers 40 years of age or over, where the risk (171.7 cases per 100 000 women) was about 13 times as high as the overall risk (12.4 per 100 000) for women under 40 years of age. For the latter group, those aged under 20 years apparently experienced a higher risk than those 20–24 years of age, who registered the lowest rate. A slight decline in risk was also observed in the group aged 30–34 years followed by an appreciable increase in those aged 35–39 years. The difference in rates between the various groups under 40 years of age, however, was not statistically significant ($\chi^2 = 6.59$; d.f. $= 4$; $P > 0.1$).

An increased risk associated with a large number of pregnancies was also observed. The rate for subjects who had had six or more pregnancies was four times higher than the combined rate for those who had had fewer pregnancies and the excess was significant ($\chi^2 = 34.2$, d.f. $= 1$, $P < 0.001$). The risks

Table 2. Incidence of choriocarcinoma per 100 000 live births according to maternal age and number of pregnancies. Maternal age: $\chi^2 = 212.2$; d.f. $= 5$; $P < 0.001$. No. of pregnancies: $\chi^2 = 34.5$; d.f. $= 5$; $P < 0.001$

Maternal age (years)	Number of pregnancies														
	1		2		3		4		5		6+		unknown	total	
	No. of cases	rate	No. of cases	rate	No. of cases	rate	No. of cases	rate	No. of cases	rate	No. of cases	rate	No. of cases	No. of cases	rate
<20	2	5.3	2	19.8	1	55.2	0	0	0	0	0	0	2	7	13.7
20–24	3	3.7	2	4.6	2	8.5	2	17.9	1	28.6	0	0	3	13	7.8
25–29	5	12.7	6	18.2	3	11.5	2	9.2	1	7.9	2	16.4	3	22	14.9
30–34	1	9.8	1	8.4	1	7.5	1	6.3	1	7.6	3	10.3	3	11	11.5
35–39	1	36.8	0	0	0	0	1	20.3	1	20.3	5	14.3	2	10	21.2
40+	1	387.6[a]	0	0	0	0	1	70.0	0	0	18	198.4	4	24	171.7
Unknown	0	—	1	—	0	—	0	—	0	—	0	—	3	4	—
Total	13	7.6	12	11.6	7	10.0	7	12.6	4	11.4	28	36.4	20	91	17.4

[a] The denominator is less than 1000 live births.

for those who had had 1–5 pregnancies did not differ significantly from each other.

The figures in Table 2 reveal a slightly elevated risk for women under 20 years of age and a tendency for the risk to increase with increasing maternal age over 40 years in each gravidity class studied. The trend of increasing risk with number of pregnancies was limited to those under 25 and those 40 years of age or over. For women between 25 and 34 years of age, there was almost no increase in risk with number of pregnancies and a downward trend was noted in those aged 35–39 years. Apparently, women who were pregnant for the first time at the age of 35–39 years experienced a higher risk than those in the same age group who had had several pregnancies. No great significance could be attached to the very high incidence of choriocarcinoma in those who were first pregnant when 40 years of age or over because of the small number of live births in this group. Those who were over 40 years of age and had had six or more pregnancies had the highest risk. Because of the rarity of the disease the study group was rather small, particularly for analysing rates within maternal age and gravidity groups; hence, caution should be exercised in the interpretation of the rates shown in Table 2.

The incidence of the disease increased with the number of fetal losses (Table 3). Fetal wastage represented the difference between the gravidity and parity figures shown in the records and was therefore based on recognized pregnancies. The risks for women with one, two, and three or more fetal losses, compared with those for women whose recognized pregnancies all terminated in live births, were 21, 32, and 34 times higher, respectively. Of the 73 women with choriocarcinoma for whom adequate informa-

tion was available, the pregnancy previous to diagnosis terminated in abortion in 33 (45%), hydatidiform mole in 21 (29%), and a live birth in 19 (26%).

To correct for the effect of maternal age on the number of previous fetal losses, the risk of contracting the disease according to previous fetal losses was examined within each age group (Table 4). Some groups were combined because they had relatively small numbers of live births. Within each age group examined, the incidence of choriocarcinoma increased markedly in those who had had one or two or more fetal losses. The risk associated with an increasing number of fetal losses was therefore not dependent on maternal age. However, whereas the high risk associated with mothers aged 40 years and over was apparent even for those with no history of fetal wastage, the slightly higher risk among mothers under 25 years of age was observed only for women who had previously lost one or more fetuses.

Of the 82 cases of known nationality, 79 were Filipinos and 3 Chinese. The number of live births to Chinese mothers was relatively large. The Chinese registered a higher risk (72.5 per 100 000) than the Filipinos (15.2 per 100 000). Under the null hypothesis of no difference in choriocarcinoma incidence rates, the probability that the observed or a higher ratio between Filipinos and Chinese would occur is 0.03. All of the women with choriocarcinoma studied were married. Information relating to other variables, e.g., the occupation of the woman and of her husband and their religion were usually not adequately recorded. These items of information were missing for between one-third and two-thirds of the 91 cases.

Case–control study

Of the 120 women with choriocarcinoma who were residents of the four cities and the nearby province of Rizal, 34 were shown by hospital records to be deceased and 15 had died during the interval between discharge from hospital and the time when the study was conducted. Twenty-eight of the remaining 71 (39%) were actually interviewed. Of the remainder, 30 had moved to an unknown address, 12 could not be located, and 1 refused to cooperate. Four hundred controls were chosen and 187 (47%) were interviewed. Of the rest, 67% had moved to an unknown address, 30% could not be traced, and 3% refused to cooperate. The mean age at diagnosis of the cases interviewed was 32.1 years and that of the interviewed controls 31.5 years. The mean age of the cases who did not cooperate was 33.1 years and that

Table 3. Incidence of choriocarcinoma according to number of fetal losses. $\chi^2 = 295.7$; d.f. $= 2$; $P < 0.001$

No. of fetal losses	No. of patients	Incidence per 100 000 live births
0	15	3.4
1	37	72.4
2	13	110.4
3 +	7	115.3
Total	72 [a]	17.4

[a] The number of fetal losses was not known for 19 patients.

Table 4. Incidence of choriocarcinoma per 100 000 live births according to maternal age and number of fetal losses

Maternal age (years)	Number of fetal losses								
	0		1		2 +		unknown	total	
	No. of cases	rate	No. of cases	rate	No. of cases	rate	No. of cases	No. of cases	rate
≤ 24	2	1.0	11	95.3	3	154.4	4	20	9.2
25–29	5	3.9	11	89.3	3	80.0	3	22	14.9
30–34	2	2.7	4	28.0	2	36.8	3	11	11.5
35–39	1	3.3	4	41.7	3	55.2	2	10	21.2
40 +	5	54.4	6	177.9	9	696.1	4	24	171.7
Unknown	0	—	1	—	0	—	3	4	—
Total	15	3.4	37	72.4	20	112.0	19	91	17.4

of the non-cooperating control subjects was 32.3 years. Of those who cooperated in the study, a larger proportion had had the disease diagnosed (cases) or had borne children (controls) in the latter half of the 5-year study period.

Ward patients accounted for 68% of the women who cooperated in the study and for 71% of those who did not. All the cases were Filipinos except for one Chinese who was not interviewed. The average number of pregnancies was four for those who cooperated and five for those who did not.

Body weight and previous illness. The health of the study subjects prior to diagnosis of the disease was retrospectively investigated. The normal body weights of the cases and the control subjects were similar, the averages being 46.9 and 46.4 kg, respectively. These were based on the body weights of 23 cases and 172 control subjects.

Data on two selected illnesses experienced by the study subjects prior to the diagnosis of choriocarcinoma (cases) or prior to the index pregnancy (controls) are presented in Table 5. Some of the totals in Table 5 and in subsequent tables do not add up to 28 cases and 187 controls because specific information was not provided by some respondents. The proportion of cases for which there was a history of suspected pulmonary tuberculosis was 18% against 4% for the control subjects. The risk ratio (RR) for subjects with a history of suspected pulmonary tuberculosis was 5.6 times higher than for those who had a negative history. Anaemia, on the other hand, had no apparent association with choriocarcinoma:

Table 5. Number of cases and controls according to suspected previous history of pulmonary tuberculosis and anaemia

History	Pulmonary tuberculosis			Anaemia		
	cases	controls	RR	cases	controls	RR
Negative	23	179	1	17	131	1
Positive	5	7	5.6[a]	11	55	1.5[b]
Total	28	186	—	28	186	—

[a] 95% confidence limits, 1.6–19.1.
[b] 95% confidence limits, 0.7–3.4.

the risk among subjects with a history of anaemia was only 1.5 times as great as in those without.

Reproductive history. The ages at menarche of the cases and the control subjects were almost the same, the mean ages being 14.0 years for the former and 13.8 years for the latter. Other items related to reproductive history, such as number of pregnancies and fetal wastage, have been discussed earlier in this paper.

The use of contraceptive pills prior to diagnosis (cases) or to the index pregnancy (controls) is given in Table 6. The data indicated a significant association (RR = 6.4) with the disease. Contraceptive pills had been used by the cases for an average of 1.8 years and by the control subjects for an average of 1.6 years.

Table 6. Number of cases and controls according to the use of contraceptive pills

	Cases	Controls	RR
Non-users	19	175	1.0
Users	7	10	6.4 [a]
Total	26	185	—

[a] 95 % confidence limits, 2.2–18.8.

Tea, coffee, and tobacco. The previous smoking and drinking (coffee and tea) habits of the cases and the control subjects are compared in Table 7. The associations between the disease and each of these factors were weak. Although those who smoked had a risk that was double that of non-smokers, the difference was not statistically significant. The proportion of coffee drinkers was very similar in both groups. The negative association of risk with tea drinking was also not significant.

Multiple cases. There had been no cases of choriocarcinoma among the mothers and sisters of the 26 cases and 185 control subjects interviewed.

Table 7. Number of cases and controls according to coffe and tea drinking and smoking habits

Habit	Cases	Controls	RR
Cigarette smoking			
Non-smokers	21	164	1.0
Smokers	6	23	2.0 [a]
Total	27	187	—
Coffee drinking			
Non-drinkers	3	20	1.0
Drinkers	24	167	0.96 [b]
Total	27	187	—
Tea drinking			
Non-drinkers	19	115	1.0
Drinkers	8	72	0.67 [c]
Total	27	187	—

[a] 95 % confidence limits, 0.7–5.5
[b] 95 % confidence limits, 0.3–3.8
[c] 95 % confidence limits, 0.3–1.6

Table 8. Numbers and percentages of cases and controls according to selected socioeconomic characteristics

Characteristic	Cases		Controls	
	No.	%	No.	%
Occupation of husband				
Professional/managerial	—	—	21	11.35
Skilled or non-manual	5	17.86	44	23.78
Unskilled or manual	20	71.43	109	58.92
Unemployed	3	10.71	11	5.95
Total	28	100.00	185	100.00
Years of education completed by husband				
1–6	2	8.00	21	11.29
7–10	12	48.00	84	45.16
11–14	10	40.00	74	39.78
15 +	1	4.00	7	3.76
Total	25	100.00	186	100.00
Type of dwelling unit				
Single	15	53.57	118	63.10
Duplex	—	—	2	1.07
Apartment	10	35.71	29	15.51
Makeshift house	3	10.71	38	20.32
Total	28	100.00	187	100.00

Socioeconomic status. Some of the indices of socioeconomic status presented in Table 8 failed to show a consistent pattern of association with the disease. A higher proportion of the husbands of the cases tended to be either unemployed or engaged in manual jobs compared with the husbands of control subjects, and while more than 10% of the husbands of control subjects were professionals or holders of managerial positions, none of the husbands of the cases belonged to this category. However, the difference in the distribution of the two groups was not statistically significant ($\chi^2 = 5.11$, d.f. = 3, $P > 0.1$). The number of years of formal education completed by the husband was similar in the two groups. There were also no significant differences between the two groups in the type of dwelling unit and the average number of persons per room was virtually the same (2.85 for the cases and 2.76 for the control subjects).

DISCUSSION

The limitations of this study include the large amount of inadequately recorded information for some variables in the reviewed records, the low and unequal level of cooperation among the cases and the control subjects, and the relatively small number of study subjects. However, a comparison of those who cooperated with those who did not, with respect to some known characteristics, showed that the two groups were similar within broad limits.

A high incidence of choriocarcinoma in the Far East has been documented by earlier investigators. Frequencies such as 1 in 912 pregnancies, 1 in 1382 pregnancies, and 1 in 4298 deliveries have been reported from India (24), the Philippines (1), and Singapore (29), respectively. The rate for Singapore was based on all deliveries in the area, whereas those for the other two countries were based on hospital deliveries. In the USA, on the other hand, a round figure estimate was 1 in 40 000 terminated pregnancies (31). England (17) has reported an incidence similar to that of the USA, as has Puerto Rico (1 in 32 000 deliveries). Australia (1 in 14 567 pregnancies) (27) and Israel (1 in 19 700 live births) (15) have reported incidence figures intermediate between those from countries in the Far East and in the West.

The overall incidence of 1 in 5753 live births or 1 in 6392 pregnancies reported in this study is appreciably lower than an earlier estimate for this country. The earlier estimate was based on pregnancies and, as other studies have shown, rates for hospitals were higher than for the population as a whole. Not all pregnancies were terminated in hospital. For the study area, about 78% of all births occurred in hospital (23). In Hong Kong, an incidence of 1 in 1333 hospital deliveries was corrected to 1 in 6250 pregnancies for the colony (5). The incidence rate derived from the present study is comparable with the figures for Hong Kong and Singapore. The population-based incidence estimates for countries of the Far East, although lower than hospital-based figures, remained substantially higher than those for Western countries.

Another explanation for the difference between the two estimates for the Philippines could be a change in the trend of the disease with time. This alternative, however, was not investigated because of the lack of pertinent data. In Israel, the disease has shown a significant decline within a 15-year period (15).

The variation in incidence in different parts of the world cannot be explained by differences in diagnostic criteria in various countries. Previous studies on the incidence of histologically diagnosed malginant trophoblastic neoplasia, i.e., choriocarcinoma and malignant mole, in Singapore were compared with results from Connecticut, Norway, and Sweden. The microscope slides from the four sources were reassessed by a single person. The Singapore incidence was some three to nine times greater than that in Connecticut and Scandinavia (25). Furthermore, in 1953, the Joint Project for the Study of Choriocarcinoma and Hydatidiform Mole in Asia collected clinical and pathological material from trophoblastic tumours in Asia and compared the histological criteria of diagnosis with those used in large pathology laboratories in the USA. No significant differences in the histology of these tumours were found (11).

The significant influence of maternal age on the risk of developing the disease demonstrated in this study is in agreement with the findings of previous investigators. The sharp rise in incidence beyond the age of 40 years has been a constant finding (3, 6, 15, 21, 22). The slightly elevated risk for women under 20 years of age has been observed in Puerto Rico (3) and Singapore (29) but not in Israel (15). Although an association between the disease and parity had been reported from Singapore (6) and India (21), studies conducted in Israel (15) and the USA (20) did not support such an association. In the present study, the effect of the number of pregnancies was noted only within certain age groups. The above findings suggest that maternal age may well be an important risk factor whereas the number of pregnancies may play only a minor role.

While some investigators have suspected that racial differences are related to the observed distribution of trophoblastic disease, others have not found evidence to support the relationship. The present study showed a difference between persons of two nationalities in the Philippines, the risk being higher in Chinese than in Filipinos, but in this case nationality does not necessarily reflect the ethnic background. Information on race was not available in the reviewed records. Specific rates for each nationality, adjusted for maternal age, were not computed because of the very small number of cases among the Chinese. One study revealed different frequencies of choriocarcinoma among the various ethnic groups living in Singapore (29): 1 in 9857 Malays, 1 in 15 681 Chinese, and 1 in 78 300 Indians. However, no definite ethnic differences were observed between

Asian- and African-born and between European- and American-born women in Israel. A study in Hawaii in 1967 showed that hydatidiform mole was more common in the Oriental than in the Caucasian group and that the Hawaiian and part-Hawaiian groups had a relatively low incidence despite their generally lower socioeconomic level (16, 19). The incidence in Mexico has been found to be comparable to that in some Asian countries, but in a study in Los Angeles, the percentage of Mexicans in the study group did not differ significantly from that in the control group (30).

Socioeconomic status had been associated with the occurrence of hydatidiform mole among women in Eastern countries but this has not been found to be the case in the USA (31) and Hawaii (16). A dietary factor, probably protein deficiency, has been suggested by Acosta-Sison (2) to explain the frequency of the disease among less privileged women. This author also observed that, among patients with hydatidiform mole, especially those who eventually developed malignant disease, a great proportion showed evidence of previous pulmonary tuberculosis; however, no mention was made of the frequency of pulmonary tuberculosis among patients with hydatidiform mole who did not develop malignancy. She believed that pulmonary tuberculosis or advanced age had a deteriorating effect on the nutritional status of the patient. The present study revealed that a greater proportion of patients than control subjects had a history of suspected pulmonary tuberculosis. If Acosta-Sison's hypothesis is correct, differences should exist between cases and controls regarding some aspects of nutritional status.

Data on normal body weight and history of anaemia were not significantly different between the cases and the control subjects. Body weights were compared directly on the assumption that there was no difference in average height between the members of the two groups. Should an association between poor nutrition and choriocarcinoma exist, the present findings concerning these two variables may be due to one of the following possibilities: (a) the method employed (interview) to obtain information on these variables was not satisfactory; (b) those who cooperated were not representative of the total population; (c) there was systematic bias in the information given concerning these variables; or (d) for body weight alone, either the assumption

mentioned above was not valid or normal body weight is not a sensitive measure of nutritional status.

Socioeconomic status was investigated in terms of the occupation and educational attainment of the husband, the type of dwelling unit, and the average number of persons per room in the household. Data on the incidence of choriocarcinoma in relation to these characteristics were not available and the case–control study did not furnish conclusive evidence on the relationship between the disease and socioeconomic status. However, the suggested association with regard to the occupation of the husband, which did not attain a conventional level of significance possibly because of an inadequate sample size, should be investigated further.

Different rates of occurrence of choriocarcinoma following different types of pregnancy have been reported. Between 27% and 80% of patients with choriocarcinoma have been reported to have a history of hydatidiform mole (1, 3, 5, 9, 12, 15, 22, 24, 29); between 10% and 40% of patients had previously had an abortion (1, 3, 5, 24), between 5% and 33% had had a full-term pregnancy; and a very small number had had an ectopic pregnancy (5, 29). The present study has shown that there is an increasing risk of choriocarcinoma with the number of fetal losses; this could lend support to the theory that choriocarcinoma results from a defective gene giving rise to a pathological ovum (2). The factors responsible for the production of a defective gene remain unclear.

The significant association between choriocarcinoma and the previous use of contraceptive pills merits further investigation. This particular information was elicited mainly as a result of interviews with the study subjects. However, the possibility must be considered that the cases were better able to recall the use of the pills than the control subjects.

Sex hormones have been shown to increase the incidence of tumours, both benign and malignant, in experimental animals. In man, however, the administration of oral contraceptive pills to women " has not as yet been shown to alter the risk of cancer of the breast. The evidence with respect to cancer of the cervix is somewhat less consistent " (10). This author is not aware of any published data pertaining to a relationship between the use of oral contraceptives and choriocarcinoma.

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RÉSUMÉ

CARACTÈRES ÉPIDÉMIOLOGIQUES DU CHORIOCARCINOME

A l'aide de dossiers hospitaliers et de certificats de décès, 91 cas de choriocarcinome ont été identifiés dans les villes de Manille, Quezon, Pasay et Caloocan aux Philippines sur une période de cinq ans (1970-1974). L'incidence globale a été de 17,4 pour 100 000 naissances vivantes. Les autres résultats fournis par cette étude concernaient principalement l'âge maternel, les antécédents de grossesses improductives et le nombre de grossesses. Des taux extrêmement élevés ont été enregistrés pour les mères de 40 ans et plus; il y avait aussi un risque un peu supérieur à la moyenne pour les femmes de moins de 20 ans. Le risque augmentait avec le nombre de morts fœtales. L'effet du nombre de grossesses n'apparaissait clairement que pour les mères très vieilles ou très jeunes. Une étude de cas avec témoins a été menée sur 28 des malades présentant un choriocarcinome et sur 187 témoins d'âges appariés; toutes ces femmes avaient vu leur maladie diagnostiquée (cas) ou avaient donné naissance à des enfants (témoins) entre 1970 et 1975. Par rapport au groupe témoin, il y avait dans le groupe des cas une proportion plus élevée de femmes ayant des antécédents de tuberculose pulmonaire et ayant utilisé des pilules contraceptives. La coopération ayant été faible et inégale parmi les malades et les témoins, ces constatations demandent à être confirmées.

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