PROGRESS IN THE TREATMENT OF MALIGNANT TROPHOBLASTIC TUMORS DURING THE LAST TWO DECADES IN THE PEKING FANTI HOSPITAL**

During a period of 20 years from 1949 to 1968, a total of 581 cases of malignant trophoblastic tumors, consisting 294 cases of choriocarcinoma and 287 cases of chorioadenoma destruens, were admitted into this hospital. Some of these cases have been reported previously. (1-4)

Our investigation in the treatment of trophoblastic tumors during the last 20 years can be divided into 3 periods. First period: from 1949, when the People's Republic of China was established, to July 1958. Second period: from August 1958 to 1965. Third period: from 1965 to the end of 1968. The reason for this division into these 3 periods is due to the fact that the various country-wide political movements have exercised great influence on the research work of this particular line and have given it a significant impetus. The Great Leap Forward of 1958 enabled us to break away from convention, thus opening up a new line of treatment for the disease—the chemotherapy. 1966 ushered in the unprecedented Great Proletarian Cultural Revolution, which further liberated the mind of the broad masses of medical workers and mobilized their initiative, thus creating a brand new aspect in the treatment of this disease.

The therapeutic results in 3 different periods is shown in Table 1.

Table 1. Therapeutic results in three different periods

Period	Method of treatment	Choriocarcinoma			Chorioadenoma			Total		
		No. of cases	No. of deaths	%	No. of cases	No. of deaths	%	No. of cases	No. of deaths	%
1949.1— 1958.7	Surgery	37	33	89.2	27	7	25.9	64	40	62.5
1958.8— 1965.12	6PM with surgery	131	75	57.3	107	14	13.1	238	89	37.4
1966.1— 1968.12	5Fu, KMS* 6MP, MTX with surgery	126	49	38.9	153	8	5.2	279	57	20.4

Mortality includes all deaths up to Nov. 1970.

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Diagnostic criteria and clinical staging.

Clinical diagnosis was based on history, physical examination, roentgenological examination of the lungs and determination of the urinary chorionic gonadotrophin. In some of the patients treated by chemotherapy alone for preservation of fertility, hysterosalpingography and occasionally pelvic arteriography were performed. Electroencephalographic examination was made in all cases suspected of brain metastasis. When metastasis of the liver was suspected, hepatoscanning was performed.

Pathologic diagnosis was mainly based on the uterine specimens and autopsy materials with the exception of a few taken from surgically removed vaginal, pulmonary metastatic nodules or other materials. In no case was pathologic diagnosis based on uterine curetting. The criterion for the differentiation between choriocarcinoma and chorioadenoma destruens agreed with that of Novak which is based on the absence or presence of chorionic villi. Cases with even a single ghost villus were classified as chorioadenoma destruens. (4)

Patients with chorioadenoma destruens had far better prognosis than those with choriocarcinoma. As shown in Table 1, the mortality rate of choriocarcinoma was higher than that of chorioadenoma destruens in all three periods irrespective of the improvement of treatment. In the 1st period it was 3 times higher. And in the 2nd period and 3rd period it was 4 and 7 times higher respectively.

The criteria used in determining the clinical stages followed those reported in 1962 (3) (Fig. 1). According to our experience the clinical staging exerts remarkable effect

Fig. 1. Criteria of clinical staging, Stage I: The lesion is limited to the uterus. Stage II: The lesion has extended outside the uterus, but is still confined to the genital organs. A. Extension to parametrium or appendages. B. Vaginal metastasis. Stage III:

Pulmonary metastasis. A Cotton ball-like shadows not exceeding 3 cm. or the covered by patchy shadows not exceeding half the lung on one side, B Conditions exceeding the above. Stage Iv: Generalised metastases to the brain, liver, kidney, spleen, intestines, skin, etc.

on the prognosis. The later the clinical stage of the patient, the worse is the outcome. In this series a large proportion of the total 294 choriocarcinoma patients were late cases (Stage IIIB & IV). In the 1st period the proportion of late cases was 62.2% (23 in 37 patients), in the 2nd period 46.6% (61 in 131) and in the 3rd period 49.3% (62 in 126).

The therapeutic results in relation to the clinical staging in 3 periods are shown in Fig. 2.

Fig. 2. Comparison of mortality rate in relation to clinical staging.

Therapeutic methods

Period I (1949-1958). Chiefly surgery.

Part of the patients received deep X-ray irradiation and/or chemotherapy (nitrogen mustard and nitromin).

Period II (1958-1965). Chemotherapy in combination with surgery.

The main chemotherapeutic agent was 6-Mercaptopurine (6MP). Methotrexate (MTX) was used occasionally. Since 1964-5-Fluorouracil (5Fu) and Kengshengmycin (KSM) had been used in a few cases. In all patients besides those intending to preserve fertility, subradical hysterectomy in which the parametrial and ovarian venous plexuses were resected together with the uterus was the operation.

Period III (1966-1968). Chemotherapy in combination with surgery.

The chief therapeutic agents were 5Fu and KSM. 6MP and MTX were used occasionally.

The methods of administration of different chemotherapeutic agents are listed in Table 2.

Table 2. Method of administration of chemotherapeutic agents

Agent	Route	Daily dosage	Duration of course (days)	Interval between courses (weeks)
6MP	Oral	6.0-6.5mg/kg in 2 divided doses	10	3-4
MTX	Oral	0.45-0.5mg/kg in 2 divided doses	5	3-4
	i.v. drip	10-15 mg	6-8	2-3
	Intrathecal	10-15 mg each time		
5Fu	i.v. drip	25-30mg/kg	10	2
	Local injection	250-500 mg each time		
KSM	i.v. drip	300-400	10	2
5Fu & KSM	i.v. drip	5Fu 23-25mg/kg		
		KSM 300 mcg	8-10	3

For intravenous drip the daily dose of drug is added to 500 ml dextrose. The rate of 5Fu infusion should be slow (500 ml given in 6-8 hr.) For the combined use of 5Fu and KSM the daily dose of each is added to 500 ml dextrose. They are given by one-half portions alternately. Dosage for arterial infusion is essentially the same as that for intravenous drip or may be slightly lower. The duration of course may be prolonged or shortened for 1-2 days depending on the degree of severity of the disease and toxic effect of the drug. In case of severe toxic reactions the interval between courses should be prolonged accordingly.

Among the 4 drugs used at present 5Fu and KSM, on account of their better therapeutic effect and milder toxicity, are the agents of first choice. In those patients who become resistant to 5Fu and KSM, 6MP or MTX is used instead. The treatment should proceed until complete recovery is achieved. That is to say no clinical symptoms are present, pulmonary metastatic shadows have completely disappeared and male toad test has become negative with the urine concentration method. In other words, the presence of any residual cancer tissue in the body is no longer detectable by the available methods. Hence, 1-2 consolidating courses should be given to the patient before discharge.

Results

157 cases of choriocarcinoma and 29 cases of chorioadenoma destruens had died either in the hospital or during follow-up up to Nov. 1970 (Table 1). There were 17 patients (8 cases of choriocarcinoma and 9 cases of chorioadenoma destruens) lost to follow-up. All these 17 cases achieved complete recovery at the time of discharge. The duration of follow-up for the survivors is shown in Table 3.

The therapeutic results in patients with metastases (Stage II-IV) are shown in Table 4.

Table 3. Duration of survival

Years	-1	-2	-3	-4	-5	-6	-7	-8	-9	10	-10.	Total
Choriocarcinoma	13	29	19	30	18	3	6	5	-	1	5	129
Chorioadenoma	23	45	52	47	31	19	5	4	1	-	22	249
Total	36	74	71	77	49	22	11	9	1	1	27	378

Table 4. Mortality in patients with metastases

	Choriocarcinoma			Chorioadenoma			Total		
	No. case	No. death	%	No. case	No. death	%	No. case	No. death	%
1958-1965	116	75	64.7	79	12	15.2	195	87	44.6
1966-1968	109	46	42.2	115	7	6.1	224	53	23.6

Chemotherapy of malignant trophoblastic tumors with preservation of fertility

From 1959 to 1968 there were 99 young patients desirous of children treated by chemotherapy alone with preservation of fertility. Part of the cases have been reported before (5). Successful results were achieved in 85 cases as shown in Table 5.

Table 5. Results of chemotherapy in preserving fertility

	Total no. cases	No. success	% success
Chorioadenoma	86	77	89.5
Choriocarcinoma	13	8	61.5
Total	99	85	85.9

The clinical staging of 85 patients with their fertility successfully preserved is shown in Table 6.

Table 6. Clinical stage in patients with successfully preserved fertility

Clinical Stage	I	II	III		IV	Total
			A	B		
Chorioadenoma	28	7	40	1	1*	77
Choriocarcinoma	1	5	0	2	0	8
Total	29	12	40	3	1	85

*A patient with brain metastasis.

Of the 85 patients, only 29 (34.1%) were stage I cases and all the remaining 56 (65.9%) had metastasis. Therefore, metastases in itself is by no means a contraindication for the preservation of fertility provided that the uterus is not too bulky and uterine hemorrhage not uncontrollable.

Among 14 failures, all the 9 cases of chorioadenoma destruens and 4 out of 5 cases of choriocarcinoma recovered after subradical hysterectomy and further chemotherapy. One choriocarcinoma patient died of brain metastasis even after hysterectomy. Since the degree of malignancy of choriocarcinoma is much higher than that of chorioadenoma destruens the selection of cases for chemotherapy alone should be done with utmost care.

The patients in whom reproductive function was preserved were warned to take strict contraceptive measures for 1-2 years after completion of therapy. During follow-up, 46 of the 85 cases became pregnant, a conception rate of 54.1%. Thirty-eight patients (including one brain metastasis) had normal term deliveries, 10 of them had 2 deliveries and 5 had 3 deliveries. All the 58 babies delivered except 2 (one neonatal death with unknown cause and one with Tetralogy of Fallot) developed normally.

Recurrent mole occurred in a case of chorioadenoma destruens treated by chemotherapy alone but the patient recovered after curettage and further treatment. Another patient of chorioadenoma destruens treated in 1964 developed choriocarcinoma in 1970 after a full-term delivery in 1968. She is now readmitted and under intensive treatment. This case warned us that recurrence is still possible even after a full-term delivery in patients with preserved uterus, and close follow-up examinations are indispensable.

Toxic Reactions.

All the 4 above-mentioned chemotherapeutic agents have the disadvantage of causing toxic reactions of different degrees which effect chiefly the hemopoietic system and digestive system.

Inhibition of hemopoietic system. The toxic reactions are manifested by granulocytopenia and thrombocytopenia. As shown in Table 7, the lowering of white cells was most promi-

Table 7. Comparison of blood picture after medication

Drug (No. courses)			Lowest value of WBC (thousand/mm ³)					Lowest value of platelet (ten thousand/mm ³)				
			< 1	1-2	2-3	3-4	> 4	< 1	1-3	3-5	5-10	> 10
6MP	(138)	%	5.1	31.2	47.7	10.1	6.5	8.0	33.0	26.1	24.6	7.2
MTX	(66)	%	9.1	30.4	30.4	55.1	15.1	7.6	28.8	22.7	30.3	10.6
5Fu	(713)	%	0.8	4.6	10.0	18.5	66.0	0.7	3.5	6.9	30.4	58.5
KSM	(402)	%	0.2	0.7	4.0	8.2	86.8	0.5	7.7	8.0	29.4	54.5
5Fu & KSM	(39)	%	0	30.8	17.9	12.8	38.5	2.6	12.8	20.5	28.2	35.9

nent in patients treated with MTX. In 39.5% of them the count dropped to below 2,000/mm³, while in those treated with KSM only 0.9% of the patients had the count dropped to similar level. The drop of white cells caused by the combined use of 5Fu and KSM was far greater (30.8%) than when they were used individually. The lowering of platelet count was most prominent in patients treated with 6MP. In 42.0% of them the count dropped to below 30,000/mm³. The thrombocytopenic effect of 5Fu is the mildest, only 4.2% of the patients had the count dropped to the same level. The combined effect of 5Fu and KSM was greater than either used alone. The inhibition of hemopoietic system was temporary in most cases, thus no interference of the resumption of the treatment was incurred. However, prolonged inhibition of platelet had occasionally been encountered in patients treated with KSM.

Liver damage after medication. The liver damage was most prominent in patients treated with 6MP and mildest with 5Fu (Table 8).

Table 8 Liver damage after medication

Drug	No. courses	% Elevation of SGPT
6MP	138	42.7
MTX	66	23.0
KSM	360	15.0
5Fu	567	7.7

Gastro-intestinal system reactions. Anorexia, nausea and vomiting were common. Abdominal cramps and diarrhea were frequent in patients treated with 5Fu. In severe cases there might be melena. Occasionally pseudomembranous colitis might result after improper treatment of diarrhoea.

Stomatitis and ulceration of oral mucosa. These manifestations were most prominent in patients treated with MTX and mildest with 5Fu.

Alopecia. Alopecia was most frequently seen in patients treated with MTX and KSM.

Skin rash. This was most frequent in patients treated with MTX and rarely seen in patients treated with 5Fu.

Generally speaking, all the toxic reaction will subside after the cessation of medication. However, if they are not properly managed, serious complication may develop and may even become fatal. During the 2nd period from 1958 to 1965 there were 14 deaths (5.9%) caused by toxic reaction among 238 cases, and during the 3rd period from 1966 to 1968 there were 5 deaths (1.8%) among 279 cases. Of the 19 deaths related to medication, 13 occurred after the use of 6MP, 2 after MTX, 2 after 5Fu and 2 after KSM. Septicemia and toxic shock after severe granulocytopenia and massive hemorrhage from gastro-intestinal tract after thrombocytopenia were usually the direct causes of death.

ILLUSTRATIVE CASES

Case 1.

H. L., Wu, a poor peasant's daughter aged 25, complained persisted vaginal bleeding for 6 months after a full-term delivery and bedridden for one month. Pelvic examination revealed a slightly enlarged uterus. Urinary HCG content was 512 iu./ml by hemoagglutination-inhibition method. Multiple metastatic shadows were seen in both lungs. Hepatoscanning with radio-active gold revealed multiple space-occupying lesions in the left lobe of liver. Choriocarcinoma of uterus with pulmonary and hepatic metastases was diagnosed. After a course of combined 5Fu and KSM therapy the general condition of the patient was remarkably improved and the urinary gonadotrophin decreased to 8 iu/ml. In the second course, laparotomy was performed. During exploration the uterus was found to be the size of 6 week pregnancy. More than 20 metastatic nodules were found on both lobes of liver. There were a metastatic tumor with the size of $7 \times 6 \times 4$ cm in the spleen and one of $2.5 \times 1.5 \times 1.5$ cm at the lower pole of the right kidney (Fig. 3).

From the past experience none of Stage IV patient with such extensive metastases recovered. However, armed with Mao Tse tung's thought and tempered in the Great Proletarian Cultural Revolution, we decided to surmount every difficulty to win victory. Subradical hysterectomy, splenectomy, right nephrectomy and hepatic artery intubation were performed at one stage. Postoperatively 5500 mcg of 5Fu and 20 mg of MTX were given through the hepatic artery and 2400 mcg of KSM and 6000 mg of 5Fu were

Fig. 3. Case 1. Diagram showing sites of metastasis

administered intravenously. Serious toxic reaction manifested by granulocytopenia and thrombocytopenia, high fever and extensive ulceration of oral mucosa occurred after cessation of medication. Through proper management and careful nursing, she overcame the toxic reactions eventually. The urine concentration test became negative and pulmonary metastatic shadows resolved completely. She was discharged after three consolidating combined courses of 5Fu and KSM. She is now in good health and has been followed up for one and a half year with no evidence of recurrence.

Case 2.

A. M., Ts'ao, a nurse aged 26, was admitted on account of hemoptysis and headache 2+ months after hysterectomy for choriocarcinoma. A purplish nodule was found in the orifice of urethra. Chest film revealed more than ten metastatic nodules of different sizes in both lungs. Neurologic examination showed mild hemiplegia on the right side, enlarged right pupil and papilloedema. Choriocarcinoma with metastases to vagina, lungs and brain was diagnosed. Dehydration and chemotherapy were initiated at once. After two courses of MTX the neurologic symptoms were essentially controlled, but the pulmonary metastases did not resolve appreciably. 5Fu was then administered. The Urine concentration test became negative and the pulmonary metastases resolved markedly leaving only three small roundish shadows. At 5th course the electroencephalogram became normal and the hemiplegia disappeared completely. In spite of further treatment with KSM and, 6MP, the pulmonary shadows remained unchanged. She has been followed up for 3 years after discharge. The urine concentration test persisted to be negative. The residual pulmonary shadows are still under resolution. She is now working on the northwest plateau and in good health.

Case 3.

S. C., Yang a shop worker aged 33, was admitted in the Dept. of Int. Medicine on account of a huge shadow in the right lower lung. Bronchogenic carcinoma was diagnosed. There was no improvement after one course of nitrogen mustard. On further inquiry, a history of hydatidiform mole 4 years ago was revealed. The urine pregnancy toad test was positive at 1/32 dilution. Choriocarcinoma was then diagnosed. She was referred to the Dept. of Thoracic Surgery for exploration. At operation the tumor was found to be of the size of double fists. Its extensive adhesions to the Diaphragm rendered the resection impossible. She was then referred to the Dept. of Gynecology. After 8 courses of 5Fu alone and 4 courses of combined 5Fu and KSM, the huge pulmonary metastatic shadow resolved completely. The urine concentration test persisted to be negative. Follow-up for 2 years showed no evidence of recurrence.

Case 4.

C. S., Shu, a cadre aged 29, gravida I para 0, complained persistent vaginal bleeding 4 months after curettage for hydatidiform mole. The uterus was enlarged to the size of 6 week pregnancy and pulsation was felt on the left parametrium. Hysterosal-

pingogram revealed an enlarged uterine cavity with infiltration of iodized oil into the myometrium. The urine pregnancy test was positive at 1/64 dilution. Chest film showed a small roundish shadow in the right lower lung. Chorioadenoma destruens with pulmonary metastasis was diagnosed. After 3 courses of 5Fu the urine concentration test became negative and pulmonary shadow completely resolved. An additional course of 5Fu was given to her before discharge. Hysterosalpingography performed 3 months later revealed that the outline of the right cornua was slightly irregular, otherwise the uterine cavity was normal. Follow up for 2 years showed no evidence of recurrence. At the time of writing she is 7 months pregnant with an uneventful course.

DISCUSSION

Chairman Mao Tsetung, the great leader of the Chinese people, has pointed out:

"The history of mankind is one of continuous development from the realm of necessity to the realm of freedom. This process is neverending. In the fields of the struggle for production and scientific experiment, mankind makes constant progress and nature undergoes constant change; they never remain at the same level."

The progress in the treatment of malignant trophoblastic tumors during the last two decades in the Peking Fanti Hospital fully prove the truth of scientific thesis of Chairman Mao's. The fact that the fatal choriocarcinoma is becoming curable has opened up a thoroughfare in the conquest of malignant disease by mankind.

Chemotherapy of malignant trophoblastic tumors has made great advances in the last decade. Advancement was obtained in this hospital through efforts in three respects:

1. Through ceaseless efforts in search of more and better anticancer drugs.

Prior to the use of 6MP and MTX, choriocarcinoma was regarded as a fatal disease. Its mortality was about 90%. Our traditional methods of management before 1958 were surgical extirpation of the uterus supplemented by irradiation. Nitrogen mustard and nitrovin were added to some of the cases. All the patients with choriocarcinoma except for 4 out of 6 Stage I cases ended fatally.

In 1958, under the influence of the Great Leap Forward, the workers of the Dept. of Gynecology of this hospital started to tackle choriocarcinoma which seriously threatened the lives of women. During the course of an investigative drug the embryocidal qualities of 6MP was first observed. Since trophoblastic tumors are embryonic in origin, it occurred to us that this drug might prove to be effective in treating trophoblastic tumors. The usual dosage for leukemia (2.5mg/kg/day) was first tried. And it was found to be of no avail. Therefore it was gradually increased to the present dose of 6.0-6.5mg/kg/day. Effective arrest of trophoblastic growths was obtained. But it was also found that severity of toxic reactions was proportional to the increment

of dosage, especially occurring in the hemopoietic system which often interfered with the course of therapy. Through the conjoint efforts of physician and nurses, the rule and course of toxic reaction of 6MP were mastered and active measures to prevent serious complications were acquired thus enabling the use of large dosage of 6MP as a practical and effective method of therapy.

Since 1961 MTX which was introduced by Hertz (6,7) was used to manage 6MP-resistant cases.

"Ultra-large dosage" of 5Fu (mixed in dextrose and given by i.v. drip) was found in 1964 to be superior to 6MP in therapeutic effects. In addition to its usefulness in treating 6MP and MTX resistant cases it was found to be less toxic than either of the two.

Since 1965 KSM was also successfully used in managing antimetabolites (6MP, MTX, and 5Fu) resistant cases. It was found to be most effective in dealing with pulmonary metastasis. The combined use of KSM and 5Fu had achieved spectacular results in not a few far-advanced cases.

The Great Proletarian Cultural Revolution which began in 1966 brought about a new upsurge in the learning of Mao Tsetung's thought. Mass efforts in participating scientific research began anew. Under the inspiration of the spirit of serving the sick heart and soul, of undertaking every step from the interests of the patient, research work on malignant trophoblastic tumors made a new leap forward. Through the combined efforts of the medical and nursing personnel, not a few would be fatal cases with metastases to the brain, liver, kidney and G-I tract recovered by the combined use of the chemotherapeutic agents. Through administration of drugs by various routes, meticulous observations, scrupulous nursing care and many other auxiliary measures the mortality rate of choriocarcinoma was further reduced from 57.3% to 38.9%. Naturally the summit has not yet been reached. Some of the cases which were resistant to all the drugs used failed to recover. Therefore, searching for better and more effective chemotherapeutic agents remains a task as yet to be fulfilled.

2. Through a rational handling of the relation between drug dosage and toxic reactions.

The problem we are facing now is the contradiction between effective dosage and toxic reactions. Our task, therefore, is to enhance the effectiveness and lower the toxicity.

The question of dosage and toxicity was most acute when 6MP was used as the chief therapeutic agent. The toxicity was serious that it threatened the life of the patient when the dose was increased to above 6.5mg/kg/day. On the other hand when the dose was below 6.0 mg/kg/day the therapeutic results were usually unsatisfactory. In order to attain a cure the daily dose must be kept above 6.0 mg/kg/day and the same time effective measures were enforced, namely close observation and meticulous nursing care,

prevention of secondary infection and hemorrhage and using Chinese herb to treat stomatitis and toxic hepatitis, thus minimizing the toxicity and safeguarding the purpose of obtaining a recovery.

Improving the method of the administration of drugs is another aspect of attaining the same purpose. According to the Wisconsin Plan, by the large-dosage regime 5Fu was given 15mg/kg/day intravenously for 5 days in succession, after which it was reduced to 7.5 mg/kg every other day until the appearance of toxic symptoms. The toxic reactions with such regime were severe. In Ansfield's series of 1091 cases⁽¹¹⁾ the white count lowered to below 2,000/mm³ in 32%, diarrhea occurred in 64%, stomatitis in 48% and 22 cases (about 2%) succumbed to toxicity. Cudmore reported in his review that some of the mortality rate were as high as 6.9%⁽¹²⁾.

In this hospital, 5Fu is given by means of slow dripping method, taking 6-8 hours to complete the daily dose. By such a way, we found that the dose could be increased to 25-30 mg/kg/day for 10 days. Such an improvement was named "ultra-large" dosage. In using such a method of administration the toxicity was less than of Wisconsin Plan. The white count was lowered to below 2,000/mm³ in only 5.4%. Deaths due to toxicity were only 2 in 236 (< 1%). By slow dripping of 5Fu an effective concentration of drug can be maintained for a long duration, thus preventing the sudden rise of blood level followed by a quick drop which is unfavorable in achieving an effective result. In addition the continuous dripping of drug also favors the pharmacologic action of the anti-metabolites, thus the recovery rate is increased.

3. Through the individualization of the methods of management.

The choice of medicine, method of administration and time of surgery were planned according to the condition of each case.

The selection of a therapeutic agent depends upon the actual condition of each patient and the special merits of drug. Experience through years of practice uncovered the fact that the action of each of the 4 drugs are different in different conditions and at different sites of metastases. For example, 5Fu is more effective in cervical and vaginal metastases, KSM more effective in pulmonary metastasis and MTX in brain metastasis. Favorable results were often obtained on rapidly-progressing cases with widespread metastases by using 5Fu and KSM conjointly. Therefore, before deciding on any drug the condition of the patient should be carefully analyzed, such as extent and site of metastasis, the function of bone marrow and liver, etc.. Unfortunately, we have not yet found a method in selection any anti-cancer agent similar to the drug susceptibility test used in the choice of antibiotics. Therefore, it is often necessary to use another drug when a case is found unresponsive or resistant to certain agent.

In addition to the commonly used route of administration, drugs can be given locally to particular sites of metastasis. 5Fu can be directly injected into the vaginal

metastatic nodules. MTX can be given intrathecally in brain metastasis. Internal carotid artery or hepatic artery intubation can be used for administering medicine in cases of brain or liver metastasis.

Before 1964, subradical hysterectomy was routinely performed at the 3rd day of the initial course. Since 1965 owing to the introduction of 5Fu and KSM, surgery was usually postponed in patients of poor operative risk or cases with extensive lesion until the patients' conditions became more favorable. This was made possible due to the fact that the toxicity of these two drugs on the bone marrow were much less than 6MP or MTX. Thus the occurrence of secondary hemorrhage or infection due to medication was very much reduced.

According to our experience that the plan of management must be based upon the actual conditions of individual cases through careful investigation and scientific analysis. In order to obtain the expected result, no formula of treatment can be laid down as a rule to be followed rigidly.

In conclusion it is our opinion that the recovery rate of malignant trophoblastic tumors can be further raised in the future through ceaseless efforts in search of more and better anticancer drugs, rational handling of the relation between drugs dosage and toxic reaction and individualization of the methods of management according to the actual conditions of each case. Moreover, in order to finally eradicate this serious disease which endangers the health and threatens the lives of many women, intensive investigation of its pathogenesis is the urgent task of the medical workers.

SUMMARY

1. A total of 581 cases of malignant tumors were treated in this hospital from 1949 to 1968. Rate of recovery was remarkably raised during the last 20 years. The mortality rate for choriocarcinoma was reduced from 89.2% prior to 1958 to 57.3% after the Great Leap Forward, the chorioadenoma destruens from 25.9% to 13.1%. Since the Great Proletarian Cultural Revolution the mortality rate was further reduced to 38.9% and 5.2% respectively.
2. Preservation of fertility was successfully achieved in 85 cases by chemotherapy alone since 1959, 46 of which became pregnant, a rate of conception of 54.1%.
3. The effective chemotherapeutic agents available at present are 6MP, MTX, 5Fu and KSM. The drugs in favor in recent years are 5Fu, and KSM due to their relatively low toxicity.
4. The toxic manifestations of different drugs were different. Bone marrow depression and liver damage were prominent features of 6MP and MTX. Diarrhea and other gastro-intestinal tract reactions were most frequent with 5Fu. Alopecia and stomatitis were frequently seen with MTX and KSM.
5. With more, better, less toxic anti-cancer drugs, the recovery rate of malignant trophoblastic tumors can be further raised in the future.

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