

canal some 3-4 cm in length. Traction exerted every 24 hr will result in a final length of 9 cm.

About 7-8 days after the operation, the traction apparatus is removed and the olive and threads are extracted via the vagina. Phalluses of gradually increasing size are then inserted.

This technique has been applied in 159 cases. A functionally successful result was achieved in all but two cases. These were patients who had married without revealing their deformity. The operation was initially successful, but marital differences resulted in abandonment of intercourse and reduction in the length of the vagina. Divorce followed in one case.

With our technique, the newly formed vagina is covered by the mucosa of the pseudohymenal canal as this is gradually stretched by increasing traction. Over a period of time, this new wall acquires the anatomical and functional features of a normal vaginal wall. The cytohormonal picture becomes almost normal; a virtually normal histological and histochemical pattern is also observed and pH values range between 5 and 7.

#### SUMMARY

The Author describes the aetiopathogenetics, anatomo-pathological, diagnostic and therapeutic aspects of the Rokitansky-Küster-Hauser syndrome.

A personal technique of surgical therapy applied on 159 cases is referred.

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## The antimetabolic drugs in the treatment of gynaecological cancer

by

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In the study of gynaecological neoplasias chemotherapy has attained a validity of clinical application which, for certain drugs and with the appropriate route of administration and in suitable combinations, is decisive for the treatment of some neoplasms (ovarian or trophoblastic tumours; other uterine tumours, metastases, etc) they are effective although only as a palliative. From this a « combined therapy » has been developed which has been carried out extensively in our school and in which we have had considerable experience (<sup>1, 2, 3, 4, 5</sup>). Chemo-isotope-radio-surgical treatment appears to be especially suitable and to be capable of actual control of some neoplasms of the female genitalia (<sup>6, 3, 4</sup>) and in our

opinion adequate chemotherapy should be included in the scheme of treatment of gynaecological neoplasia.

In our clinical experience we have used antimetabolites as follows:

- a) in combination with other chemotherapy
- b) combined with radiotherapy
- c) in the treatment of trophoblastic tumours.

With the antifolics (Amethopterine) alone or in combination with other drugs and by systemic, intrauterine, intra-arterial and local administration we have treated over 500 patients affected by malignant tumours of various histological types and sites (ovarian, uterine body, cervix, vagina and vulva) chorionepithelioma (gesto- and teratochorionepithelioma), chorioadenoma, malignant vesicular mole, and also those belonging to potentially malignant categories. We have often used other antimetabolites (antipurines, antipyrimidines) in combination with antifolics and with alkylating agents which were introduced into the scheme to increase drug potentiation. Local treatment by intraperitoneal or intra-arterial infusion is also of great interest as it is almost without danger or trauma to the patient, requiring little in the way of clinical attention.

The concentration of the antiblastic drug in the tumour by infusion or by regional intra-arterial perfusion, whether to the area or to the organ actually supplied, enables the *lack of selectivity of the drug* to be obviated, though only partially, by *selective topographic* treatment.

This is often used in our clinic and the infusion of antifolics (Methotrexate) is used in the treatment of trophoblastic tumours or in combination with chemo- and radiotherapy for the treatment of other genital tumours.

Intra-aortic infusion by transcutaneous and transfemoral catheterisation of the lumbar aorta (pelvic douche) gives a regional therapy with only slight trauma to the patient. Transcutaneous transfemoral catheterisation of the hypogastric arteries and of their branches (<sup>7,8</sup>), on the other hand, is more advantageous because it enables the drug to be infused directly into the pelvic blood supply or actually into the blood supply of certain organs (bladder, uterus, vagina, vulva).

In addition, arterial catheterisation also enables the regional vascular system to be explored radiologically, thus giving data for a more accurate diagnosis of the spread of the neoplasm.

In our experience the combination of antimetabolics (antifolics, antipurines and antipyrimidines) with the alkylating radiomimetics and with drugs affecting mitosis (alkaloids of *Vinca rosea*) appear to be generally suitable in raising considerably the therapeutic quotient as shown by an improved or at least equal efficacy on the tumour and with usually definitely reduced general toxicity. By these combinations it is possible in some cases to overcome primary chemoresistance or to avoid the development of crossed or parallel secondary chemoresistance.

The combination of ovarian hormones (progestagens, oestrogens) in high dosage can increase the blood supply to the neoplasm and can therefore potentiate, even indirectly, the effects of chemotherapy.

In view of the fact that medical treatment is greatly complicated by multiple factors linked to the biochemistry of the neoplastic cells as well as by the mechanisms of action of the drugs, pharmacological combinations can definitely potentiate the therapeutic effects. An example of *combined antiblastic* therapy is the following:

systemic or local treatment with substances with an antimitotic action; plus

systemic or local treatment with antimetabolites; plus systemic or local treatment with radiomimetic alkylating agents; plus systemic or local treatment by hypoglycaemic drugs and/or oestrogens; plus local hyperoxygenation or the use of vasodilators.

We believe that chemotherapy must be started as early as possible from the patient's first attendance so as to increase the possibility of success, but all too often it is found that recourse is made to this treatment when the neoplasm is either in an advanced stage or is terminal through the failure of traditional therapy.

The administration of antimetabolites, especially of antifolics (Methotrexate) and antipyrimidines (5-fluor-uracil), is interesting through the heightening of the radiosensitivity of the neoplastic elements. Intra-arterial chemotherapy with simultaneous local hyperoxygenation by infusion of  $O_2$  directly into the afferent vessels to the tumour during radiotherapy gives better results. In fact it is known that the efficacy of ionizing radiation is directly related to the oxygenation or to the temperature of the tissues and that the failure of radiation therapy is often referable to anoxic elements which are therefore resistant to ionizing radiation. Oxygenation of tumour tissue is particularly suitable if radiotherapy is combined with antimetabolite therapy in order to potentiate the focal effect without increasing the effects on the skin.

Antimetabolites (amethopterin combined with 6-mercaptopurine) seem suitable in the control of trophoblastic tumours.

From our clinical experience supported by data in world literature, we can confirm that if given in adequate doses and by the most suitable route the antifolics are particularly suitable for the early treatment and control of metagradid trophoblastic tumours and should definitely be prescribed today whatever other treatment, surgical, or radio-therapeutic is given<sup>(9, 10, 11)</sup>.

In conclusion, we feel that we have shown that the antimetabolites, particularly the antifolics, are drugs of undoubted value in gynaecologic tumours but we believe that their use, as also any other antitlastic chemotherapy, must be dependent on the clinical results of the antitlastic chemotherapy, must be dependent on the clinical results of the timely use of the maximal dosage tolerated and by the selection of the most suitable routes of administration in combination with chemo-radiosurgical treatment. Against this, whatever scheme of treatment is prescribed and whatever diagnostic schedule is used to suggest the required treatment, it must be adapted to each individual case as only by these means will we be able to bring to fruition with a real chance of success the possibilities that pharmacology offers today in the treatment of malignant gynaecological tumours.

### SUMMARY

The clinical application of antimetabolic drugs in the treatment of gynaecological cancer, alone or in combination with other drugs and with the radiotherapy is described.

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## Medical treatment of trophoblastic disease

by

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Antiblastic drugs in the treatment of trophoblastic tumors are important therapeutic agents ensuring frequent success in modern gynaecology and are often surprising as regards final results.

In the study of trophoblastic tumors numerous reports in the literature indicate both the possibility of a therapeutic association between antiblastic preparations, radiotherapy and surgery, and the possibility of equal success with chemotherapy alone.

The experiences of our unit (<sup>1</sup>) are decidedly favourable as regards treatment with antiblastic preparations alone, combining them with surgery and radiotherapy only in those rare cases of failure.

Chemotherapy in the control of trophoblastic tumors must be applied alone (<sup>2, 3, 4, 5</sup>). This has the ability, in many patients, to prevent the evolution of trophoblastic disease, leading to a final clinical cure (<sup>6, 7</sup>).

The reduction of mortality from chorion-epithelioma, chorio-adenoma and malignant mole observed in recent years, due to the contribution of chemotherapy, is notable in world literature; mortality has been reduced from the 80-100% that was recorded before the advent of chemotherapy (<sup>8</sup>) to about 30% with the use of suitable preparations singly or together with traditional therapy (<sup>7</sup>).

An abundance literature since 1967 shows that the best results are achieved with chemotherapy alone, while combining chemotherapy with surgery, although giving satisfactory results, is less effective. We do not consider that the reservations of various writers on the reliability of the diagnosis of trophoblastic malignancy are sufficient to cast doubts on the real efficacy of chemotherapy.

There is no doubt that these diagnostic difficulties frequently lead to some forms being considered highly malignant, when in fact they are not, and to a