SEVENTY-FIVE CASES OF SOLID TUMOURS TREATED BY A MODIFIED QUADRUPLE CHEMOTHERAPY REGIME

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SUMMARY.—Seventy-five cases of malignant solid tumours treated by a quadruple chemotherapy regime are described. These tumours originated in the breast, head and neck, bronchus, genital tract, cutaneous melanoma, soft tissue and gastro-intestinal tract. All 14 patients with breast carcinoma underwent remission and in 6 this was complete. Significant remissions were seen in gastro-intestinal and head and neck malignancies, and also in the soft tissue group. A short response was noted in 6 of 14 cases of bronchial carcinoma. Malignant melanoma, testicular, ovarian and cervical carcinomata failed to respond.

In all, 40 of 75 patients underwent objective remission.

RESULTS of treatment of solid tumours (as distinct from reticuloses and leukaemias) by individual chemotherapeutic agents have been disappointing, although short remissions in 50% of breast cancer cases have been observed with cyclophosphamide (Kunkler *et al.*, 1968) and 30% with 5-fluorouracil (Heidelberger and Ansfield, 1963). It was at one time hoped that concentration of dose by intra-arterial techniques would improve the response rate for localised tumours, but this method has fallen into disfavour at this Centre owing to frequent relapses and a disturbing incidence of complications. The position of intra-arterial chemotherapy, certainly in head and neck cancer, has further been weakened by the results of intermittent high dose intravenous injections of Methotrexate, which have given a 57% remission rate in one series (Leone *et al.*, 1968).

In an effort to improve the generally disappointing results associated with single cytotoxic agents, intravenous injection of a combination of the 4 cytotoxic agents, cyclophosphamide, Methotrexate, Vincristine and 5-fluorouracil, originally advocated by Constanzi and Coltman (1969) has been selected, though in a reduced dosage (Table I).

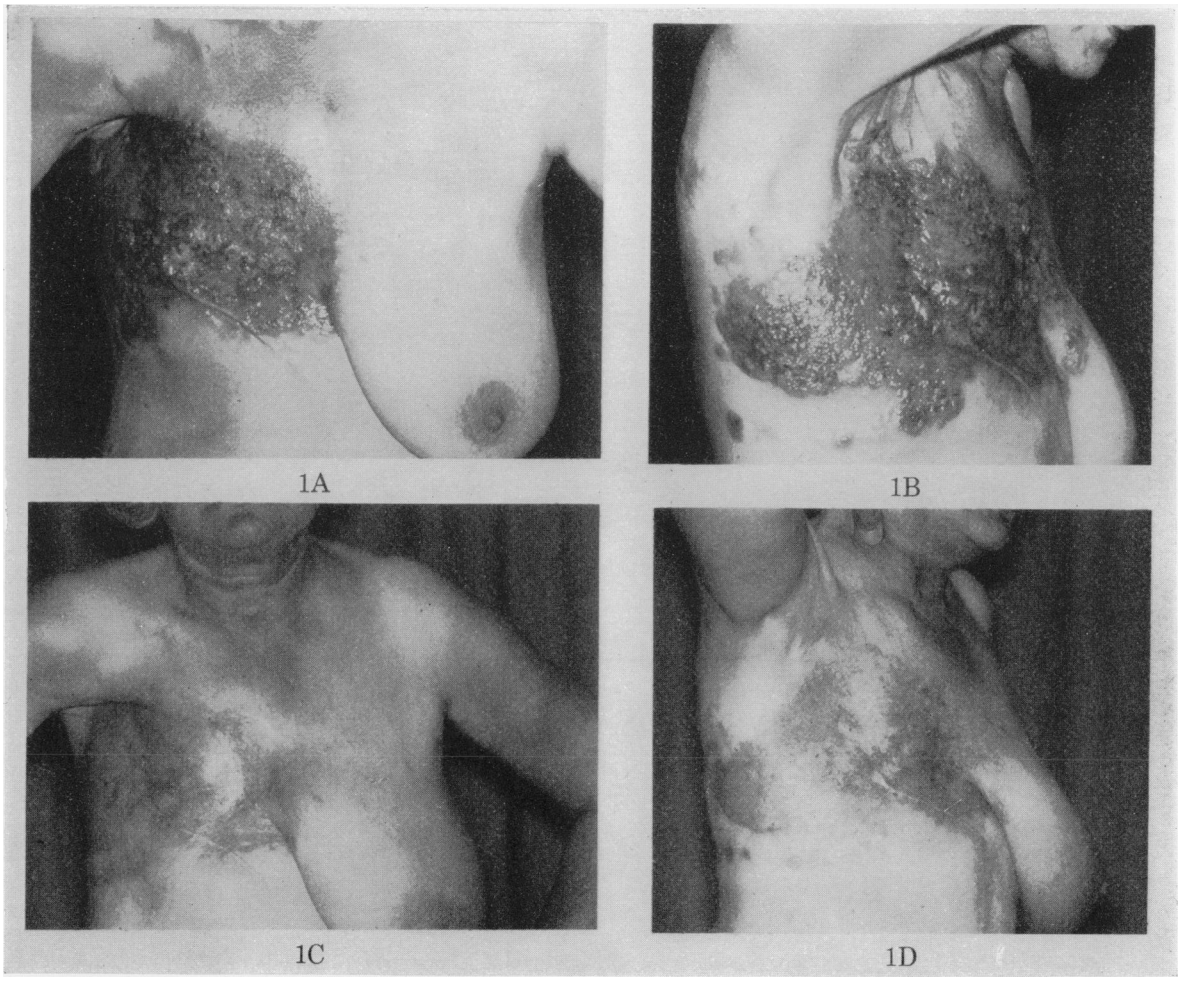
EXPLANATION OF PLATES

FIG. 1.—Nodular carcinoma en cuirasse before (A and B) and 3 months after (C and D) chemotherapy.

FIG. 2.—Breast carcinoma. Widespread diffuse opacities both lung fields, before (A) and 2 months after (B) chemotherapy.

FIG. 3.—Carcinoma of bronchus with cutaneous metastases before (A) and 1 month after (B) chemotherapy, showing partial response.

FIG. 4.—Cutaneous deposits from alveolar rhabdomyosarcoma before (A) and 2 months after (B) chemotherapy. Mediastinal deposits before (C) and 2 months after (D) chemotherapy.



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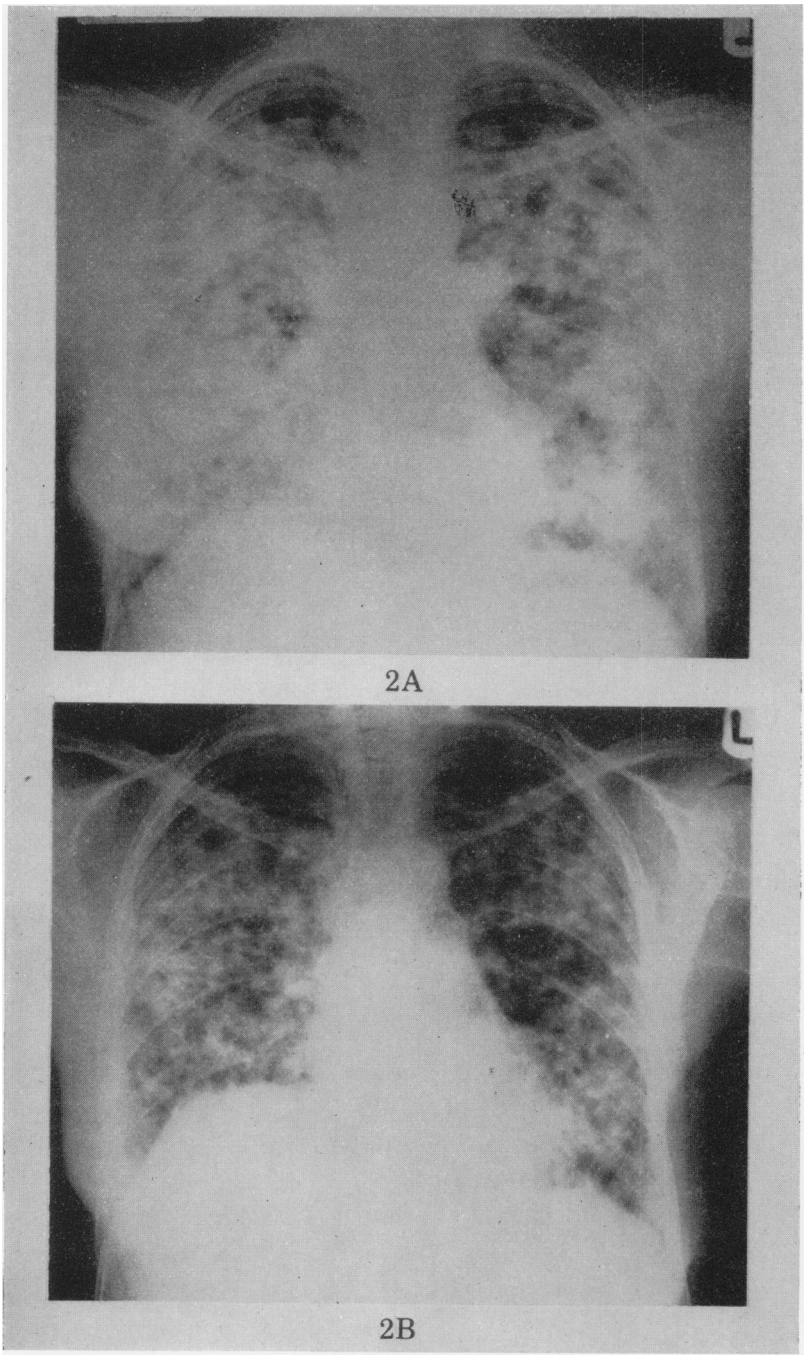

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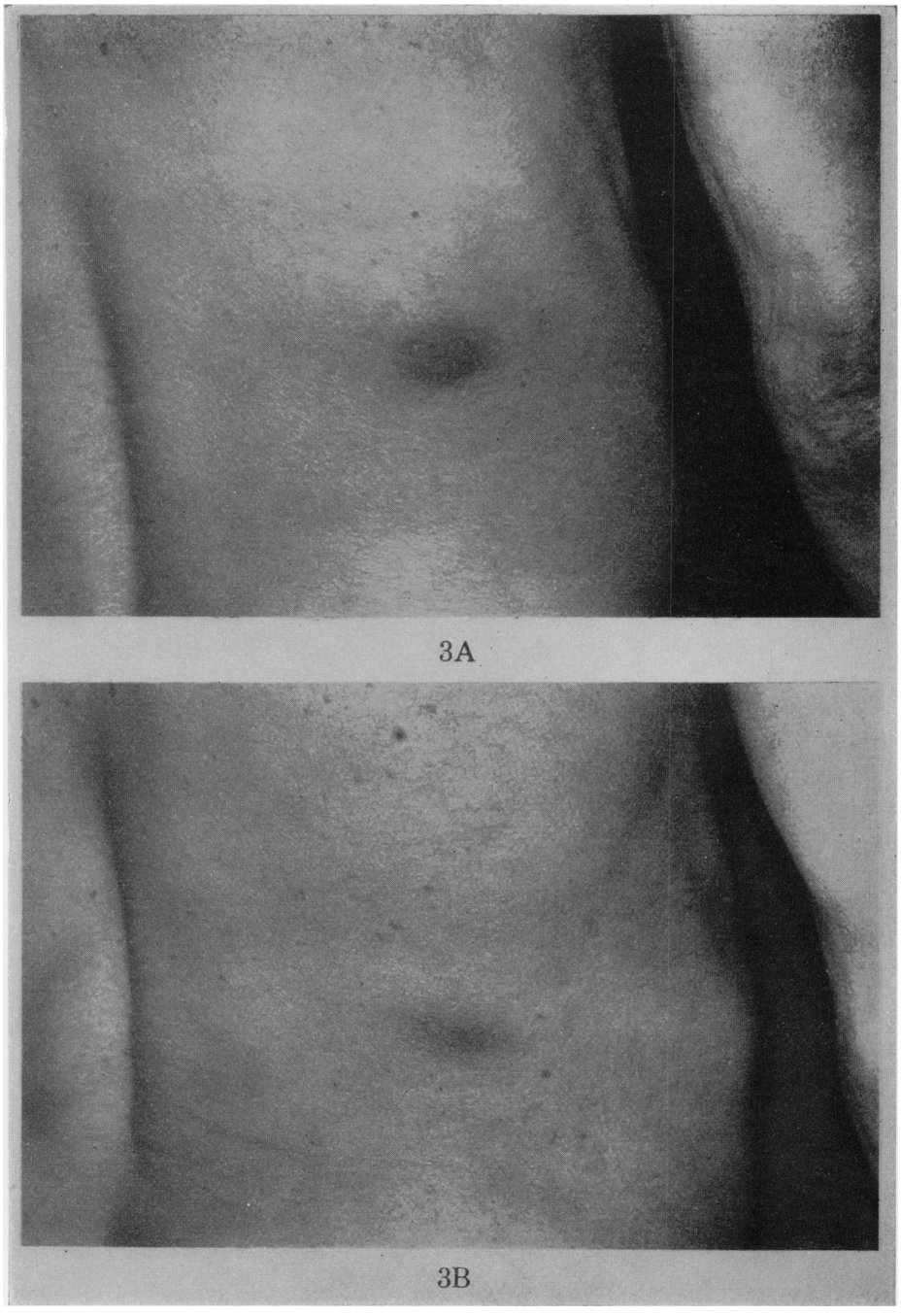

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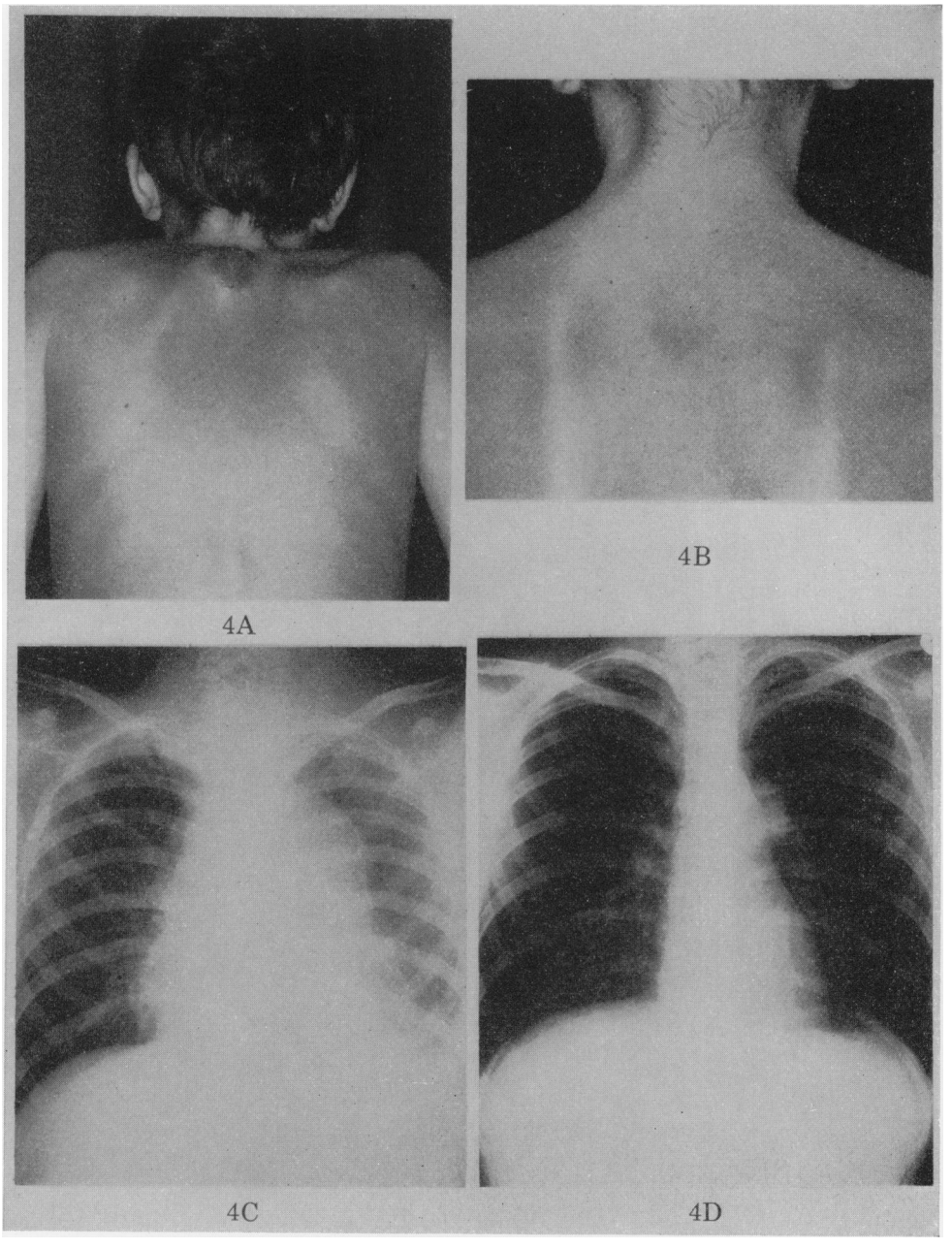

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TABLE I.—*Quadruple Chemotherapy*

Constanzi and Coltman, 1969, Cancer, **23**, 589		Modification of dosage in the adult suggested by the authors
300 mg.—2 doses days 1 and 5	Cyclophosphamide	2–300 mg.—2 doses days 1 and 5
0·5 mg./kg./day—2 doses days 1 and 4	Methotrexate	0·25 mg./kg./day—2 doses days 1 and 4
0·025 mg./kg./day—2 doses days 2 and 5	Vincristine	0·015 mg./kg./day—2 doses days 2 and 5
10 mg./kg./day, daily	5-Fluorouracil	7·5 mg./kg./day, daily for 5 days

Constanzi and Coltman (1969) suggested that the interval between the first and second course should be 2 weeks, and thereafter 4 weeks. This regime was followed in the early cases, but we now find that a 4-weekly interval throughout is effective. The modified schedule was adopted because severe toxicity was seen in early cases treated according to the original protocol. Further reduction has been made in individual cases for any of the following reasons:

1. Old age.
2. Previous chemotherapy or radiotherapy.
3. Widespread bone marrow involvement.
4. General ill health.

In the series of Constanzi and Coltman (1969) treatment was continued for an overall maximum period of 6 months. In the present series patients have been under treatment for periods up to 18 months.

Clinical material

Seventy-five patients with solid tumours have been treated: Table II indicates

TABLE II.—*Types of Tumour Treated and Degree of Response Achieved*

	Objective remissions			
	Complete	Partial	Failure	Total
Breast carcinoma	6	8	0	14
Head and neck carcinoma	1	7	2	10
Bronchial carcinoma	0	8	6	14
Ovarian carcinoma	0	0	4	4
Testicular carcinoma	0	0	4	4
Cervical carcinoma	0	3	0	3
Malignant melanoma	0	0	10	10
Soft tissue sarcoma	0	5	1	6
Various				
Nephroblastoma	0	1	1	2
Hepatoma	0	0	1	1
Stomach carcinoma	1	1	0	2
Large bowel carcinoma	1	1	1	3
Bone carcinoma	0	0	2	2
Total	9	34	32	75

the type of tumour and the degree of response achieved. Objective response was graded as:

1. Complete
2. Partial
3. Failure

The Karnofsky scale, Table III (Karnofsky and Burchenal, 1948) to indicate subjective response and improvement in the general condition of the patient.

TABLE III.—*Karnofsky's Rating for Chemotherapy Response*

	%
Normal	100
Minor signs or symptoms	90
Normal activity with effort	80
Unable to carry on normal activity, but cares for self	70
Requires occasional assistance with personal needs	60
Requires considerable assistance and medical care	50
Disabled	40
Severely disabled and hospitalized	30
Very sick: active supportive treatment necessary	20
Moribund	10
Death	0

Complications

Thirty-six cases were treated without side effects. In the remainder the most frequent was evidence of toxicity, leucopenia (2000 white cells or less), followed by alopecia, nausea and vomiting, stomatitis and peripheral neuropathy.

Bone marrow depression (16 cases) was no more frequent or profound than with standard courses of, *e.g.* Methotrexate, 5-fluorouracil or cyclophosphamide used singly.

Alopecia occurred in 15 cases, mostly in the early part of the series. It is possible that this incidence would have been greater had it not been for a scalp tourniquet applied during and for 5 minutes after injection.

In 3 patients with peripheral neuropathy Vinblastine was substituted for Vincristine in view of the known neurotoxic effect of the latter compound.

Three patients failed to complete their treatment because of side effects.

RESULTS

Breast Carcinoma (Table IV)

These were patients with advanced and uncontrolled disease, which had previously been treated by hormones or adrenalectomy, and/or 5-fluorouracil or cyclophosphamide by injection. All cases showed some response; in 6 out of 14 this was complete and maintained for more than 6 months.

Subjective improvement was manifested by relief of bone pain and improvement in general well-being. Objective remission was observed in chest wall recurrence (Fig. 1A, B, C, D), in liver deposits and in pulmonary metastases.

In 1 patient lung function studies were carried out before and after 2 courses of chemotherapy. They showed an increase in total lung and initial residual capacity and in maximum expiratory flow rate (Table V, Fig. 2A, B). Chest X-ray confirmed some clearing of disease.

Two patients were considered too ill for endocrine ablative procedure, but following good objective and subjective response to quadruple chemotherapy, successfully underwent bilateral adrenalectomy and oophorectomy. Remission continued without further chemotherapy in both cases.

Four patients with carcinoma en cuirasse were treated; 1 showed complete response and 3 partial response. In our experience this type of disease has proved unresponsive to single agent chemotherapy.

TABLE V

	Predicted normal	Before	2 months after
a. *Spirometry* (litres)			
P.E.F.R.	417	165	185
F.V.C.	2·44	1·27	1·43
F.E.V. (1 sec.)	2·09	0·84	1·09
$\frac{\text{F.E.V.}}{\text{F.V.C.}}$	86%	66%	76%
M.M.E.F.R. L/Sec.	2·99	0·56	0·84
M.M.I.F.R. L/Sec.	3·74	1·43	2·16
$\frac{\text{M.M.E.F.R.}}{\text{M.M.I.F.R.}}$ Ratio	0·8	0·39	0·38
b. *Lung volumes* (litres)			
Slow V.C.	2·44	1·27	1·43
F.R.C.	2·26	1·7	1·64
T.L.C.	4·05	2·53	2·47
$\frac{\text{R.V.\%}}{\text{T.L.C.}}$	35%	49·9%	41·1%

Head and neck carcinoma (Table VI)

The palliation of uncontrolled head and neck cancer presents a challenging problem to the chemotherapist. Intra-arterial methods have fallen from favour in this Centre, and, as already mentioned, single intravenous weekly injections of Methotrexate have produced comparable results with far less morbidity. One of us (I.H.) has observed objective response in 50% of patients treated by intravenous Methotrexate, but palliation was generally short-lived, seldom exceeding 3 months.

Quadruple chemotherapy has been used mainly in those cases showing failure of control with, or relapse following intravenous Methotrexate. Further remission has been achieved in 6 of 10 patients, lasting up to 6 months in 1 case.

In view of these findings we suggest that quadruple chemotherapy should replace the use of a single agent in this group of cases.

Bronchial carcinoma (Table VII)

Fourteen cases have been treated. None showed complete regression of disease, but in 8 patients there was a partial, short-lived, response (maximum duration 3 months). Rapid, though transient, regression of cutaneous metastases was noted in 3 patients (Fig. 3A, B). One patient with superior vena cava obstruction, which had relapsed after radiotherapy, was treated (by injection into the veins of the uninvolved lower limbs) with rapid resolution of symptoms.

Our experience suggests that the results may not be better than those following single weekly intravenous injections of cyclophosphamide, though admittedly this series is small.

Genital carcinoma (Table VIII)

Four testicular and 4 ovarian carcinomas were treated, without effect. Wiltshaw (1965) claimed 43% remission for at least 2 months in ovarian cancer using chlorambucil; Bateman (1962) reported a similar remission rate with ThioTepa, and Burns *et al.* (1969) claimed 50% response in carcinoma of the ovary treated with phenylalanine mustard. The poor response to quadruple chemotherapy is therefore surprising.

TABLE IV.—*Fourteen Cases of Breast Carcinoma*

Patient	Age	Sex	Site of metastases	Previous chemotherapy and/or hormone therapy	Number of courses	Side effects	Response			Duration of response (months)	Comment
							Objective	Karnofsky Pre-%	Karnofsky Post-%		
L.D.	63	F	carcinoma-lymphangiitis, soft tissue bone	Norethisterone 5-fluorouracil	5	Alopecia	Complete	80	90	6	Alive, successful adrenalectomy and oophorectomy 5 months after quadruple
M.D.	43	F	Bone	5-fluorouracil adrenalectomy	8	Alopecia	Partial	80	90	8	Alive
D.B.	54	F	Soft tissue en cuirasse	Control with Nandrolone a year 5-fluorouracil cyclophosphamide	9	Alopecia mild nausea	Partial	80	90	9	Alive
B. G.	56	F	Soft tissue en cuirasse	5-fluorouracil methotrexate cyclophosphamide	12	Temporary alopecia	Complete	90	100	12	Alive
B.W.	47	F	Bone	Nandrolone 5-fluorouracil cyclophosphamide	9	Alopecia anaemia leucopenia	Partial	70	90	9	Alive, relief of pain

H.C.	45	F	Soft tissue, hepatic enlargement	Norethisterone 5-fluorouracil	3	Vomiting	Partial	80	90	9	Alive, successful adrenalectomy and oophorectomy after 3rd course
P.P.	54	F	Soft tissue en cuirasse hepatic enlargement	Bilateral oophorectomy and adrenalectomy 2 months before quadruple	7	Nausea	Complete	70	100	8	Alive
M.R.	54	F	Soft tissue en cuirasse	Prednisone 5-fluorouracil methotrexate ICRF.159	9	Alopecia, mental depression	Partial	80	90	9	Alive
E.B.	56	F	Soft tissue, pulmonary metastases	Norethisterone	6	Leucopenia	Partial	50	80	6	Alive, relief of dyspnoea.
H.E.	60	F	Soft tissue bone	Nandrolone	4	Nil	Partial	60	90	4	Alive, relief of pain
D.B.	65	F	Hypercal-caemia, bone	—	3	Nil	Complete	50	80	3	Alive, relief of pain. Normal calcium
M.McC.	75	F	Soft tissue en cuirasse	Nandrolone cyclophospgamide	4	Nil	Partial	90	90	4	Alive
V.E.	74	F	Soft tissue	5-fluorouracil cyclophosphamide	6	Stomatitis, alopecia, leucopenia	Complete	80	90	6	Alive
L.O.	70	F	Bone, brain	Nandrolone, bilateral adrenalectomy	6	Peripheral neuropathy	Complete	80	90	6	Alive, relief of pain

TABLE VI.—*Ten Cases of Head and Neck Carcinoma*

Patient	Age	Sex	Diagnosis	Previous treatment	Number of courses	Side effects	Response			Duration of response (months)	Comment
							Objective	Karnofsky Pre-%	Karnofsky Post-%		
J.C.	64	M	Carcinoma of larynx	Local recurrence after radiotherapy and local surgery	6	Nil	Partial	60	80	5	Died 9 months after starting quadruple. Chemotherapy at 5 months, changed to Bleomycin
E.W.	64	M	Carcinoma of larynx	Local recurrence after radiotherapy and local surgery	4	Nil	Partial	50	50	3	Died 6 months after starting quadruple
J.S.	36	M	Carcinoma of pyriform fossa	Local recurrence after radiotherapy	1	Nil	Failure	30	—	Nil	Died during 1st course
J.R.	69	M	Carcinoma of floor of mouth	Local recurrence after radical radiotherapy. Failure of control with i.v. Methotrexate	3	Nil	Partial	70	70	3	Patient refused to continue with the regime
E.E.	69	F	Carcinoma of lip	Recurrence after radiotherapy, local recurrence after plastic surgery. Failure of control with i.v. Methotrexate	3	Nil	Partial	60	70	3	Died of bronchial pneumonia

J.B.	64	M	Carcinoma of oral cavity with cervical gland metastases	Recurrence in block dissection of neck, failure of control with i.v. Methotrexate	5	Nil	Complete	90	100	6	Continues in remission with non-active disease
G.B.	58	M	Carcinoma of naso-pharynx with cervical gland metastases	Radical radiotherapy, oral Methotrexate and ICRF 159 No control. i.v. Methotrexate control 3 months	3	Nil	Partial	50	60	3	Died 4 months after starting quadruple
H.H.	65	F	Carcinoma of floor of mouth	Radical radiotherapy. Control with i.v. Methotrexate for months	2	Leucopenia	Partial	50	50	Nil	Died 3 months after starting quadruple
G.M.	30	M	Recurrence of basal cell carcinoma of the face, with pulmonary metastases	Plastic surgery	2	Nil	Failure	60	60	Nil	Died 1 month after starting quadruple
F.R.	52	F	Leukoplakia, carcinoma of cervical node metastases	Radium implant. External radio-nodes. i.v. Methotrexate	3	Leucopenia	Partial	50	50	2	Died 3 months after starting quadruple

Three cases of cancer of the cervix were also treated and failed to respond.

Malignant melanoma (Table IX)

Ten cases of malignant melanoma were treated without response, failing to substantiate the encouraging results suggested by Constanzi and Coltman (1969). Seven patients survived for more than 6 months, but it is unlikely that quadruple chemotherapy altered the natural history of their disease. It could be argued that our modification of the dose regime contributed to these poor results, but our overall clinical impression is that this drug combination is of little value in malignant melanoma.

Soft tissue sarcoma (Table X)

The value of chemotherapy in soft tissue sarcoma is not generally recognised, although Wiltshaw (1967) has reported benefit following oral Methotrexate. Arterial infusion or perfusion may also produce regression in these lesions (Newton, 1967).

We have treated 6 patients, using the quadruple regime. A boy, aged 14, with metastases from an alveolar rhabdomyosarcoma involving mediastinum, liver, pancreas and skin, showed complete clinical regression within 2 months of starting treatment. This patient continued in reasonably good general health for a further 15 months, but isolated recurrences in the right inguinal region, pancreas (proven at laparotomy) and mediastinum required local radiotherapy (Fig. 4). Unfortunately this patient has now died from intestinal haemorrhage, 20 months after starting chemotherapy.

Four other cases continued to show partial response.

One case only, a leiomyosarcoma, failed to show objective response.

Carcinoma of gastrointestinal tract (Table XI)

Two patients with carcinoma of the stomach and 2 with carcinoma of the colon, and 1 with squamous carcinoma of the ano-rectal junction have been treated. All showed some response; this was clinically complete in 1 case of carcinoma of the stomach who remained in remission for 3 months, eating normally and gaining weight. Barium meal examination showed reduction in size of the growth.

The patient with metastatic carcinoma of the ano-rectal junction is now in complete remission, 6 months after commencement of treatment.

Miscellaneous (Table XII)

No benefit followed treatment in the remainder of the series, which included patients with nephroblastoma, hepatoma and bone sarcoma.

DISCUSSION

Seventy-five patients have been treated by a modification of a regime originally reported by Constanzi and Coltman (1969). This modification was necessary because of unacceptable toxicity in our earlier cases. Using the modified regime, treatment now present no undue problems of toxicity, yet still retains a therapeutic effect. It is practical to treat the majority of cases as out-patients. The most troublesome side effect (especially for female patients) is alopecia, 20%. Haemato-

TABLE VII.—*Fourteen Cases of Bronchial Carcinoma*

Patient	Age	Sex	Site of metastases	Number of courses	Side effects	Response: Objective	Response: Karnofsky Pre-%	Response: Karnofsky Post-%	Duration of response (months)	Comment
H.D.	62	M	Cutaneous	4	Leucopenia	Partial	70	80	3	Died after 4th course
E.H.	55	M	Superior venacaval obstruction	4	Nil	Partial	60	80	3	Died after 4th course
R.McB.	64	M	Cerebral	2	Nil	Failure	50	50	Nil	Died after 2nd course
M.McL.	62	F	Cutaneous	5	Nil	Partial	80	80	3	Died after 5th course
F.M.	55	M	Cerebral	2	Nil	Failure	50	50	Nil	Died after 2nd course
K.	52	M	Lymph nodes, cerebral	3	Nausea	Failure	70	70	Nil	Died 3 months after 3rd course. Treatment abandoned
W.H.	43	M	Visceral	2	Nil	Partial	80	80	2	Died 1 month after 2nd course
M.A.	34	F	Lymph nodes	2	Nil	Failure	30	20	Nil	Died after 2nd course
W.M.	64	M	Bone	2	Nil	Failure	60	60	Nil	Died after 2nd course
H.C.P.	60	M	Bone	2	Alopecia nausea	Partial	50	60	1	Died after 2nd course
W.T.H.	65	M	Cutaneous	1	Nil	Failure	60	50	Nil	Died after 1st course
N.B.	47	M	Cutaneous	2	Stomatitis	Partial	60	80	1	Continues in remission
J.E.	45	F	Cutaneous, superior venacaval obstruction	2	Nil	Partial	60	70	1	Died after 2nd course
G.B.	45	M	Bone	4	Leucopenia	Partial	50	50	3	Died after 4th course

TABLE VIII.—*Eleven Cases of Genital Carcinoma*

Patient	Age	Sex	Previous treatment	Number of courses	Side effects	Response: Objective	Response: Karnofsky Pre-%	Response: Karnofsky Post-%	Duration of response	Comment
Ovarian carcinoma										
F.S.	66	F	Radiotherapy alkylating agents	1	Nausea	Failure	30	0	Nil	Died 2 weeks after starting quadruple
M.R.	67	F	Radiotherapy alkylating agents	2	Alopecia, nausea	Failure	80	70	Nil	Died 3 months after 2nd course, refused further treatment
G.K.	64	F	Radiotherapy Chlorambucil	1	Nil	Failure	40	0	Nil	Died 2 weeks after starting quadruple
M.N.	65	F	Radiotherapy	1	Nil	Failure	40	0	Nil	Died 2 weeks after starting quadruple
Cervical carcinoma										
J.R.	28	F	Bone metastases	1	Alopecia	Failure	20	0	Nil	Died 2 weeks after starting quadruple
B.C.	69	F	Bone and supra-clavicular nodes	3	Nil	Failure	40	30	Nil	Died 3 months after starting quadruple
W.P.	60	F	Pelvic recurrence	3	Nil	Failure	60	60	Nil	Alive. Quadruple discontinued after resection of deposit in small bowel
Testicular carcinoma										
R.B.	31	M	Orchidectomy radiotherapy	2	Nil	Failure	30	30	Nil	Died 2 months after starting quadruple
C.S.	27	M	Orchidectomy radiotherapy	2	Nil	Failure	30	0	Nil	Died 1 month after starting quadruple
J.S.	19	M	Nil	2	Nausea	Failure	70	70	Nil	Alive, responding to Mithramycin
D.L.	21	M	Orchidectomy	1	Nil	Failure	30	0	Nil	Died 2 weeks after starting quadruple

TABLE IX.—*Ten Cases of Malignant Melanoma*

Patient	Age	Sex	Site of metastases	Number of courses	Side effects	Response			Duration of response	Comment
						Objective	Karnofsky Pre-%	Karnofsky Post-%		
P.D.	54	F	Pleural deposits, local recurrence	2	Leucopenia	Failure	40	40	Nil	Died 6 months after starting quadruple
R.S.	42	F	Cutaneous lymph nodes, lungs	2	Leucopenia	Failure	60	50	Nil	Died 6 months after starting quadruple
E.B.	39	M	Cervical nodes, liver	1	Nil	Failure	50	50	Nil	Discontinued because of obstructive jaundice. Died 3 months after starting quadruple
R.K.	42	M	Small bowel, brain	3	Alopecia, nausea	Failure	70	70	Nil	Died 10 months after starting quadruple. Patient refused to continue
J.W.	39	M	Small bowel, brain	5	Leucopenia	Failure	70	70	Nil	Died suddenly 6 months after starting quadruple due to cerebral haemorrhage
D.W.	27	M	Small bowel, liver, lungs	4	Leucopenia	Failure	70	60	Nil	Died 10 months after starting quadruple. Patient refused to continue
E.P.	55	F	Bone, lungs	3	Nil	Failure	50	50	Nil	4 months after starting quadruple
V.P.	60	F	Local cutaneous recurrence	2	Nil	Failure	80	80	Nil	Alive following ablation of affected leg
S.E.	39	F	Local cutaneous recurrence, ovarian, retro-peritoneal nodes, liver	2	Nil	Failure	50	70	Nil	Died 3 months after starting quadruple
S.O.	40	M	Local cutaneous recurrence of lower limb	1	Nil	Failure	70	70	Nil	Alive after ablation of limb

TABLE X.—*Six Cases of Soft Tissue Sarcoma*

Patient	Age	Sex	Diagnosis	Indication	Number of courses	Side effects	Response			Duration of response (months)	Comment
							Objective	Karnofsky Pre-%	Karnofsky Post-%		
S.P.	61	F	Leiomyosarcoma mesentry	Disseminated local disease	2	Nil	Failure	30	30	Nil	Died 2 months after starting quadruple
L.F.	66	M	Liposarcoma thigh	Disseminated to soft tissue disease, lungs	12	Nil	Partial	80	90	9	Alive with control of disease
B.	30	M	Fibrosarcoma in cervical tissue	Recurrent local disease	6	Nil	Partial	90	90	6	Alive
R.W.	14	M	Alveolar rhabdomyosarcoma	Disseminated disease, cutaneous, pancreas, mediastinal lymph nodes	18	Alopecia leucopenia	Complete to partial	30	90	20	Died from intestinal haemorrhage
B.H.	23	M	Rhabdomyosarcoma of thigh	Residual disease after radiotherapy. Recurrent pneumothorax	6	Alopecia	Partial	80	80	3	Alive, recent recurrent pleurodoesis
O.E.	60	F	Retroperitoneal leiomyosarcoma	Local recurrence after surgery and radiotherapy	2	Leucopenia	Failure	50	20	Nil	Died 1 month after starting quadruple

TABLE XI.—*Carcinoma of Gastrointestinal Tract*

Patient	Age	Sex	Diagnosis	Indication	Number of courses	Side effects	Response			Duration of response (months)	Comment
							Objective	Karnofsky Pre-%	Karnofsky Post-%		
R.H.	68	M	Carcinoma of stomach	Local recurrence gastrectomy	7	Peripheral neuropathy	Complete	50	90	8	Alive
O.C.	60	M	Carcinoma of stomach	Cerebral metastases	2	Nil	Partial	50	80	2	Alive
B.S.	55	F	Squamous carcinoma of anorectal junction	Liver, supraclavicular lymph nodes lymph nodes	6	Nil	Complete	80	100	6	Alive
C.K.	47	M	Carcinoma of colon	Local recurrence and liver	4	Peripheral neuropathy	Partial	60	60	3	Alive
A.H.	77	F	Carcinoma of colon	Local recurrence after palliative radiotherapy	1	Severe stomatitis, alopecia	Partial	60	60	1	Changed to 5-flourouracil alone because of severe stomatitis

TABLE XII.—*Miscellaneous*

Patient	Age	Sex	Diagnosis	Indication	Number of courses	Side effects	Response			Duration of response (months)	Comment
							Objective	Karnofsky Pre-%	Karnofsky Post-%		
A.A.	19 months	M	Nephroblastoma	Lung metastases controlled for 4 months with actinomycin D	3	Nil	Failure	40	40	Nil	Died 3 months after starting course
J.H.	31	F	Recurrent nephroblastoma	Recurrence after 27 yeats	3	Leucopenia	Partial	50	80	3	Died 4 months after starting quadruple from marrow infiltration
C.P.	17	F	Hepatoma	Local recurrence after radical surgery, lungs, peritoneal	4	Leucopenia	Failure	60	70	Nil	Alive, drug changed to ICRF.159
K.H.	6	M	Osteosarcoma tibia	Lung metastases	3	Leucopenia	Failure	40	30	Nil	Died 3 months after starting quadruple
D.O.	11	F	Round cell sarcoma of femur	Lung metastases	3	Nil	Failure	30	30	Nil	Died 3 months after starting quadruple

logical side effects are now a minor problem and in no patient was treatment discontinued for this reason.

The most consistent response was seen in carcinoma of the breast, where all patients responded in some degree. Regression was clinically complete in 6 out of 14 cases. As all these patients had undergone previous hormonal or cytotoxic treatment these results can be considered encouraging.

There were only 10 patients with head and neck cancer, but a remission in 8 cases compared well with the report of Leone *et al.* (1968), and considerably better than the results of intra-arterial chemotherapy at this Centre.

Fourteen cases of carcinoma of bronchus were treated and 8 underwent brief remission (3 months or less). It is recognised that it is difficult to palliate bronchial carcinoma with cytotoxic agents and the use of quadruple chemotherapy in this small series is not encouraging.

Surprisingly no remissions were achieved with carcinoma of the ovary cervix or testicle.

The success claimed by Constanzi and Coltman (1969) was not confirmed in this series of melanomas, and we no longer treat this tumour with the quadruple regime.

In a small group of 6 soft tissue sarcomata only 1 failed to respond. If in a larger series this response rate were to be maintained it would be an improvement on previous experience (Newton, 1967; Wiltshaw, 1967).

In the small group of gastro-intestinal cancers, 4 out of 5 cases of carcinoma of the large bowel and stomach responded, and it is felt that where 5-fluorouracil has failed, quadruple chemotherapy may be of value.

TABLE XIII.—*Response of Different Groups of Solid Tumours to the Modified Quadruple Regime*

Good remission	Moderate remission	No remission
Breast carcinoma	Head and neck carcinoma	Malignant melanoma
	Soft tissue sarcoma	Ovarian carcinoma
	Cervical carcinoma	Testicular carcinoma
	Bronchial carcinoma	Bone sarcoma
	Stomach and large bowel carcinoma	

Table XIII summarises the value of this modified quadruple regime in the different groups of solid tumours.

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