Each patient has been maintained in reasonably good health by the continued administration of cortisone.

I am grateful to Dr. Ernest Bulmer for permission to publish Cases 1 and 2, and to Dr. A. G. W. Whitfield for Case 3, and to both for their encouragement and helpful criticism. I am indebted to the late Dr. A. L. Peeney, who undertook the pathological investigations.

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RESULTS OF A PLANNED ATTACK ON CARCINOMA OF THE VULVA

BY

STANLEY WAY, F.R.C.O.G.

*Gynaecologist, Newcastle Regional Cancer Organization;
Associate Surgeon, Gynaecological Department, Royal
Victoria Infirmary, Newcastle-upon-Tyne*

In 1939 during the course of a discussion at the Royal Society of Medicine on the treatment of carcinoma of the vulva, F. J. Browne suggested that since this was a fairly uncommon disease the results might be improved by concentrating all the cases in the hands of a few surgeons, who might thereby gain greater experience in handling the disease than if the cases were scattered in various clinics all over the country, usually in ones and twos.

My interest in the disease was aroused by my former chief, Clifford White, who suggested that a study of it might prove useful, especially as the incidence appeared comparatively high in Newcastle-upon-Tyne.

The more academic aspects of that study I have reported elsewhere (Way, 1951), but, briefly, the research showed that the previously poor results were due not only to lack of experience on the part of those responsible for its treatment but also to the fact that standard treatments at that time were based on unsound pathological and anatomical principles. The removal of the vulva was insufficiently wide in most cases to prevent recurrence, and the node dissections were not extensive enough to deal with the metastases.

As a result of this study, I devised the extended radical vulvectomy and node dissection which I have described elsewhere in full (Way, 1951), but which in brief consists of the complete removal of the vulva from the mons to the anus, extending deep enough to expose the pubic bones and their associated muscles; the excision of wedges of skin from the groins and saphenous regions with the underlying lymph nodes which remain undetached from the skin during the operation; the division of the inguinal ligament; and the removal of the external iliac lymph nodes as far as the bifurcation of the common iliac artery. The groin wounds are sutured, but the vulval wound is so wide that it has to be left to granulate. If the vulval wound can be sutured then the cardinal principle of cancer surgery is violated and recurrence can be expected in a fair proportion of cases.

The first of these operations I performed rather in the nature of an experiment in 1941. The patient had involved nodes, and died nine years later of coronary thrombosis without recurrence of the tumour or metastases.

From 1943 onwards, with the help of my colleagues in the gynaecological and radiotherapy departments, all the cases seen in the centre were handled by me and were assessed for this radical operation; in addition, most of the cases occurring in the gynaecological departments of neighbouring hospitals, in particular the Newcastle-upon-Tyne General Hospital, were also referred. The early cases were all performed in the Royal Victoria Infirmary, but the serious bed situation created by the long stay of these patients necessitated the provision of beds specially for them, and these were provided by the Newcastle Regional Cancer Organization in their associated hospitals, where more than half of the patients described in this paper were treated. The unselfish attitude of my colleagues and the co-operation of the Regional Cancer Organization, both before and after the advent of the National Health Service, played a great part in the excellent results that have been achieved, but without the very great assistance and encouragement of Professor Harvey Evers, who was quick to see the advantages of and to encourage the establishment of a special unit for this type of case, and Mr. John Thurgar, who, in the most difficult time, handed over radiotherapy beds for the surgical treatment of these cases, this planned attack could never have been carried out.

This paper describes the results of 79 cases seen prior to March 31, 1949. A five-year follow-up is available on all these patients, and they represent an unselected group who presented themselves for treatment at Newcastle hospitals. The results are believed to be representative of what can be achieved in any large centre where these cases are concentrated in the hands of a medical and nursing staff who see enough cases to become conversant with the problems involved.

Operability Rate

The higher the operability rate of a particular surgical technique the more useful the operation becomes. Table I shows that in this series the operability rate was 83%, and

TABLE I.—Operability

Total Cases Seen	Refused Treatment	Considered Unsuitable For Radical Operation	Operated Upon
79	1	13	65 (83%)

this would appear to be reasonably satisfactory. With increasing experience—and I have now performed this operation more than 150 times—this can be increased, and were I faced with the same group of cases now I am sure that I could have successfully operated on even more of them. The causes of rejection are given in Table II. It will be noticed that most of the cases rejected because the tumour was too advanced survived only a short while, and were in most cases dying when I first saw them. It is doubtful whether I could do anything for this group even now, but cases of heart disease now present little difficulty if the operation is carried out in stages. Diabetes remains a serious problem owing to the fact that inevitable infection of the raw wound tends to make control of the diabetes exceedingly difficult. However, by staging the operation and by increasing the time interval between the stages much can be done for these patients. Age of the patient may

TABLE II.—*Rejected Cases*

No.	Cause of Rejection	Alternative Treatment, If Any	Result
1	Diabetes	Wide local vulvectomy	Died of gas gangrene from infected insulin injection
2	Severe asthma	" " "	Died at 4 years from heart failure. No recurrence
3	Age (81)	Local excision of tumour	Died 1 year. Local recurrence
4	Heart disease	Radium and local vulvectomy	Alive and well at 6 years
5	Tumour too advanced	None	Died at 8 weeks
6	" " "	"	" " 6 "
7	" " "	"	" " 9 "
8	" " "	"	" " 11 "
9	" " "	"	" " 3 "
10	" " "	"	" " 11 months
12	Tumour too advanced, diabetes, and age (85)	Diathermy coagulation	Died from diabetes in 1 month. Tumour still active
13	Heart disease	Radium; local excision; superficial node dissection	Died at 3 years. Heart failure. No recurrence

One patient, who refused treatment, died three years later with extensive local disease but no evidence of metastases.

necessitate staging the operation, and in some cases in which node involvement is extensive and a one-stage operation is imperative because there is too little margin of safety between the primary and the lymph nodes, age may be the deciding factor between operation and rejection.

Material

The age distribution (Table III) of all these cases was not different from that in other published series of this disease—52% of all patients were over the age of 60. Over the age of 60 the operability rate was 78%; under 60 it was 90%.

TABLE III

Age Group	Total Cases Seen	Treated	Positive Nodes	Rejected	Refused Treatment	5-year Survivors
0-20	0	—	—	—	—	—
21-30	2	2	0	0	0	2
31-40	3	3	1	0	0	3
41-50	10	9	2	1	0	9
51-60	23	20	9	3	0	13
61-70	34	27	8	6	1	19
71-80	5	4	1	1	0	2
81+	2	0	—	2	0	0
	79	65	21	13	1	48

Size of tumour *per se* was seldom an indication for rejection, although in the 13 rejected cases the average size of the tumour was twice that of the operated cases (30 square cm. as compared with 16 square cm.).

Involvement of urethra, vagina, and rectum was not a contraindication to operation. Removal of a large part of the urethra led to only temporary incontinence, and the anus was removed with the performance of a colostomy in four patients, three of whom survived five years. The largest tumour in the rejected group was 90 square cm. The largest in the operated group was 102 square cm. The smallest tumour operated on was 0.25 square cm. This patient had a mass of nodes in her left groin 204 square cm. in area. It had been incised six times in three months by her doctor, who mistook it for an abscess. She died at one year of a groin recurrence, the only groin recurrence so far in the whole series.

Node involvement *per se* was never a contraindication to operation, and one patient with nodes fixed to the inguinal ligament and ulcerating the skin was treated and, furthermore, became a five-year survivor. Rejection was almost always decided on a combination of advanced tumour, advanced age, and concomitant disease. There was no significant difference between the average size of the tumours in the node-free cases (16.5 square cm.) and those in the node-involved cases (15.5 square cm.).

More recently our material has consisted of even more advanced cases, many of which are coming to us from far afield, but our operability rate still remains at the level

described in this series. We still see too many recurrent cases which have already been the victims of timid surgery before they reach us.

Results

An operation stands or falls by its results. The results of the treatment of carcinoma of the vulva by methods other than those described in this paper have been far from satisfactory. The five-year survival rate achieved in this clinic prior to this experiment was a relative five-year one of 26%. This figure is on an equality with those reported from other centres, with the exception of Taussig (1941), who in a smaller series of cases with an operation which was more extensive than any described up to that time reported a relative figure of 58%.

Table IV shows the absolute five-year survival rate for this group of cases—that is, the percentage surviving at five years out of all cases seen, whether they were treated or

TABLE IV.—*Absolute Five-year Survival Rate*

Total cases seen	79
Refused treatment	1
Total cases considered for operation	78
Total operations performed	65
Alive and well at 5 years	48 (61%)

not. This absolute figure of 61% is very much higher than other published relative figures. The relative five-year survival rate in this series—that is, the survivors out of all the cases operated on—is 74% (Table V).

TABLE V.—*Relative Five-year Survival Rate*

Total operations	65
Operative deaths	8 (12%)
Intercurrent deaths without recurrence before 5 years	5 (8%)
Deaths from cancer	4 (6%)
Alive and well at 5 years	48 (74%)

The influence of node involvement in cancer at any site is of great importance, since the results are always worse when the nodes are involved (Table VI). It may be argued that the node involvement (32%) in this series is not as high as it might be and therefore the results are influenced

TABLE VI.—*Node Involvement*

Total No. of cases operated upon	65
Nodes involved	21 (32%)
" not involved	44

Five-year Results According to Node Involvement

Nodes not involved:	
Total cases	44
Alive and well at 5 years	38 (86%)
Died of intercurrent disease before 5 years	2
" operation	4 (9%)
" metastases	0
" local tumour	0
Nodes involved:	
Total cases	21
Alive and well at 5 years	10 (48%)
Died of intercurrent disease before 5 years	3
" operation	4 (19%)
" metastases	4
" local tumour	0

by this. There is no doubt that to some extent this is the case, and in our larger series the incidence of node involvement is 47%, but it should be pointed out that in this series 9 out of 21 patients with node involvement had their iliac nodes involved as well as the inguinal—that is, 43% of the node-involved cases. In our larger series this incidence of deep node involvement was found to be only 22% of all node-involved cases. With increasing experience, and making allowance for the rather higher proportion of widespread node involvement in this early series, I believe that the lower incidence of node involvement has not made a great difference to the results.

The relative five-year survival rate in the node-free cases of 86% is an excellent one by any standards, and the fact that no patient in this group died of cancer is extremely satisfactory. It does, however, raise the question whether it is necessary to remove the nodes. I have pointed out elsewhere (Way, 1951) the impossibility of being certain on clinical examination whether or not the nodes are involved, and the 48% survival when the nodes are involved leaves me in no doubt about the wisdom of removing the superficial nodes in all cases in which this is possible. The

survival rate in the node-involved cases is reduced to 48%, but here again only four patients died of cancer, and here also there were no local recurrences. Many of these operations were extremely difficult, and this is reflected in the high operative mortality. However, of the nine patients with deep pelvic node involvement two survived and are well, one at 10½ years and one at 6½ years. This may suggest that the removal of the deep nodes is not an important step in the operation.

At the time these cases were treated we had little knowledge about the incidence and pattern of deep node involvement and no way of knowing if this step in the operation was vital. As a result of a far larger series we now know that the anatomical spread of cancer of the vulva in the lymphatics is fairly regular, and that involvement of the deep nodes is seen in only about 15% of all cases. As a result of this and the development by Dr. Ruth Dearing (1952) of her rapid node-smear technique we now modify this part of the operation by exposing the external iliac nodes and removing the lowest medial node (the node of Cloquet) and the lowest lateral external iliac node. These are smeared and stained (this takes no longer than seven minutes) whilst the superficial nodes are removed. If the deep nodes are negative the inguinal ligament is not divided and no further dissection of the iliac region is carried out. If they are involved then we proceed as we did with all the cases in this series. The greatest advance of this technique is undoubtedly the wide excision of the vulval area, because we have had no local recurrences in this series up to five years.

Discussion

The results really speak for themselves. The operation is more complicated than difficult and does require constant practice. The nursing is very complex, and the technique requires a fair amount of ancillary help and experience, especially in cytology since the introduction of the modification described above. The experiment—it has long since ceased to be one so far as I am concerned—may be said to have paid a handsome dividend, and the results are more than gratifying. It would seem well within the scope of any large centre which is prepared to concentrate its material and study the pathological and anatomical features of this disease.

Summary

Owing to the comparative rarity of carcinoma of the vulva few people see sufficient cases to become very familiar with the problems concerned in its treatment.

After research into the causes of failure to cure the disease an experiment was tried in which all the cases in a wide area were referred to one surgeon, who applied a more extensive operation based on the lessons of the preliminary research.

The results of the treatment of 79 cases seen before March 31, 1949, are reviewed.

One patient refused treatment and 13 were considered unfit. The operability rate was 83%. The absolute five-year survival rate was 61% and the relative five-year survival rate—that is, the survival of all cases operated on—was 74%. When the lymph nodes were involved the five-year survival rate was 48% and when they were not involved it was 86%.

These figures are a great improvement on other published figures and it is believed that they are well within the reach of any centre which decides to pool its cases into the hands of a special team which will carry out a radical approach to the disease.

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TREATMENT OF GOUT WITH H.P.C.

BY

D. N. ROSS, M.D., F.R.F.P.S.

Assistant Physician, the General Hospital,
Newcastle-upon-Tyne

One feature of the revival of interest in the rheumatic diseases following the introduction of cortisone and A.C.T.H. has been the screening of a great variety of substances for evidence of a cortisone-like action on the collagen group of diseases. Among the therapeutic agents, old and new, which have been examined is a cinchoninic acid derivative—namely, 3-hydroxy-2-phenylcinchoninic acid (H.P.C.). In the U.S.A. Blanchard *et al.* (1950) reported promising results with H.P.C. in cases of acute rheumatic fever, chronic rheumatoid arthritis, and disseminated lupus erythematosus. In this country Rennie *et al.* (1951) found the drug of value in a small group of cases of rheumatic fever and scleroderma. This preliminary report suggested that a further investigation was justifiable, and in the summer of 1951 a small supply of H.P.C. was obtained for trial and was used in a few early cases of rheumatoid arthritis. The results were not dramatic, and it was felt that H.P.C., being a derivative of cinchophen, might be of greater value in the treatment of gout. Accordingly, the small supply was hoarded until suitable cases were seen, but, as often happens, no patient with typical gout attended for many months; then several cropped up within a few weeks.

To date, 12 cases have been treated with H.P.C., a bitter yellow powder compressed into white-coated tablets containing 250 mg. The initial dosage recommended by Blanchard *et al.* (1950) was 20 mg. per kg. of body weight daily, in divided doses, by mouth, with an equal amount of sodium bicarbonate to prevent gastric upset. The amounts used in the trial, and the results, are described in the case abstracts.

Case 1

A farm worker aged 58 had his first attack of gouty arthritis in 1947, when his left hand, feet, and ankles were affected; subsequent acute attacks led to progressive involvement of the knees, elbows, and shoulders. He was admitted to Harrogate Royal Bath Hospital for a course of physical treatment in 1950 and had colchicine therapy during several acute episodes, with moderate benefit. At home he experienced general deterioration and was re-admitted in January, 1952, when he joined a test group of cases which were given A.C.T.H. by intravenous infusion. The first infusion contained 10 mg. of A.C.T.H., and his condition improved during the next seven days; the second infusion contained 20 mg. of A.C.T.H., and his arthritis was appreciably relieved for 24 hours. The following day he relapsed to his original state, and the next day he developed a typical acute attack of gout with extremely painful tender joints and constitutional upset with pyrexia. At this stage H.P.C. was given in daily doses of 2 g., and he improved rapidly, being able to walk within 24 hours; after six days he had made such good progress that the dose was halved, and he continued to do well on 1 g. daily for another eight days. At this point he developed a recurrence of pain in his knees when walking, and began to complain of some nausea and looseness of the bowels. These symptoms became more severe next day, but treatment had to be interrupted in any event, as the available supplies of H.P.C. had been used.

During the next 12 days he deteriorated very much, until a fresh supply of H.P.C. enabled treatment to be resumed.