FROM THE DEPARTMENT OF GYNECOLOGIC RADIOTHERAPY (DIRECTOR: OLLE KJELLGREN), UNIVERSITY OF UMEÅ, SWEDEN.

EFFICACY OF PRIMARY RADIATION IN CARCINOMA OF THE ENDOMETRIUM

Preliminary study of unselected material from a specific region in the north of Sweden

by

O. KJELLGREN and S. S. MAGNÚSSON

Carcinoma of the corpus uteri is notifiable in Sweden. Analysis of the Cancer Registry records (see ref. 27) reveals that endometrial carcinoma constitutes 6 % of all malignant neoplasms in women. The annual incidence rate is 17 per 100 000 women, and 600 to 650 new cases are reported every year. The probability that a Swedish woman will develop endometrial carcinoma sometime during her lifetime is 1 in 66. It is a disease of later life, and is rare in women under the age of forty (1 %). In women over forty years of age, the incidence rate is 37 per 100 000 women. Between fifty-nine and seventy-nine years of age, the incidence rate is about 47 per 100 000 women, reaching a peak of 57 per 100 000 women in the 65 to 69 year group (Fig. 1). The age distribution in the 2 524 cases reported in Sweden during the period 1958—1961 is given in Fig. 2.

The management of carcinoma of the endometrium has for years been a subject of controversy all over the world. Two main lines of treatment are advocated: primary surgery with or without postoperative radiation, and primary

Submitted for publication 21 February 1969.

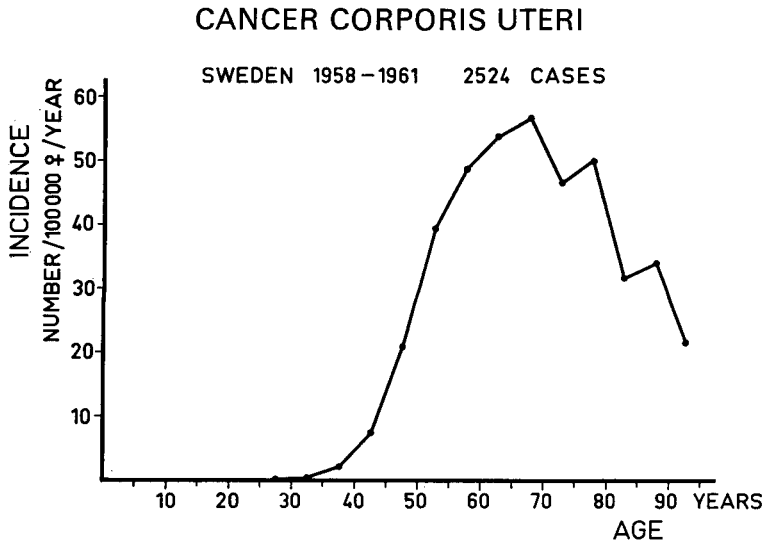

Fig. 1. Incidence of endometrial carcinoma in different age groups in Sweden.

radiation with or without supplementary operation (2—10, 12—17, 20—23, 29—30). Most authorities now agree that primary surgery for early adenocarcinoma of the highly differentiated type gives excellent results; it should be followed by vaginal vault irradiation in order to decrease the risk of vaginal recurrence. This procedure reduces the incidence of recurrence from 12 to 3 or 4 % (3, 16, 24, 28). In late cases with advanced changes, management is more difficult. These growths, even if highly differentiated, should probably be irradiated prior to operation. In carcinoma of the undifferentiated type, primary radiation followed by total hysterectomy and bilateral salpingo-oophorectomy is the treatment of choice. The prognosis in anaplastic carcinoma treated by primary surgical resection is very poor, even if the tumor is localized to the uterine cavity (17).

Evaluation of the clinical results of treatment of endometrial carcinoma is beset by many difficulties. Although a vast literature has grown up around the subject, the diversity of methods of management has made it difficult to collect a significant number of cases treated by any single technique. Another difficulty is the matter of classification. As KOTTMEIER (16) has pointed out, there is no justification in comparing statistics based on surgically classified cases with those collected from clinically classified cases. Finally, and most importantly, the problem of patient selection arises. If the significance of this is disregarded or

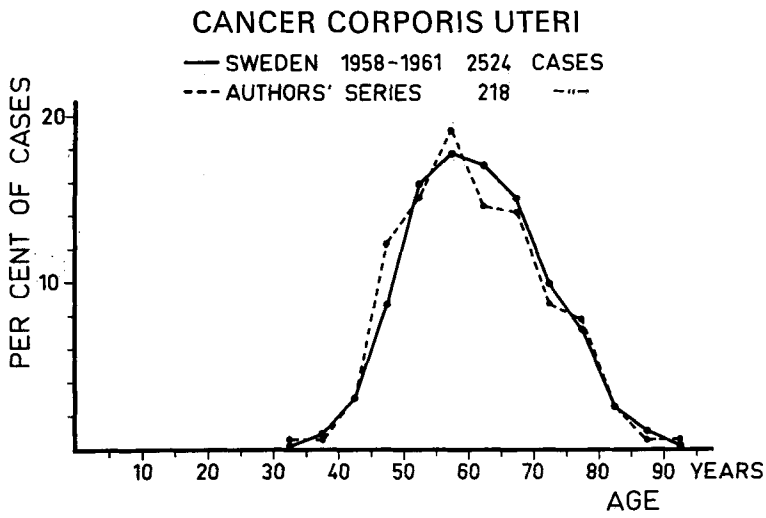

Fig. 2. Age distribution in the material compared to that of a larger Swedish series.

minimized, unwarranted conclusions can too easily be drawn. For example, the results obtained with primary surgical resection followed by intravaginal radium are statistically excellent. It is, however, often overlooked that the case material on which these results are based is always highly selected, since it does not include cases of tumors that are either advanced or disseminated, nor those in which operation is contraindicated by concomitant disease. Furthermore, the criteria by which the cases are selected are often obscure, if given at all.

Many of the protagonists of primary surgery maintain that radiation is an ineffective form of treatment for endometrial carcinoma, pointing out that the 5-year recovery rates are much inferior to those obtained with primary surgery. A moment's reflection will reveal the fallacy in this reasoning. In most countries, the cases referred to radiotherapy centres are the unfavourable ones, those that have not been accepted for primary operation for the reasons stated above. In other words, the element of selection is again just as much in evidence, but this time the factors are weighted the other way. It should be stressed that the excellent results of primary radiation at Radiumhemmet have been achieved in a selected material, since about 20 % of the cases referred to the institution have already been operated upon elsewhere. Incidentally, KOTTMEIER has never advocated radiation alone as the treatment of choice for endometrial carcinoma on the basis of these results, as has sometimes erroneously been maintained, but he advocates that operation should always be preceded by radiation.

With reservation for the obviously limited value of statistics, where the treatment of endometrial carcinoma is concerned, the following figures give an idea of what can be achieved with different methods of management (19). Primary surgery followed by intravaginal radium, in selected cases of early malignancy confined to the endometrium or invading the inner half of the myometrium, gives a 90 % 5-year recovery rate. In more advanced cases, with invasion of the outer half of the myometrium, it is about 60 %, and in cases of pelvic recurrence treated with radiotherapy after primary surgery it is 40 %. The 5-year recovery rate for cases in stage I, group 1 (clinically operable) treated with primary intracavitary radium with the Heyman packing technique alone is 85 %; the corresponding figure for stage I, group 2 (technically operable) cases is about 50 %. Cases which have been secondarily operated upon because of a recurrent growth have been included in these figures; the incidence of such operations is about 14 %. The recovery rate for cases operated upon because of failure of radiotherapy is about 60 % (ref. 12—16).

GRAHAM, writing in 1956 on the treatment of choice for carcinoma of the endometrium, stated that he knew of no papers in which all the cases from a given geographic area were included. We are now able to present the preliminary results of such a study. Our department, which has full radiologic and surgical facilities, serves a specific region in the northern part of Sweden with about 700 000 inhabitants. There are no other radiotherapy centres in the area. All cases of possible or manifest endometrial carcinoma in this region are referred to the department for review and treatment. By arrangement with the gynecologic and surgical services within the area, no therapeutic procedures are carried out on these cases prior to their admission to our department. The only exceptions are occasional cases in which endometrial carcinoma has been an incidental finding at hysterectomy for some other condition, and which are thereafter referred to the department for postoperative radiotherapy. This therapeutic centralization has made it possible to carry out a uniform plan of management on an unselected material, comprising all the known cases of endometrial carcinoma occurring in a specific region. The preliminary results of a therapeutic trial of this nature are presented in this paper. The efficacy of primary radiation for stage I and stage II endometrial carcinoma determined by the microscopic study of specimens obtained at major surgery or post-radiation curettage is discussed. The term 'primary cure rate' conveniently expresses the proportion of cases in which no residual malignancy was evident.

Material. Between 1963 and 1967, 242 cases of malignant tumors of the corpus uteri were treated. A total of 218 cases (90 %) had endometrial carcinomas, and these make up the material. The remaining 24 cases (10 %) of

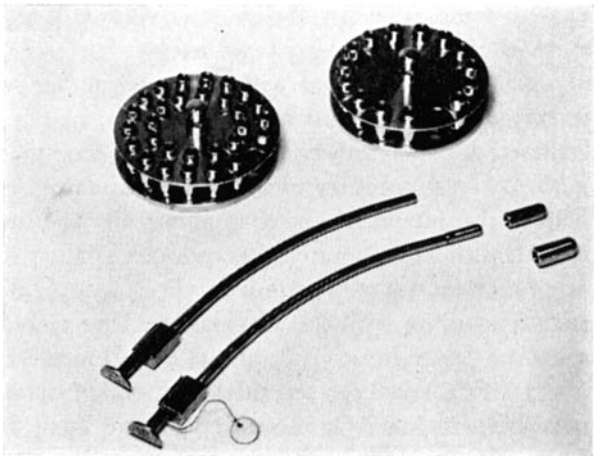

Fig. 3. Instrumentarium used for intrauterine packing. Two jacket holders are seen uppermost; two applicators, of which the lower one is loaded with an irradiator with thread and tag are seen below and to the right are two jackets of different size.

sarcoma have been excluded from the study. The age distributions, in our material and in the 2 524 cases registered at the Swedish Cancer Registry during the period 1958—1961, are given in Fig. 2. The material is unselected and is made up of all known cases of endometrial carcinoma occurring over a period of three years in the region served by the department. The staging of invasive carcinoma of the corpus uteri according to the international classification is as follows:

Stage I. The carcinoma is confined to the corpus;

Stage II. The carcinoma has involved the corpus and the cervix;

Stage III. The carcinoma has extended outside the uterus but not outside the true pelvis;

Stage IV. The carcinoma has extended outside the true pelvis or has obviously involved the mucosa of the bladder or rectum.

According to this classification our material included 158 cases (75.6 %) in stage I, 32 cases (15.8 %) in stage II, 7 cases (3.3 %) in stage III, and 11 cases (5.3 %) in stage IV.

Management. Since 1963 the department has carried out a clinical experiment whereby all cases of endometrial carcinoma irrespective of the clinical stage, have been treated with primary radiation. Intracavitary and vaginal radium was the initial treatment selected in most cases (200) and external radiotherapy in the remainder.

Evaluation of the patient's general state of health was made on admission and the presence of associated conditions such as obesity, hypertension, diabetes or cardiovascular disease was noted. This was followed by a pelvic examination

Table 1

Irradiators used in treatment of carcinoma of the uterine corpus

Length mm	Diameter mm		Wall thickness mm steel	Radium tube	Total filtration mm Pb	Dose rate at 1.5 cm
	Inner	Outer				
Permanently sealed irradiator (No. 0)						
20	3	6	1.5	Radium content 10 mg External length 17 mm Active » 10 mm Diameter 2.9 mm Filtration 2 mm Pb	2.4	32.2 rad/h = 100 %
Additional jackets						
22.5	6.1	8	1 No. 1		2.6	30.8 rad/h = 96 %
23.5	6.1	10	2 No. 2		2.7	29.9 rad/h = 93 %

under anesthesia and cervical dilatation and fractional curettage in order to determine uterine size and the depth and extent of tumor involvement. The procedure was carried out by a senior staff member with both gynecologic and radiotherapeutic qualifications. After clinical staging, a preliminary plan of management was drawn up. Treatment was usually instituted forthwith, as most of the patients had previously undergone curettage at local hospitals. In a few cases, the uterine neoplasm was sometimes found to be secondary to carcinoma of the cervix or the ovaries and these cases have of course been excluded.

The cases in stage I and stage II were treated with intracavitary radium. The Heyman packing methods as modified by KJELLGREN & JONSSON (11) was used in 187 cases (98.4 %). The uterus was packed on three separate occasions fortnightly; it was sometimes necessary to insert a tandem at the third application on account of uterine shrinkage. The uterus was so atrophic in three cases (1.6 %) that adequate packing could not be carried out and a tandem was inserted on each occasion.

Capsules containing 10 mg of radium were used for packing. The details of size and filtration are given in Fig. 3 and Table 1. The number and size of the capsules determined the duration of irradiation in each individual case (Table 2). The estimated delivered radiation dose at a distance of 1.5 cm from the nearest radium source was 3 000 rad.

The packing technique is simple. The idea is to fill the cavity with radium, and, if possible, to distend and thin out the walls, thus shortening the distance

Table 2

Treatment times in hours required to deliver 1 000 rad at 1.5 cm depth with different numbers and sizes of irradiators in the treatment of carcinoma of the uterine corpus

Number of irradiators	Irradiator size		
	0	1	2
6	15 1/2	19	21 1/2
7	14 3/4	18	20
8	14	17	18 3/4
9	13	16 1/4	17 1/2
10	12 1/4	15 1/4	16 1/2
11	11 1/2	14 1/2	15 1/2
12	10 3/4	13 3/4	14 3/4
13	10 1/4	13 1/4	14
14	9 3/4	12 3/4	13 1/2
15	9 1/4	12 1/4	13

between the radium and the outermost layers of the uterus. Each capsule has a thread attached, which is tagged and numbered for easy removal. The cavity is packed in rows from the fundus downwards, the length of thread lying outside the vagina and held in the hand, indicating the position of the capsules. The cavity is packed as tightly as possible, to accomplish which Hegar's dilators may be carefully burrowed between the capsules lying in the uterus to make room for more. The normal uterus is not readily distensible, but a uterus which is the site of a carcinoma can usually be ballooned out, thus ensuring satisfactory contact between the radium and the tumor. In experienced hands, perforations are uncommon and, as will be shown later, rarely troublesome. One or two capsules are usually placed in the cervix. Should the uterine cavity be very large, the capsules may be enlarged by the addition of jackets (Fig. 3 and Tables 1 and 2). Bladder and rectal dosimetry is carried out after each application. Roentgen examination is performed if perforation is suspected. If the capsules are found to be well clustered this damage is improbable.

Vaginal radium was inserted at the first two packings in order to diminish the risk of vaginal metastases. The estimated radiation dose delivered to the vault was 3 000 rad at a depth of 1 cm. Following radium, cases in stage II were usually given supplementary external radiotherapy with ^{60}Co or 34 MeV betatron units, 4 000 rad being delivered to the parametria and the pelvic walls. Cases with advanced disease or large tumor volumes in stages I and II were treated preliminarily with external radiotherapy followed by intracavitary radium.

Table 3

Type of treatment in carcinoma of the uterine corpus stage I to IV

	Cases treated	
	Number	Per cent
Intracavitary radium eventually followed by external radiation	200	91.7
External radiation only	8	3.7
Primary surgery	10	4.6
Total	218	100

Table 4

Method of judging the effect of primary radiotherapy in carcinoma of the uterine corpus stage I and stage II

	Number of cases		Total	Per cent
	Stage I	Stage II		
Total hysterectomy ± bilateral salpingo-oophorectomy	99	20	119	63
Control curettage	59	11	70	37
Total	158	31*	189	100

* One additional patient died of intercurrent disease one week before control curettage was planned.

Of the 208 cases in all stages treated with primary radiotherapy 200 received intracavitary radium (Table 3).

Six weeks after the completion of the radium treatment, total hysterectomy and bilateral salpingo-oophorectomy was performed in all suitable cases with stage I or stage II carcinoma. In the poor surgical risk cases, where operation was considered inadvisable because of e.g. old age, hypertensive cardiovascular disease or diabetes, dilatation and curettage were carried out three months after radiation (Table 4).

Primary surgery was performed in only ten cases of the total material (Table 3). These operations were performed at local hospitals as a result of the incorrect interpretation of the clinical or histologic findings, and the cases were later referred to the department for further care.

Results

The histologic studies were carried out jointly by the senior staffs of the departments of Pathology and Gynecological Radiotherapy. The primary cure rate in the 189 cases with stage I or stage II endometrial carcinoma treated with primary radiation was 174 cases (92.3 %). The 5-year recovery rates are obviously not yet available.

The primary cure rate in stage I was 149 cases out of 158 (94.5 %). The histologic specimens in 87 % of the cases presented no traces of malignancy, a hyaline membrane replacing the endometrium. Epithelium without signs of vitality was present in 8 % of these cases, and residual viable carcinoma in 5 %. Further analysis revealed that the primary cure rate in the 99 cases in which supplementary hysterectomy was performed was 91 %. No residual malignancy was present in the specimens obtained from curettage.

The primary cure rate in cases in stage II of endometrial carcinoma was 25 out of 31 (80.8 %). Death of intercurrent disease occurred in an additional case one week before control curettage was planned and the effect of radiation could not be judged.

Analysis of the complications arising from packing disclosed that these were few and far between and to all intents and purposes without clinical significance. The hospital records of the 200 cases of endometrial carcinoma in all stages receiving intracavitary radium were studied, and the following complications were noted. A 100 % follow-up was maintained.

Pyometra. Six cases (3 %) had pyometra at the time of admission. Packing was carried out as planned, and the condition cleared up spontaneously as treatment progressed. In six other cases (3 %), pyometra developed in the course of the treatment; in two of these, packing was delayed for a few days while the uterus was drained. Apart from this, the management was unaffected by this complication.

Perforation of the uterus. Diagnostic procedures carried out before the treatment began resulted in performation of the uterus in twelve cases (6 %). Seven of these occurred in local hospitals and five in our department. The uterus could be packed as planned in all cases but one, in which a tandem was inserted at the first application. In nine other cases (4.5 %) the uterus was perforated as a direct result of the packing. Eight of these cases were in stage I, the other in stage II. In one case, a tandem was substituted. In another case the perforation necessitated a reversal of the usual time sequence of therapy, and the patient was given external radiotherapy followed by packing; the fact that she had ex-

tensive disease contributed to this decision. In the remaining cases, the uterus could be packed despite the perforation. There were no cervical tears.

Laceration of the vaginal mucosa attributable to excessive vaginal packing with gauze occurred in two cases (1 %). In one of these, the laceration had to be stitched.

Hemorrhage during packing occurred in two cases (1 %). In one of these, there was associated perforation of the uterus and a small blood transfusion (450 ml) was given.

Fever. The presence of radium in the uterus often resulted in a slight rise in body temperature but this did not appear to have any clinical significance. Only ten cases (5 %) ran a temperature of 38° C or more for two or more days; five were in stage I, three in stage II, and two in stage IV. The fever responded satisfactorily to antibiotics. Management was otherwise unaffected. None of the patients developed salpingitis. However, all those with a past history of salpingitis were given antibiotics for a week as a prophylactic measure.

Radiation necrosis of the vaginal vault. This complication was noted in two cases (1 %). Intracavitary radium had been supplemented by externad radiotherapy in both and the lesions made their appearance after subsequent hysterectomy. They caused little or no trouble and healed spontaneously.

Deep venous thrombosis of the leg developed in one case a few days after the second radium application. The patient was 75 years old and had had recurring pyometra prior to treatment; in addition, she had carcinoma of the breast and skin. The case was treated with anticoagulants but was otherwise managed according to plan.

Late bladder and rectal complications. The analysis is of course incomplete as the observation time is short. Five cases (2.5 %) complained of bladder trouble one to three years after treatment, with cystoscopic evidence of trigonal oedema. In two of these necrotic areas in the bladder mucosa were revealed. The symptoms were in all instances temporary and responded to simple treatment with urinary antiseptics. In four cases (2 %) there were late symptoms from the sigmoid colon or the rectum; these were mild and of short duration and no ulcerated areas were seen at sigmoidoscopy.

There were no deaths attributable to packing.

Discussion

Several authors (1, 3, 18, 21, 25) have reported the incidence of residual carcinoma after primary radiation for endometrial carcinoma. The superiority

of the packing over the tandem technique has been well documented (1, 18). ARNESON (1), for example, stated that the proportion of cases of residual malignancy dropped from 77 to 26 % on changing from the tandem to the packing technique. The present results, a primary cure rate of 95 % in an unselected material with endometrial stage I carcinoma, are much better than any hitherto published. It should be borne in mind that the material is heterogenous with large variations in the differentiation and extension of the growth as well as in uterine size.

Sceptics may query the validity of the histologic studies, both in respect of the number of histologic sections examined and the criteria by which cell vitality has been assessed. We are fully aware that even careful curettage may fail to reveal malignancy lurking deep in the myometrium. Although these considerations may somewhat limit the value of the study, it is hoped that it may provide food for thought. Ever since REYNAUD's contribution in 1922, the impression has prevailed in many quarters that endometrial carcinoma, being derived from adenomatous tissue, cannot be cured by irradiation. It cannot be disputed that the intrauterine application of multiple sources delivers a lethal radiation dose to most endometrial carcinomas. The application must, however, be carried out properly in order to ensure the delivery of a uniform dose to the entire tumor. Of equal importance is adequate dosage, since a very high irradiation dose is necessary to cure this relatively radioresistent growth. Fortunately, the extreme radioresistance of the uterine walls makes the intracavitary application of such doses feasible.

We do not advocate radiotherapy alone as the treatment of choice for endometrial carcinoma. The fact that failure is occasionally encountered makes supplementary surgery mandatory in the good risk case. Cases with early carcinoma of the highly differentiated type may very well be treated with primary surgery. Their selection is not always so easy, however, and error of judgment may lead to serious consequences. We therefore believe that the standard treatment of all cases of endometrial carcinoma should be primary radiation, supplemented where possible by hysterectomy and bilateral salpingo-oophorectomy. The radiation-induced uterine shrinkage makes operation easier, and the above-mentioned cancerocidal effect diminishes the risk of squeezing tumor cells into surrounding lymphatic and vascular channels at operation. Even if radiation fails to eradicate the growth, there is experimental evidence that irradiated malignant cells dispersed at the time of surgery are less liable to implantation elsewhere. Finally, the adoption of preliminary radiotherapy as a standard measure ensures that all cases of endometrial carcinoma are referred to a therapeutic centre. It is reasonable to suppose that centralization must lead to a degree of diagnostic and therapeutic expertize that cannot easily be obtained in any other way.

SUMMARY

The preliminary results of a three-year investigation of an unselected material of all known cases of endometrial carcinoma in a specific region of the north of Sweden are presented. Cases in stage I and stage II were treated with intracavitary radium, followed if possible by hysterectomy and bilateral salpingo-oophorectomy. Curettage was performed three months after radiotherapy in the remainder. The 'primary cure rate' was 95 % in the stage I cases and 81 % in the stage II cases.

ZUSAMMENFASSUNG

Es wird über die vorläufigen Resultate einer dreijährigen Untersuchung sämtlicher behandelten Fälle von Endometrialcarcinom in einem gewissen Bezirk in Nord-Schweden berichtet. Fälle im ersten und zweiten Stadium der Erkrankung wurden intracavitär mit Radium behandelt und wo möglich erfolgte anschliessend Hysterektomie und beiderseitige Entfernung der Tuben und Ovarien. Curettage wurde in den anderen Fällen drei Monate nach der Bestrahlung ausgeführt. Die primäre Heilungsrate war 95 % der Fälle im Stadium I und 81 % im Stadium II.

RÉSUMÉ

Les auteurs présentent les résultats préliminaires d'une étude ayant duré trois ans dans tous les cas non sélectionnés de cancers de l'endomètre dans une région déterminée du nord de la Suède. Les cas aux stades I et II ont été traités par le radium intracavitaire, suivi si possible d'une hystérectomie et d'une salpingo-oophorectomie bilatérale. Un curetage a été fait dans les autres cas trois mois après la radiothérapie. Le taux de guérison primaire a été de 95 % dans les cas du stade I et de 81 % au stade II.

REFERENCES

1. Arneson A. N., Stanbro W. and Nolan J. F.: The use of multiple sources of radium within the uterus in the treatment of endometrial cancer. Amer. J. Obstet. Gynec. 55 (1948), 64.
2. Candis D. J.: Cervical treatment of patients with corporal carcinoma. *In:* Carcinoma of the uterine cervix, endometrium and ovary, p. 257. Year Book Medical Publishers, Chicago 1962.
3. Chau P. M.: Technique and evaluation of pre-operative radium therapy in adenocarcinoma of the uterine corpus. *In:* Carcinoma of the uterine cervix, endometrium and ovary, p. 235. Year Book Medical Publishers, Chicago 1962.
4. Corscaden J. A.: Gynecologic cancer. Third edition. Williams & Wilkins, Baltimore 1962.
5. Furuhjelm M.: Surgical treatment of carcinoma corporis uteri. Acta obstet. gynec. scand. 36 (1967), 420.
6. Graham J. B.: Treatment of choice in cancer of the uterine corpus. New Engl. J. Med. 254 (1956), 1112.
7. Heyman J.: The Radiumhemmet experience in postoperative radiological treatment of cancer of the corpus uteri. Acta radiol. 18 (1937), 93.

8. — and BENNER S.: Further experience with radiotherapy in cancer of the corpus of the uterus. Acta radiol. 27 (1946), 328.
9. — REUTERWALL O. and BENNER S.: The Radiumhemmet experience with radiotherapy in cancer of the corpus of the uterus. Acta radiol. 22 (1941), 14.
10. JAVERT C. T. and RENNING E. L.: Endometrial cancer. Survey of 610 cases treated at woman's hospital (1919—1960). Cancer 16 (1963), 1057.
11. KJELLGREN O. and JONSSON L.: Further development of the Heyman radium packing method. Acta radiol. Ther. Phys. Biol. 3 (1965), 143.
12. KOTTMEIER H.-L.: Radiotherapy in uterine cancer. Progr. Gynec. 2 (1950), 574.
13. — Carcinoma of the female genitalia. Williams & Wilkins, Baltimore 1953.
14. — Carcinoma of the corpus. Its classification and treatment. Gynaecologia 138 (1954), 287.
15. — Klinische Fortschritte. *In:* Gynäkologie, p. 419. Herausgegeben von T. Antoine. Urban & Schwarzenberg, Wien 1954.
16. — Carcinoma of the corpus uteri. Diagnosis and therapy. Amer. J. Obstet. Gynec. 78 (1959), 1127.
17. — The role of radiotherapy in gynecology. Postgrad. Med. 25 (1959), 124.
18. LEMPE I.: Combined surgical and radiological treatment for endometrial carcinoma. Proc. nat. Cancer Conf. 1 (1952), 753.
19. LINDGREN L.: The prognosis of carcinoma of the endometrium in its different stages treated by surgery combined with post-operative radiotherapy. Acta obstet. gynec. scand. 36 (1957), 426.
20. LONG R. T. L., SPRATT J. S. and SALA J. S.: Problems in the management of advanced endometrial carcinoma. Amer. J. Obstet. Gynec. 87 (1953), 942.
20. LONG R. T. L., SPRATT J. S. and SALA J. S.: Problems in the management of advanced endometrial carcinoma. Amer. J. Obstet. Gynec. 87 (1963), 942.
21. MARTIN C. L. and MARTIN J. A.: Can endometrial carcinoma of the uterine fundus be eradicated with radium therapy? Amer. J. Roentgenol. 89 (1963), 491.
22. NOLAN J. F.: Symposium on endometrial cancer. Amer. J. Obstet. Gynec. 81 (1961), 1099.
23. NORDLANDER E.: Operative treatment of carcinoma of the corpus uteri. Acta obstet. gynec. scand. 32 (1953), 211.
24. PRICE J. J., HAHN G. A. and ROMINGER C. J.: Vaginal involvement in endometrial carcinoma. Amer. J. Obstet. Gynec. 91 (1965), 1060.
25. RANDALL I. H. and GODDARD W. B.: A study of 531 cases of endometrial carcinoma. Surg. Gynec. Obstet. 103 (1956), 221.
26. REGAUD C.: Influence de la durée d'irradiation sur les effets déterminés dans le testicule par le radion. C. R. Soc. Biol. (Paris) 86 (1922), 787.
27. RINGERTZ N., SJÖSTRÖM Å., TÖRNBERG O. and SWENSON D. (Editors): Cancer incidence in Sweden 1958—1961. The Cancer Registry. The National Board of Health, Stockholm 1960, 1962, 1963 and 1965.
28. RUBIN P., GERLE R. D., QUICK R. and GREENLAW R. H.: Significance of vaginal recurrence in endometrial carcinoma. Amer. J. Roentgenol. 89 (1963), 91.
29. SHERMAN A. I.: Cancer of the female reproductive organs. C. V. Mosby, St. Louis 1963.
30. WAY S.: Malignant disease of the female genital tract. J. & A. Churchill, London 1951.