CARCINOMA OF THE PROSTATE

A REVIEW OF VARIOUS METHODS OF TREATMENT

A. J. S. BURGER, *Urologist, Karl Bremer Hospital, Bellville, and Groote Schuur Hospital, Cape Town*

Sufferers from carcinoma of the prostate seldom consult the urologist in the first instance, unless they have symptoms of obstruction or urinary infection.

Their reluctance to consult a urologist may be for social reasons or from sheer ignorance. In the absence of urological symptoms they may mistake the late symptoms caused by metastases for attacks of rheumatism, and resort to liniments or patent medicines for relief.

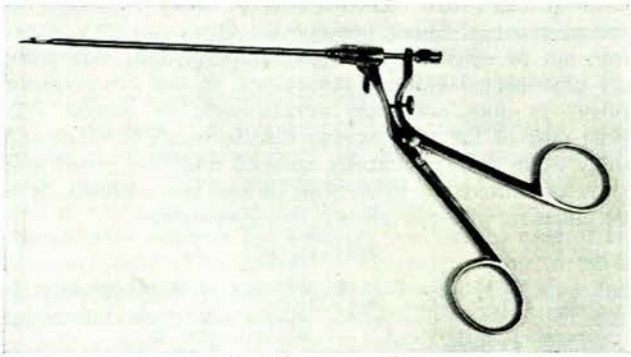
Bearing in mind that the tendency to carcinoma of the prostate in men between the ages of 40 and 90 is greater than is generally believed, the public should be educated about the need for a routine check-up on all men over 40. Few men will submit to such a routine check-up, with the result, in my experience, that only the most advanced cases are seen. All urologists know that diagnosis may be very difficult in the early stages.

DIAGNOSIS

I have in the past made use of different biopsy needles to obtain specimens *via* the transperineal route. This procedure was difficult and inaccurate, and it was not easy to pinpoint the nodule *via* this route; in addition, the needles used at this stage were not reliable. The open method of obtaining a specimen transperineally is a major operation, with a high percentage of error, and is not one I would advise.

On doing needle biopsy *via* the perineal route I discovered that in a high proportion of cases the rectum was buttonholed, but with no ill-effects on the patient. As a result of this experience I have resorted to the trans-

rectal route. In this way specimens can be taken much more accurately. Originally I thought the Veenema biopsy needle would suit our purpose, were it not for the fact that it cuts circumferentially. We have devised our own biopsy punch needle, which is simply a sizable needle telescoping within the lumen of a thicker cannula (see illustration). This is a very cheap and easily made instrument.* What is more, this instrument will cut in one direction only. It can be burrowed under the rectal mucosa *via* the transrectal route, and the specimen can be taken from the suspected nodule with the greatest precision.



The biopsy needle

I hope that in future we shall be able to include this method in the routine examination of all or most male patients above the age of 50 years. If we do such check-ups, more patients may be found suitable for total prostatectomy. Whether this will make much difference to the prognosis is an open question.

TREATMENT

According to statistics gathered by Franks and others, including our Groote Schuur Hospital statistics, we find that for total prostatectomy plus hormone treatment, 31·6% will survive the five-year period. Of patients treated with hormones only, 25% survive the five-year period.

This proves that total prostatectomy for carcinoma of the prostate is not the answer. The gland is too closely surrounded by important structures like the rectum and large blood vessels. It can hardly be considered possible to be able to clear the surrounding field of malignant cells. Lymph vessels and glands are abundantly related to the gland. The candidates for total prostatectomy are naturally the younger patients, and it is just in these men that we do not want disabling complications such as incontinence, etc., for such little gain.

The easiest treatment adopted during the last 15 - 20 years was hormone treatment only, and different brands of oestrogens, synthetic and otherwise, were used. All sufferers from prostatic cancer were treated in this way, supplemented by a transurethral resection and orchidectomy when necessary. Of these patients, 25% survived the five-year period, and very few lived after five years without further treatment.

Considering then that 25% outlive the five-year period when treated with hormones, that another 7% survive after five years without treatment, and that 20% of patients are not affected by hormone treatment, it can be seen that approximately 50% of patients improve, if only temporarily.

There must be a specific reason for this temporary improvement; undoubtedly it must result from the effects of the hormone therapy—these effects are directly proportional to the degree of differentiation of the neoplasm. This means that the most differentiated growth may be destroyed totally, leaving the undifferentiated growth almost undisturbed. Working on this theoretical basis, we have added a cytotoxin to the endocrine treatment.

After using many hormone preparations in turn, we finally decided to use the most concentrated preparation, namely, stilboestrol diphosphate. This preparation appears to have given new hope for a longer survival in the relapsed cases, but it is not the final answer.

COMBINED HORMONE AND CYTOTOXIN

Having come to the conclusion that none of the hormone preparations were sufficient, we combined stilboestrol diphosphate ('honvan') with a cytotoxin. 'Thio-tepa' infiltration of the neoplasm at monthly intervals on two or three occasions, combined with prolonged, intravenous, concentrated hormone therapy, gave encouraging results, and the patients have remained well for more than three years.

A number of patients who were unable to come for infiltration with thio-tepa, were given courses of intravenous nitrogen mustard combined with prolonged daily administration of concentrated hormones, with good results.

Method of Administration

We are now using prolonged stilboestrol diphosphate (honvan) therapy in combination with 'endoxan'. The neoplasm is infiltrated transrectally with 200 mg. of endoxan, in 50% dilution. Subsequently endoxan is given in increasing doses to reach a maximum of 1,000 mg. twice weekly. The honvan dosage is also increased at this stage; thereafter it is decreased slowly until after two or three months a maintenance dose of 2 - 3 tablets of honvan per day alone is used. This was reduced in some cases to monthly doses of 4 mg. of 'estradurin'.

In other cases the endoxan has been given in daily doses of 200 mg., until the patient showed signs of toxic symptoms, which prevented us from continuing the treatment.

From our past experience with the combination treatment, it is not yet possible to lay down any rule for the best dosage. It seems that the amount administered varies with every patient according to his constitution and according to his capacity for enduring a specific dose.

We intend to use different brands of hormone preparations with different cytotoxin preparations. The object is to try to achieve better results with cheaper preparations. The response to the combination treatment with hormone and cytotoxin is very encouraging, especially when one takes into account that most of the patients treated in this way had relapsed on hormone treatment combined with transurethral resection and orchidectomy. Most of these patients now have a new hope. We have been fortunate to be able to change the life expectancy from weeks up to 3 years and longer. We have been using this treatment now for some 3 years. In a high proportion large carci-

*Manufactured by Frederick Marcus (Pty.) Ltd., P.O. Box 3039, Cape Town.

noma masses have disappeared almost completely. It is, however, more difficult to assess the effect on the metastases. In a number of cases local spread has been checked, and tumour masses have disappeared completely.

Complications

To infiltrate the neoplasm evenly all over is almost impossible. Areas of hardness are encountered which can probably be overcome only if we use a pressure syringe.

In our experience a too concentrated material can be injected into a single area with disastrous results. Some of these patients tolerated the treatment very well for some time, after which they suddenly became temporarily intolerant and the treatment had to be discontinued.

Up to now we have seen 5 patients developing symptoms resembling infarcts of the lung. They coughed up streaks of blood in large quantities of sputum. In all these patients a rise in evening temperature was found, and they were all very depressed. They recovered from their lung complications and the primary growth was found to have disappeared completely. A general practitioner used PAS on his patient with a good result.

CASE REPORT

One of the patients we treated has a very interesting history.

A European male, 65 years of age, presented himself in 1959 with urinary obstruction, after which a transvesical prostatectomy was performed. Histology of the gland indicated benign glandular hyperplasia, but one piece showed an area where the glands had lost their differentiation and there was infiltration of the surrounding muscle; this indicated a focus of adenocarcinoma. The patient was given estradurin, 40 mg. once a month, as well as TACE, 1 tablet *t.d.s.* for one month and *b.d.* after that.

He returned in October 1961, this time presenting with a large prostatic mass and metastases in the bones and lungs. His general condition had deteriorated markedly and his main complaint was pain in the back and weakness of the lower limbs.

Transrectal infiltration of 200 mg. of endoxan into the neoplasm was carried out and intravenous therapy was administered as follows: 250 mg. of honvan *b.d.* and 400 mg. of endoxan three times a week. Initially the patient took his treatment well, but developed a temperature in the evening which lasted for several months and which was believed to be due to the metastases. The patient was completely bedridden at this stage.

Gradually, however, his general condition improved, and on examination in January 1962 it was found that his prostate could no longer be felt, and X-ray examination showed that the metastases were sclerotic. He still had an elevated temperature.

At present, about one year after treatment began, reports from his doctor state that the temperature has subsided and the patient is now well enough to walk again. The course of this case gives us hope for even better results in those cases of prostatic carcinoma which are detected early.

CONCLUSION

Three cases in this series did not respond, the prostatic tumours being resistant to the treatment given. In 1 of these 3 cases, complete de-differentiation of the cancer cells was reported.

It is our intention to classify cases according to the degree of differentiation of the carcinoma tissue, which will put us in a better position to determine the type of treatment. For this purpose we have a biopsy needle which is simple and cheap; it is by means of biopsy that we hope to be able to make this classification. In future, patients must be followed-up by taking regular transrectal prostatic biopsies in the consulting room or in the outpatient department. This will be of great help in our assessment of the success of the treatment already given.

In summing up, we are glad to say that there is an improved prognosis for at least 50% of patients suffering from carcinoma of the prostate. It must be realized that the combination treatment used by us was carried out in the beginning on relapsing cases only. It is too early to say that we have discovered a permanent cure, or even what proportion of patients will have a 5-year survival rate, yet we know that many patients who would have been dead by now are still alive and active.

With this treatment we hope to create new hope for all men suffering from carcinoma of the prostate.