otherwise of the profession I suppose it was poor Stephenson with his lifetime of ill health, but when I first read it, it struck me as so adulatory that, to say the least of it, it would be a little difficult for the average doctor to hang it on his

own wall. As the years rolled on I began to realize that Stevenson was only expressing what were the sentiments of a large section of the community towards their own doctors, and it was an intensely sobering thought.

PAIN IN MALIGNANT DISEASE OF THE UTERUS

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Pain is seldom encountered as an early symptom of carcinoma of the uterus, but in advanced and recurrent cases, especially in carcinoma of the cervix, it is an extremely common symptom and one which frequently calls for treatment in the later stages of the disease.

Types of Pain

It is usual to differentiate between the two main types of pain in carcinoma of the uterus (a) visceral and (b) somatic. These types of pain have a different aetiology and call for very different types of treatment.

Visceral Pain

Visceral pain is so called because it is referred to the pelvic viscera and is chiefly referred to the bladder and the rectum. It is experienced when either of these organs is involved by direct extension of the tumour, or it may be due to radium necrosis if radium has been employed in the treatment of such a case. It is frequently difficult to distinguish between radium necrosis and recurrent tumour, but obviously from a prognostic viewpoint it is essential to do so.

Rectal Pain

The complaint of rectal pain in a patient who has been treated for a carcinoma of the cervix by radiotherapeutic measures should immediately arouse the suspicion of radium necrosis. Involvement of the rectum with tumour, even in late stages of the disease, is not common, but irradiation injury to the rectal mucosa is the most common manifestation of radium necrosis and some form of rectal disturbance occurs in probably as many as 8 per cent. of cases of carcinoma of the cervix treated with radium. Todd, in 1938, drew attention to this disorder, which he called "pseudocarcinoma of the rectum," and he believed

that it was due to over irradiation of the parametrial triangle. In some cases he believed it was due to slipped vaginal applicators or to retroversion, for in this latter case the uterine tube is brought close to the rectum and may increase the dose of irradiation by as much as 20 per cent. The onset of the disease may be noticed a few days or weeks after the completion of radium treatment, when the patient suffers from a mild proctitis with diarrhoea and tenesmus. If the necrosis progresses defaecation becomes exceedingly painful, there is constant tenesmus and these patients are unable to sit with comfort and frequently have localized pain in the perineum and anal region, accompanied by the passage of mucus and slime. Vaginal examination reveals a typical area of rubbery thickening in the posterior fornix, and rectal examination shows an ulcer on the anterior rectal wall behind the cervix. Bleeding is always present but is usually slight; occasionally very severe haemorrhage from the rectum takes place.

Treatment. If the necrosis is mild and the pain not too severe, astringent enemata such as tannic acid may considerably relieve the discomfort, but if it progresses it is a clear indication for presacral neurectomy. Colostomy is not indicated for the relief of pain and is only necessary if a very large recto-vaginal fistula occurs, or if a rectal stricture completely occludes the bowel.

Bladder Pain

The mucosa of the bladder is more resistant to the effects of irradiation than that of the rectum, and furthermore the bladder is much more frequently involved by local spread of the carcinoma of the cervix than is the rectum. Pain referred to the bladder is, therefore, often of more serious import than pain referred to the rectum. Some degree of cystitis is extremely common after radium treatment of carcinoma of the cervix, and

the mere presence of dysuria and frequency is not necessarily the forerunner of necrosis or further local spread of the disease.

It is extremely difficult to differentiate between recurrent tumour involving the bladder base and radium necrosis. The syndrome presented by both complications is the same, namely the onset of pain which is usually mild at first, gradually becomes worse, is particularly severe at the end of micturition and is associated with great frequency. Haematuria may occur in both conditions, and since the cystoscopic appearances are frequently the same it is usually necessary to re-cystoscope the patient at intervals to see whether the lesion progresses or regresses. If the former the lesion is most probably due to growth, and if the latter to radium necrosis. Radium necrosis of the bladder tends to make its appearance later than rectal necrosis and is usually not seen before a year after treatment. The formation of fistulae, due to bladder necrosis, is rare.

Treatment. Presacral neurectomy is indicated, but if the lesion is very severe or is due to progressive extension of the tumour, ureteric transplant may have to be undertaken.

One other cause of pain of the visceral type, rarely seen, is the occurrence of a pyometra in the body of the uterus after irradiation. The pain is frequently intermittent and may be wave-like, resembling labour pains, and is frequently relieved by the discharge of pus from the cervix. This is not a common complication but it may occur after successful irradiation, and if after repeated drainage and oestrogen therapy it still recurs it is an indication for sub-total hysterectomy.

Somatic Pain

This type of pain is referred not to the pelvic viscera but to the leg, hip, skin of the abdomen and back, and it is very common in advanced cases. The most common site in which this type of pain is encountered is along the course of the sciatic nerve and it is usually referred to the back of the thigh, buttock, knee, calf and sole of the foot and it may be extremely severe. It may be necessary to adopt heroic measures to relieve it.

Aetiology. The exact aetiology of this type of pain is unknown and it has been commonly ascribed to a 'radiculitis.' I have drawn attention (Way, 1951) to the frequency with which this type of pain is associated with involvement by growth of the regional lymph nodes in the pelvis. My attention was first attracted to this at laparotomy for what appeared to be an early carcinoma of the cervix, in a woman who complained of right sided sciatica. Indeed at operation the primary tumour appeared to be limited to the cervix itself, but there was a mass of involved

lymph nodes densely adherent to the right sacral plexus from which it could not be removed. This striking association of sciatic pain with involvement of the sacral plexus with growth from the lymph nodes did not appear to be coincidental, and in a subsequent series of laparotomies on patients complaining of pain of sciatic distribution I did not fail to find involved lymph nodes, most of which were completely inoperable, in any case. Sometimes, however, nodes were found on both sides and one has seen, from time to time, patients with gross lymph node involvement in the pelvis but without pain. In at least one case where the lymph node involvement did not appear extensive, section of the sacral plexus showed the perineural lymphatics blocked with cancer cells. I have not always been able to find at autopsy involvement of the perineural lymphatics, but it is extremely difficult to remove the entire lumbosacral plexus right up to the cord and the serial sectioning and examination of many histological slides must of necessity take a considerable amount of time. When it is remembered that involvement of a nerve trunk in one area only, anywhere in the course of that nerve, might be sufficient to cause pain it is not surprising that more examples are not seen histologically. Nevertheless, I feel that direct involvement of the nerves, either from without or through their own lymphatics, is the probable cause of this type of pain.

Pain of this type is frequently ascribed to the use of radium and it is true that many patients who have been treated with radium experience this pain, but in a long experience of this condition I have never yet encountered a case where the pain was not associated with uncontrolled growth and I am certain that somatic pain is *never* due to irradiation. One further argument in favour of lymphatic spread of growth as a cause of somatic pain may be found. Sometimes pain of the sciatic type is found associated with pain of femoral distribution and with pain referred to the ilio-inguinal region. I have had occasion to open the abdomen, both operatively and at autopsy, in such cases and generally speaking the findings have been that the higher the nerve roots to which the pain is referred the more extensive is the node involvement. Pain of femoral distribution is frequently seen in cases whose para-aortic lymph nodes are involved as well as the lower pelvic ones.

Treatment. If the pain is mild sedatives are required, but soon after its onset it often becomes so intolerable that the usual sedatives are no longer of value and the patients require morphia, to which they develop a tolerance with exceeding rapidity. Most practitioners err on the side of under dosage and if morphia alone is to be relied upon, and in some cases it is to be, it is advisable to increase the

dose rapidly, starting with $\frac{1}{4}$ gr. four-hourly and increasing, within the course of a few days, to $\frac{1}{2}$ gr. and then 1 gr. By this means it is possible to keep these patients tolerably comfortable, and I have personally used doses as high as 5 gr. four-hourly for several days. Small doses of morphia in this condition are futile.

Unless the patient is likely to die within the course of a week or so, morphia as the sole method of pain relief is not recommended and, therefore, if the usual sedatives fail measures other than morphia are indicated. Of these methods two are most frequently used, namely intrathecal injection of alcohol and cordotomy.

Intrathecal Injection of Alcohol

This technique was introduced by Dogliotti in 1931 and popularized in this country by Todd (1937). The principle is that the nerve roots to which the pain is referred are temporarily fixed with absolute alcohol, thus cutting off pain stimuli. Thus it is necessary that the injection must be made above the site of the highest root to which the pain is referred, and intrathecal alcohol is most suited to those cases where the pain is purely of sciatic distribution.

The sensory supply to the skin over the back of the leg and buttock ranges from the first lumbar to the last sacral nerve, and therefore the injection should not be made lower than the space between the twelfth dorsal and the first lumbar vertebrae. Cases with pain above this level are not suitable for treatment with intrathecal alcohol, and if this method is reserved entirely for those patients whose pain is limited to below the level of the groins and iliac crest, success will follow in a high percentage of cases.

Technique. The patient lies on the bed with no pillows and in the left or right lateral position. The side in which the pain is experienced is uppermost, that is the patient lies on the opposite side to the one in which she has the pain. The foot of the bed is raised on blocks. The easiest way in which to find the appropriate space is to draw a line from the crest of both iliac bones and cross this with a line running down the spine, the point of intersection marking the space between the third and fourth lumbar vertebrae. Having obtained this landmark the space between D.12 and L.1 and between D.11 and D.12 can then be identified quite simply.

At this site lumbar puncture is extremely difficult. The spinous processes lie much closer together and at a more acute angle than at the usual site, and therefore the needle usually needs to be inserted at an angle of about 30 degrees to the spine. The risks of hitting the cord are great. At the usual site for lumbar puncture there is no

cord present, but at this site the cord is always present. It is therefore necessary to proceed with some caution and as soon as the skin is punctured the stillette must be drawn from the needle, which is then pushed slowly in until cerebro-spinal fluid is obtained. Immediately this occurs 0.5 ml. of absolute ethyl alcohol is injected and the needle withdrawn. The patient is then turned almost on to her face, but still with the affected side slightly uppermost.

The sequence of events following this injection are usually as follows: The pain stops immediately, the patient complains of a burning sensation at the site of injection and this travels slowly downwards until it reaches the buttock, spreads into the thigh and finally encompasses the whole leg. It usually takes two to three minutes to spread as far as the buttock and half an hour or longer to reach the sole of the foot. At the end of this time the leg is numb, painless and warm. The patient is left in this position for one hour, after which she may adopt any position she wishes and is given one pillow. The end of the bed remains on blocks for eight hours. As soon as the bed is taken off the blocks she may get up and walk about, although it is probably more comfortable to remain in bed for 24 hours. Headache usually follows and lasts for about 24 hours, and a rise of temperature on the day following the injection is almost universally encountered. If the pain is on both sides two injections are given, one with the patient in the right lateral position and one in the left lateral position, with 24 hours separating the injections.

The chief limitation of the technique is the very short duration of relief from pain which is sometimes experienced. I personally know of no way of foretelling how long relief will last. I have seen cases in which relief from pain has been absolute but has lasted only three days, whilst I have recently given a second injection to a patient who has already been kept free from pain for eight months by her first injection. The average length of relief appears to be about three months. The injections can be repeated without ill effects.

Judging by autopsy appearances of cords removed from patients who have had this procedure, adhesions due to the alcohol do not form. This is in contradistinction to a modification of this method using ammonium sulphate instead of alcohol, for if this is done adhesions of the theca to the cord are almost universal and, in my experience, are more painful than the pain for which the injection was given.

Occasionally, in performing lumbar puncture, a nerve root may be hit with the needle. It is very easy to tell when this happens because the patient immediately shouts and frequently jumps and

complaints of pain having shot right down the leg from the site of injection. On the few occasions in which this has happened I have immediately injected the alcohol; pain relief has been complete and long lasting, and on one occasion I was lucky enough to repeat this accident in the same patient. This patient remained absolutely free from pain for the 18 months until she died. Injection of the cord with alcohol is followed by paralysis of all the structures supplied below that level. I have perhaps been fortunate in never having injected the cord in a series of over 200 cases.

In my series relief from pain has been complete or sufficiently complete to control the residual pain with mild sedatives, such as codeine, in 60 per cent. of cases. It has been incomplete, or a total failure, in 40 per cent. In the early part of this series, before I realized how important it was to reject the cases in which the pain was not purely of sciatic distribution, I experienced a high percentage of failures. It is sometimes justified, if the pain of sciatic distribution is extremely severe whilst that in the other areas is mild, to give an intrathecal injection of alcohol even though the pain is not completely relieved.

Cordotomy

For patients whose pain is of femoral or inguinal distribution, or when the pain is associated with metastases in the pelvic bones and the femora, cordotomy is the operation of choice. The technique of this operation lies in the province of the neurosurgeon, but I would, however, urge that if cordotomy is to be performed it should be bilateral, as one frequently sees patients who have had a unilateral cordotomy complain of pain on the opposite side in a very short while. It is probable that this pain existed all the time but was masked by very severe pain on the side on which the operation was performed. No woman wishes to have two cordotomies in the space of six weeks if this can be avoided. About one-third of my patients submitted to cordotomy have been completely relieved.

Cobra Venom

Both in India and America, especially in the areas where the cobra is found, considerable use has been made of detoxicated cobra venom for the relief of pain in malignant disease. Its use is based on the fact that patients with severe cobra bites, although fully conscious, are often completely insensitive to pain stimuli, and it is stated that an initial dose of 3 cc. followed by the weekly injection of 1 to 2 cc. will keep the patient both pain free and ambulant. My experience is very limited, as I have only recently been able to obtain the drug. Nevertheless, it does seem capable of

relieving pain, although I would doubt that such small doses will be successful.

Pre-Frontal Leucotomy

This operation has been tried in America for the relief of pain in intractable malignant disease. It does not appear to have been very successful and certainly in the only patient in my experience in which it has been done it was a complete failure. This patient proved entirely intractable to all forms of treatment, including cordotomy at two different levels in addition to pre-frontal leucotomy.

Nerve Section

Occasionally nerve section is justified. In sciatic pain in which other methods have failed I have divided the sciatic plexus with diathermy, by an intra-abdominal operation, with great success. The limb becomes painless and the only neurological complication I have encountered was foot drop. In one other case I relieved pain in the leg by dividing both sciatic and femoral nerves and leaving the patient with a useless but painless leg; she survived for two months and was extremely grateful for the relief she obtained. These operations are usually extremely difficult, as the nerves are frequently obscured by massive lymph node metastases.

Very occasionally the pain is referred solely to the *hip joint* and this is due to involvement of the obturator nerve. *Obturator neurectomy* will relieve this. The obturator nerve can be exposed extra-peritoneally with ease, but it is not recommended in cases of malignant disease as the frequent finding of involved lymph nodes leads to very great difficulty. Intra-abdominal operation is the one of choice, and the nerve should be divided high, if necessary cutting into the psoas muscle and dividing the nerve as it passes through that muscle.

Pain Due to Bone Metastases

Bony metastases occur in about 5 per cent. of cases of cancer of the uterus. They can be extremely painful and are often associated with pathological fractures, this latter condition considerably aggravating the pain. If the metastases are in the leg below the level of the knee joint the easiest and most reliable way of relieving the pain, provided there is some expectation of life, is amputation. As has already been stated, if they are in the pelvic bones or lumbar vertebrae, cordotomy is indicated. Sometimes, however, they occur in the arm bones and in the ribs, and here deep X-ray therapy may give some temporary relief, but it is by no means certain and recurrence of the pain invariably occurs. The most difficult

case which I was ever called upon to treat was a patient with pain associated with a mass of supra-clavicular lymph nodes involving the brachial plexus and a pathological fracture of the clavicle. X-ray therapy was applied without success and eventually intravenous procaine by drip method was used, again with no success, until the concentration of procaine was almost sufficient to stop respiration.

Conclusion

The problem of pain in malignant disease of the uterus is an extremely serious one. It is one which confronts the general practitioner more than the specialist. Nevertheless, as has been indicated in this article, much can be done to make the lives of these unfortunate people comfortable. If one is to achieve the best then more care and thought

must be given to each individual case, for it is certain that the haphazard prescribing of a few aspirin tablets or an occasional injection not only does not relieve the patient's suffering but tends to induce an attitude of hopelessness and neglect which has in the past been all too common in the chronic cancer case. If we cannot cure more than a relatively small percentage of these people our aim should be to keep them ambulant and occupied for as long as possible, and it is hoped that some of the ways of doing this have been indicated in this paper.

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