Infants and children in tuberculous families present a rather different problem. Presumably the best answer, as a rule, is to remove the tuberculous member of the family from the house; but if this is not practicable the children should be removed. This has got to be done temporarily in any case if they are to be vaccinated, as all the protagonists of B.C.G. insist that separation for a time is necessary if the best results are to be obtained. If temporary removal has got to be practised, it is surely worth while considering whether separation should not be continued till the tuberculous member of the family has been cured, has died, or has been admitted to an institution for chronic cases.

One more word. Is it really worth while vaccinating infants at birth? We are still ignorant of the time the antibody-producing mechanism takes to reach maturity, but we have reason for believing that the tissue response to antigenic stimuli during the first few months of life is less than it is by the end of the first year. That is why inoculation against diphtheria is usually delayed till nine to twelve months after birth. Is there any reason for believing that the tissue response to a vaccine against the tubercle bacillus is likely to be more active than that against other antigens? If not, would it not be better to remove the infant from its tuberculous home at birth and delay vaccination with B.C.G. till it is at least 6 months of age? That this objection is not purely hypothetical is borne out by the finding that infants at birth require larger doses of B.C.G. than older infants to render them tuberculin-sensitive, and take a longer time to become allergic (Wallgren, 1947).

Summary and Conclusions

Investigations are reviewed in which a control group of persons was studied along with a B.C.G. vaccinated group.

Though a presumptive case for the value of B.C.G. vaccination has been established, it is concluded that the documentary evidence so far available is insufficient to allow any estimate to be made of the degree of protection it affords or even to prove conclusively that, in a civilized population, it has any protective effect at all.

Some of the disadvantages of B.C.G. are enumerated, and it is argued that, unless the gains from its use are likely to be substantial, B.C.G. vaccination in this country may not be worth while undertaking.

Since the risk of dying from tuberculosis in the first year of life is so small, universal vaccination of infants is clearly out of the question, and vaccination, if it is used, should be restricted to specially exposed groups, like nurses, medical students, and children in tuberculous families.

It is pointed out that the tuberculosis mortality among nurses in the Prophit survey was only a third of that among the corresponding female population in England and Wales; and it is doubted whether the relative degree of immunity that might be conferred by B.C.G. vaccination would have any greater effect in lowering the mortality than measures designed to shield nurses against undue risk of exposure to tuberculous infection.

It is further pointed out that infants and children of tuberculous parents must be separated from their homes for two to three months after vaccination with B.C.G. in order to allow immunity to develop; and it is questioned whether it might not be wiser to prolong this separation till the infecting member of the household has been cured, has died, or has been removed to an institution for chronic cases.

Since the normal antibody-producing mechanism does not seem to reach maturity till towards the end of the first year of life it might be better, if B.C.G. is to be used, to remove the infant from its tuberculous home at birth and delay vaccination with B.C.G. till it is at least six months of age.

A plea is entered for the carrying out of a properly controlled trial of B.C.G. vaccination in Great Britain, or, if this

is impracticable, for the liberation of the vaccine only under strictly defined conditions.

I am indebted to Prof. A. Bradford Hill for help in assessing the evidence in some of the investigations reviewed in this paper.

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SYMPATHECTOMY AND INTRASPINAL ALCOHOL INJECTIONS FOR RELIEF OF PELVIC PAIN*

BY

J. P. GREENHILL, M.D.

Professor of Gynaecology, Cook County Graduate School of Medicine, Chicago

Pain may be either acute or chronic. In women acute pelvic pain is not infrequent, and may be due to such causes as rupture of an ectopic pregnancy or of a corpus luteum cyst, or sudden torsion of an ovarian cyst. Such causes of pain may be relieved instantly and dramatically by a surgical operation. Likewise, in many cases in which the pain is chronic, as in pelvic inflammatory disease and endometriosis, an operation that removes the source of the pain brings relief. However, there are many women who suffer severe pain and in whom removal of its cause is either impossible or inadvisable. In this category are women with inoperable carcinoma of the uterus or severe dysmenorrhoea, women subjected to repeated unsuccessful laparotomies for the relief of pelvic pain, and young women with endometriosis who should not be castrated.

For the intractable pain associated with carcinoma of the uterus, particularly of the cervix, most physicians prescribe an opium derivative such as morphine, "pantopon," codeine, or "dilaudid." These drugs are temporarily helpful, but eventually the patient becomes refractory to them. The reasons for this inadequacy are: (1) the potential tolerance for the drugs increases enormously, so that larger and larger doses are required, resulting in a constant increase in expenditure for the drugs until the poor patient can no longer afford them; (2) in some people the opium derivatives produce nausea and vomiting; and (3) a few individuals become drug addicts.

To secure more or less permanent relief from the excruciating pain which is associated with cancer of the uterus, severe dysmenorrhoea, endometriosis, and the distressing pain of unknown origin, I recommend two useful procedures. The first is pelvic sympathectomy, or removal of that part of the sympathetic nerve plexus known as the presacral nerve or the superior hypogastric plexus. The second is intraspinal injection of alcohol.

*Read before the Oxford Postgraduate School of Medicine on July 14, 1947.

Sympathectomy is an operation that any surgeon may perform readily. The risk involved is slight, the technique is not complicated, and local infiltration analgesia may be used for a large part of the operation and in some instances for the whole of it. Furthermore, since the abdomen must be opened to carry out this procedure, it enables one to determine the extent of the growth of endometriosis, the amount of carcinomatous involvement, and any pathological process not discovered before the operation.

Of the two questions that are rightfully raised the first is whether the fibres of the sympathetic system are really sensory. Ranson (1926, 1930) confirmed the proof that was offered by Edgeworth. All the motor fibres degenerate, but the sensory fibres remain intact if the roots of the spinal nerves are cut proximal to the spinal ganglia.

Vasoconstriction of the blood vessels of the internal genital organs and inhibition of the secretion of the genital glands are produced by the hypogastric plexus, whereas the parasympathetic nerves have an opposite effect. The normal menstrual cycle is not altered by section of the superior hypogastric plexus nor does it interfere with uterine contractions during labour; neither does section produce glandular atrophy or any disturbance in the motor function of the bladder or rectum. Therefore the nerve fibres of the superior hypogastric plexus are sensory and not motor. Their function is to carry sensations from the internal genital organs to the medullary centres. Hence resection of the portion of the superior hypogastric plexus above the hypogastric ganglion is a simple way of relieving a patient of severe pain arising in the pelvic organs.

The second question concerns any possible harm that may follow removal of a portion of the sympathetic nervous system. Ranson (1926, 1930) states that Cannon and his students completely removed "the sympathetic chain on both sides, from the highest cervical to the lowest sacral ganglion. Such completely sympathectomized cats have lived under laboratory conditions for many months. Everything indicates that almost any part of the sympathetic system can be removed without seriously endangering life."

Indications for Pelvic Sympathectomy

Pelvic sympathectomy will almost completely relieve the intractable pain in about half of the cases of Group III and Group IV carcinoma of the cervix, and it will partially relieve many more. The operation (Greenhill and Schmitz, 1933) should be performed as a prophylactic measure in all cases in which a laparotomy is done for carcinoma of the cervix of the corpus uteri. Should recurrence of the cancer follow the procedure there will be considerably less pain than if the sympathectomy had not been performed. It has been reported by de Sousa Pereira (1946) that in women with cancer of the cervix subjected to pelvic sympathectomy the results of the post-operative irradiation are better than if sympathectomy had not been performed, because the vasodilatation produced by the sympathectomy improves the circulation. Pelvic sympathectomy is also indicated in selected cases of primary dysmenorrhoea in which all medication, including hormones and minor surgical measures, has been tried without avail. The results in dysmenorrhoea are excellent. I have not yet had a failure in my dysmenorrhoea cases (Greenhill, 1940).

Another but infrequent indication for pelvic sympathectomy is persistent pain in the lower abdomen not relieved by repeated laparotomies. Occasionally women are seen who have had several laparotomies for the relief of pain. Usually the first operation was an appendectomy, then an operation for an ovarian cyst, and then one or more operations for adhesions. In such women, even if the cause of

the pain is not removed, dramatic relief will follow pelvic sympathectomy.

Still another field of usefulness for pelvic sympathectomy is in cases of endometriosis in which conservatism is advisable. Of course if both ovaries are removed the endometriotic areas cease to grow. However, spaying is not desirable in young women. In all instances in which conservatism is desired a pelvic sympathectomy should be performed. The operation not only relieves pain but also seems to have some beneficial effect on the endometriosis, probably due to the vasodilatation which follows the procedure.

Technique of Pelvic Sympathectomy

The operation to be described was recommended by Cotte (1931, 1932). Since some patients who are subjected to this operation are poor surgical risks it is best to open the abdomen under direct infiltration analgesia. The rest of the operation is readily performed under a short ethylene or ether anaesthesia or even under infiltration analgesia. The patient is placed in the Trendelenburg position after a midline incision of 10–12 cm. has been made from the umbilicus down towards the pubis. After the peritoneal cavity is opened the small intestine is packed off and the sigmoid and rectum are pushed to the left side and held there with a wide retractor. Then the uterus, adnexa, and bladder may be inspected readily and palpated to determine the extent of the pathogenic processes. One may also detect a complication that can be remedied surgically. The area of the two lower lumbar vertebrae and the upper part of the sacrum is exposed. In some thin women the presacral plexus can be seen immediately beneath the peritoneum. Whether or not the plexus can be seen, the parietal peritoneum above and in the middle of the sacral promontory is elevated and incised. This incision is extended upwards and down along the sacrum for 4–5 cm. A layer of fibro-cellular connective tissue covered by adipose tissue will be exposed when the peritoneal flaps are pulled aside. This tissue can be separated easily from the peritoneum and the lower end of the aorta without hazard. The presacral plexus lies in this layer of tissue. With an aneurysm needle the tissue is elevated at the bifurcation of the aorta and the dissection is carried to a still higher level. As this is done it will be observed that in most instances the tissue spreads out triangularly. The middle sacral artery should be pushed away from the nerve, but if it is injured it can be ligated readily.

After the dissection is carried as high as desired the layer of nerve tissue is separated from the underlying tissue beyond the sacral promontory into the pelvic cavity. The plexus in this area is divided into two hypogastric nerves; hence it is necessary to dissect each nerve separately. At least 2 or 3 cm. of each hypogastric nerve should be resected in addition to 4 cm. or more of the superior hypogastric and the intermesenteric plexuses. The layer of fibrous tissue containing the hypogastric nerves is much more resistant than that containing the presacral plexus. As the dissection progresses nerve filaments projecting outward will be encountered. These should be followed as far laterally as possible before they are cut. In most instances ganglia will be included in the resection. It is preferable to remove the dissected tissue in one piece. It is not necessary or advisable to ligate the presacral plexus or the hypogastric nerves before cutting them, because only insignificant vasa nervorum are in intimate contact with them. Rarely is bleeding encountered that requires more than simple temporary pressure to check it. (When the mesosigmoid is extremely short, injury to the inferior mesenteric vessels must be avoided.) After the nerve tissue is resected the

posterior parietal peritoneum is sutured with plain catgut and the abdominal wall is closed in the customary way. Since women with inoperable carcinoma are usually cachectic and therefore show poor wound healing, silkworm gut or other permanent suture material should be used in closing the abdominal wall.

Intraspinal (Subarachnoid) Alcohol Injections

The injection of alcohol into nerves for the relief of pain has been in use for many years, but not until recently has it been employed for the relief of pelvic pain. In 1931 Dogliotti recommended subarachnoid injection of alcohol for the relief of pain. He chose the subarachnoid space because this area is the most central one for attacking the nerve roots and its injection prevents all painful peripheral stimuli from reaching the medullary centres, even if the stimuli act at the level of the spinal ganglia, the intervertebral foramina, or the spinal roots. Absolute alcohol is the preferred drug because it has no secondary toxic effects. It is easily and rapidly diffused and has a specific gravity much lower than that of the spinal fluid, hence its rise immediately affects the nerves. Most of Dogliotti's patients had sciatic pains, but not one of them had carcinoma of the genitals. The first reports on the use of intraspinal alcohol injections for cervical carcinoma were published almost simultaneously in 1934 by Saltzstein and by Stern.

In 1934 I began using intraspinal injections of alcohol for excruciating pain associated with malignancy in the female pelvis (Greenhill and Schmitz, 1935, 1936). In a series of well over 100 cases of Group III and Group IV carcinoma of the cervix treated by Schmitz and myself complete relief was obtained in about 60% and partial relief in 10%. The relief usually lasts many months—sometimes until the patient dies of the cancer. The only patients with inoperable carcinoma of the cervix who are not suitable candidates for intraspinal alcohol injections are those whose pain is in the renal area and in the parametrium from stricture of the ureter associated with hydro-ureter and hydronephrosis. The technique of intraspinal (subarachnoid) injection of alcohol is simple, and it is performed quickly and with little discomfort. However, since there is a possibility that in some cases the spinal cord may be injured, the procedure should be used only in cases of cancer.

Technique of Intraspinal Alcohol Injection

No preliminary medication is given, because observation of the immediate effects of the injection is desired. The pain in most patients with advanced carcinoma of the pelvic organs is more intense on one side than on the other. The patient is placed on the side opposite to that in which most of the pain is present. A pillow or pad is placed under the pelvis and side to elevate the sacral and lumbar portions of the spine, the back is arched as much as possible, the body is turned somewhat ventrally, and the head is lowered slightly. By placing the patient in this position the sacrolumbar area of the spine is raised to the highest level, and at the same time the posterior or sensory nerve roots are caused to lie horizontally. The anterior or motor nerve roots come to lie in a plane that is usually out of reach of the alcohol. Even if the motor nerves are not removed from the field of the alcohol, as occurs in the cauda equina, they are often not affected, since sensory nerves are more susceptible than motor fibres to the effects of alcohol. This is because the sensory nerves have less myelin.

The patient should be held in the proper position. A weak solution of iodine or other antiseptic is applied over the

lumbar and upper sacral areas. Injection is made in the second, the third, or (usually) the fourth lumbar interspace with an ordinary lumbar-puncture needle with a stylet. Procaine ("novocain") is injected into the skin before the needle is inserted into the desired interspace just as for an ordinary lumbar puncture. After the needle is in the subarachnoid space, as shown by the flow of spinal fluid, 0.75 ml. of absolute or 95% alcohol is injected into the cerebrospinal fluid. For this purpose it is best to use a tuberculin syringe to ascertain that not more than 0.75 ml. of the solution is injected. Furthermore, the alcohol must be injected very slowly, drop by drop: about two minutes is allowed for the injection of the 0.75 ml. The alcohol rises and immediately surrounds the posterior roots because its specific gravity is about 806, whereas that of the spinal fluid is 1007 to 1001. No spinal fluid should be drawn into the syringe to mix with the alcohol. After the injection is made the needle is withdrawn and the puncture hole is covered with sterile gauze and adhesive tape.

Before the injection is completed the patient will complain that the upper leg feels numb or hot and that she cannot move her leg. The numbness is almost routine after the injection, but it disappears spontaneously after a few hours or days in most instances. In spite of what the patient says concerning her inability to move the leg, when she is requested to do so she will encounter no difficulty. At the same time that the patient remarks about the numbness she also says, either voluntarily or in answer to a query, that the pain has disappeared. The results are better if the patient is permitted to lie on the side for some time. Therefore she should be kept on the side for two hours after the injection; then she is permitted to get up and walk around. At times a patient may find difficulty in getting up from a chair because her "leg is asleep." In other instances the leg feels heavy and the patient experiences some trouble in walking up steps because the knee flexes readily. These sensations usually disappear in a few hours, although in some patients they may be present for a number of weeks.

Nearly all ambulatory patients may be permitted to go home within three hours after the injection without ill effects. However, it may be best to keep a patient in a hospital for twenty-four hours after the injection. I should like to emphasize that the intraspinal injection of alcohol may be carried out easily in a patient's home. This is important, since many individuals with cancer are bedridden at home, and there is no need to subject them to the inconvenience and expense of transporting them to office or hospital. If the patient has pain on both sides an intraspinal injection of alcohol is made a week later with the patient lying on the opposite side. The same amount of alcohol is injected.

Comparison of Results

An analysis of my cases of carcinoma of the cervix treated by pelvic sympathectomy and by alcohol injections revealed that better results were obtained with intraspinal injections. In addition to the greater percentage of patients relieved by injections of alcohol, this procedure is far simpler than sympathectomy, since it does not require a stay in hospital. Therefore I believe that all women who have severe pain associated with carcinoma of the cervix should have an intraspinal injection of alcohol. More than half of such women will obtain complete relief and in a few others the benefit will be partial.

Intraspinal injections of alcohol should be used only in women with cancer, because there is definite risk of injury to the spinal cord. For women who have excruciating pain due to menstruation, endometriosis, and unknown causes pelvic sympathectomy is preferred.

Summary

I have briefly described two procedures which may be used to relieve intractable pelvic pain in women. One of these—pelvic sympathectomy—has proved most helpful in cases of carcinoma of the uterus, dysmenorrhoea, endometriosis, and pelvic pain of unknown aetiology. In inoperable cases of cancer pelvic neurectomy is helpful not only for the relief of pain but also as a prophylactic procedure at the time of hysterectomy. Likewise, pelvic sympathectomy is of great benefit in cases of endometriosis treated conservatively, not only because it relieves the pain but also because it apparently improves the endometriosis. Nearly all cases of severe primary dysmenorrhoea can be cured by sympathectomy, but this operation should not be done until all conservative measures have proved futile. Finally, in cases subjected to a number of laparotomies without relief of pain pelvic sympathectomy will yield spectacular results.

Intraspinal (subarachnoid) injection of alcohol is another means of obtaining relief from excruciating pelvic pain. This procedure is much simpler than pelvic sympathectomy and does not even require treatment in hospital. Furthermore, the percentage of patients with uterine carcinoma who obtain relief is higher than with pelvic sympathectomy. Nevertheless, because this procedure may injure the spinal cord it should not be used for any individual except one with cancer.

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RELIEF OF PAIN IN INTRACTABLE CANCER OF THE PELVIS

BY

MEAVE KENNY, M.D., F.R.C.O.G.

University Reader in Obstetrics and Gynaecology, Postgraduate Medical School of London

Cancer of the pelvic organs—intractable by surgery or irradiation, or recurrent after such measures—may condemn a man or woman to unnumbered hours of pain before death. Such people may die hard, being often in the prime of life and general health, and capable of service and happiness in their remaining days if relief from pain could be given them without impairing their mental and bodily functions. Opiates in increasing doses, neurectomies, and intrathecal injection of alcohol often increase the nursing responsibilities and make the last days of the sufferer odious to himself and to his nearest.

The treatment of such patients is surely a part of the treatment of cancer, yet among the great number of papers devoted each year to the subject of cancer of the urogenital tract alone the means of relief in hopeless cases is barely mentioned, and the average practitioner, who must shoulder their care, may have the impression that skilled surgical procedures, sometimes unavailable or impracticable, offer the greatest measure of help.

Here is described a means of relief which has borne some careful trial and which is recommended for effect and simplicity and because it can be used at need again and again until the end. This is the method of caudal analgesia.

It has seemed right to me to describe it in some detail, for this paper is addressed particularly to the general practi-

tioner and to those in charge of the chronic sick in homes and infirmaries who may not be familiar with the technique.

The Method

The apparatus consists of : Surgical spirit or "dettol" cream for cleaning the skin, and tincture of iodine or other coloured antiseptic for surface-marking ; 1 5-ml. Record syringe ; 1 Record-fitting needle, 8/10×1½ in. (3.75 cm.) ; 2 10-ml. Record syringes ; 1 Record-fitting needle, 15/10×3 in. (7.5 cm.), bore 2 ; procaine, 1.5% solution ; "proctocaine," 40–60 ml. (procaine 1.5% w/v, butyl *p*-aminobenzoate 6% w/v, with benzyl alcohol in arachis oil).

The patient is placed across the bed in the left lateral position and the buttocks and sacrococcygeal area are cleansed and disinfected. The caudal opening of the sacral canal is identified (usually with ease, and more easily in men than in parous women, who may have had the coccyx displaced in childbirth) and marked with a dab of iodine. A subcutaneous wheal is raised at this point with the 1½-in. needle attached to the 5-ml. syringe charged with the procaine 1.5% solution, and through this the tissues down to the tough fibrous membrane closing the sacral canal are infiltrated. The needle is then withdrawn, and after two minutes the stout 3-in. needle is made to follow the track of the first needle, at an angle of 45 degrees to the skin, until the fibrous membrane is encountered and pierced ; then the needle is depressed to an angle of 15 degrees and pushed steadily on until the operator is sure that about 1 in. (2.5 cm.) of its length is lying freely movable within the space of the sacral canal. The needle, which after withdrawal of the piston reveals neither blood nor spinal fluid, is then attached to the 5-ml. syringe recharged with procaine and the whole is injected boldly. The beginner will know if he is posterior to the sacrum by the appearance of a subcutaneous swelling, or anterior—between rectum and sacrum—by an exploring finger in the anus. Convinced of his correct position by the free flow of the anaesthetic and by his observations, the operator detaches the syringe and replaces it with one of the 10-ml. syringes charged with warmed proctocaine. He then steadily injects the proctocaine to an amount varying with the skeletal size of the patient—usually 40 to 60 ml.—taking some ten minutes to do so, meanwhile testing every minute the levels of cutaneous anaesthesia to pin-prick of the perineum, thighs, buttocks, and abdominal wall, and asking the patient to say when relief of his pain takes place, although it is usually pleasantly evident from the gradual relaxation of attitude and expression. When this becomes known, or if the level of skin anaesthesia rises to nipple level, the injection is stopped and the syringe detached.

Sometimes complete relief is obtained at once, but sometimes it comes only when the patient is eased on to his right side, is made to stand up, or lies on his back with the foot of the bed raised for a few minutes. Sometimes the greatest relief comes after a period of lying on the back with the buttocks raised on a pillow, so as to allow the oily solution to seep higher, although it is better to inject 6 to 10 ml. more through the still present needle and obtain effect at once. For in this, as in all cases of long-continued and severe pain, the habit of suffering is best broken swiftly and convincingly. Most often the sufferer is at once so eased of the superflux of his pain that he endures the rest with fortitude ; and having co-operated to obtain the result—knowing that by such simple means relief can be obtained again if necessary and that probably the pain will come no more—a pride in living returns.

In such circumstances I have seen an old dancer brought into the clinic in a wheeled chair, with both thighs drawn up on to the abdomen in painful spasm due to cancerous infiltration of the psoas muscles, and then after the injection straighten herself off the couch, at first gingerly, and then smilingly assume several poses of the ballet before the watching delighted class of students and nurses.

I and my assistants have so treated 17 patients with cancer of the uterus, bladder, prostate, and vagina. Of these one—a man aged 58 with prostatic cancer, who was