There is at present no clinical test available which will enable us to judge the position exactly, but it is probable that a periodic thorough and careful investigation of the retinal arteries by a skilled ophthalmologist is likely to provide the best guide to whether the onset of arterial degeneration is beginning to threaten. A periodic careful investigation of the renal function is also desirable in such cases. Finally, every case must be considered on its individual merits—general, cardiological, renal, familial, and psychological.

The author would like to express his great indebtedness to Mr. E. G. Tuckwell for his very helpful and stimulating surgical co-operation.

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ROLE OF SYMPATHETIC NERVE IN CANCEROUS PAIN

AN INQUIRY ON 300 CASES

BY

MARCEL DARGENT*Surgeon to the Centre Anticancéreux de Lyon*

[WITH PHOTOGRAVURE PLATE]

The question of pain-relieving operations on the sympathetic nerve in patients with evolutive carcinoma has been widely discussed. Although by experiment we have acquired much information concerning some of the functions of the sympathetic nervous system, a yet clearer view of its sensory functions may be obtained by a study of operative results and the anatomico-pathological findings in relation to this particular cancerous pain. Indeed, some of these operations have been performed in France as an empirical attempt to relieve pain in desperate cases: they have been only partly successful.

Spinal-cord surgery, as advocated by Putnam in the U.S.A. and Leriche and Wertheimer in France, is based on well-defined experimental facts, and consequently holds an important place in "pain surgery," as did radicotomy in the past.

This inquiry, which I started in 1940 under the direction of M. Leriche and have since pursued, has enabled me, first, to gather anatomico-pathological data; secondly, to define the clinical features of sympathetic pain; and, thirdly, to determine the limits of such operations. I do not intend here to describe the anatomical sensory pathways in the sympathetic trunk but simply to record clinical facts derived from experience.

At first, after a successful cocaine infiltration test, I performed surgical sympathetic-nerve resections—12 on the lumbar trunk and 26 on the cervical. As only temporary relief was obtained I gradually gave up this operation, as I found that repeated cocaine infiltrations had produced more lasting results. I have performed over 300 infiltrations of cervical, thoracic, and lumbar parts of the sympathetic trunk, but shall not describe the technique used, as it is well known. I employ 20 to 40 ml. of a 1% solution of "scurocain."

The use of alcohol I have found to be dangerous, as it often produces such intense irritation in the sympathetic

ganglia that the results may be worse than the initial condition. It seems preferable to use repeated cocaine infiltrations.

Anatomico-pathological Data

Macroscopic and microscopical investigations of ganglia removed at operation have disclosed the existence of actual disease of the ganglion in patients undergoing pain. This fact was revealed in two different areas. First, when removing the lumbar trunk in women suffering from carcinoma of the cervix I found it to be tightly encircled by big lymph nodes extending all along the inferior vena cava or the aorta, just in front of the vertebrae and the anterior part of the psoas muscle. Often after radium therapy these patients were apparently healed as regards their pelvis, and the cancerous extension seemed to originate in the lower part of the lumbar column. The sympathetic ganglia were oedematous, with considerable congestive reactions in the surrounding area. Surgical removal was usually very difficult. Once there even occurred a wound of the inferior vena cava. The small veins passing under the psoas arches would often give rise to troublesome haemorrhages. Secondly, in the neck, when removing the upper sympathetic ganglion, I found it to be closely connected with the big lymph nodes, often suppurative, owing to carcinoma of the tongue, tonsils, or cavum, and lying under the sterno-cleido-mastoid muscle, before the splenius capitis.

I have given up removing the cervico-dorsal ganglion in malignant process due to carcinoma of the breast, having witnessed elsewhere an attempt which proved unsuccessful.

All these oedematous ganglia were submitted to microscopical examination. Arteriolitic lesions were found, with hyalinization of the media. But the most striking fact was the presence of thick clusters of lymphocytes around the sympathetic cells even when no drugs had been previously injected (Plate, Fig. 1). On further examination it was seen that the cells had irregular borders, granulous protoplasm, and a pyknotic nucleus (Fig. 2). These lesions were surrounded by normal areas, thus constituting signs of sympathetic-cell agony.

Examination of the upper sympathetic cervical ganglion revealed in one case a very curious fact:

In a 56-year-old man—in perfect condition after treatment four years earlier for carcinoma of the tongue—a big malignant lymphatic tumour was found to progress in the upper portion of the neck. Pain was intolerable. Microscopical examination of the ganglion removed by sympathectomy showed several carcinomatous areas in the centre (Fig. 3). It was not exactly a direct involvement of nervous tissue but a metastatic growth in the lumen of the small vessels of the ganglion (Fig. 4), partially obturated by inflammatory thrombosis.

Further anatomico-pathological data have been supplied by arterial surgery. It is well known that the arterial wall, when irritated, may be the origin of sympathetic pain. Here again we have found evidence of the arterial origin of pain.

Having operated upon a man who three weeks earlier had undergone ligation of the common carotid artery and resection of the upper sympathetic cervical ganglion, which proved ineffective after a three-weeks success, I found a thrombosis of the carotid bifurcation. Arteriectomy of the three carotids was then performed. This patient had cancer of the tonsil, with a large lymphatic node. Microscopical examination showed important lesions of the intima, and an organized clot was adherent to it. The tunica adventitia also was injured. After the operation pain was abolished during the two months that preceded death.

I have since examined arteries of other suffering patients. I have never found any thrombosis (which in the above case could only be explained by the ligature), but I have often

detected inflammatory or neoplastic growths in the tunica adventitia. This was observed especially in the facial and occipital arteries. Also I have always found the primitive iliac artery closely surrounded by hard neoplastic nodes, secondary to carcinoma of the cervix.

Besides these essential anatomico-pathological facts showing evidence of the sympathetic origin of this particular kind of pain two other less important facts may be mentioned. The first is the influence of sympathetic innervation on the conduction of sensibility along the peripheral nerves. On infiltration of the upper cervical ganglion anaesthesia of the cheek is observed to disappear for a few hours in patients with cancer of the upper jaw. These effects last but a short time and are not of enough therapeutic value to justify sympathetic operations for pain by compression of peripheral nerves. The second fact is the participation of periosteal nerve-branches in pain due to certain osteolytic bone metastases. In two instances when x-ray therapy was not available I performed cocaine infiltrations—once on a lumbar vertebra involved by a metastasis from breast carcinoma, and a second time on a similarly involved ischium. The result may be compared to that of an infiltration in the case of a sprain: it does not last long, and x-ray therapy, as an antalgic treatment, is far more reliable. In this case infiltration is but an emergency procedure pending the utilization of x rays.

To sum up, anatomical lesions are to be found in the sympathetic trunk and ganglia, as well as signs of reaction in the arterial wall in contact with cancerous lymph nodes—which explains the sympathetic origin of pain in some cases of evolutive cancer. The participation of the sympathetic nerve in pain due to compression or involvement of peripheral nerves, as also in pain produced by periosteal lesions, is of a much more accessory character.

Some Clinical Features of Sympathetic Pain

Prolonged observation of our patients and a close survey of the effects, whether satisfactory or not, following the infiltrations which I performed, at first as a routine, have led me to consider the features of this type of pain. Two are quite definite. They are as follows.

1. The first is encountered in the evolution of cancer of the cervix. In many cases the primary lesion is healed and the patients suffer from one-sided pain, in the buttock, the lumbar region, the posterior part of the thigh, and often in the leg. They speak, wrongly, of sciatica. But in reality they undergo paroxysmal crises, with a feeling of cold in the leg and numbness of the whole limb. Oscillometric investigations made during the crises showed a curve with a lower level for the injured side than for the opposite one.

This type of pain should be distinguished from other types:

- (a) By x-ray examination, from osteogenic pain due to involvement of the pelvic skeleton (which is mainly the case in cancer of the prostate). These patients are relieved by x-ray therapy.
- (b) Pain due to pyosalpinx and pyometritis (as shown by Ducuing, in France). In this case local operations may be successful.
- (c) Pain from hydronephrosis, caused by a tight stricture of the ureter. Here, too, operations on the urinary tract are advisable.
- (d) Pain from direct involvement of the obturator nerve, in which paralysis of the maximus adductor muscle is obvious clinically, as is the topography of the pain.
- (e) Pain due to involvement of the lower part of the pelvis, radiating to the vulva and obviously originating in the internal pudendal nerve.

In the last two instances, and in the event of associated sympathetic pain, posterior commissural myelotomy is recommended, provided the patient is in good general condition. It is generally admitted that this operation acts as a sympathetic operation on higher and more central pathways.

2. A second type of undoubted sympathetic pain may be described in relation to the malignant evolution of cervical lymph nodes secondary to carcinoma of the tongue, tonsils, etc. These patients often indicate with their hand the topo-

graphy of the pain during the crises: one side of the head, the nape, temple, ear, eye, and teeth of the lower jaw. These crises are almost unbearable, especially at night. I have even witnessed in these circumstances a certain degree of enophthalmia and watering of the eye. As Leriche and Fontaine have shown in their book *La Chirurgie de la Douleur*, the dissection and pinching of the external carotid peripheral tunic in patients operated upon under local analgesia will awaken pain in the same area. This type of pain may also occur in the case of limited radionecrosis of the lower jaw after radium therapy.

Here again pain due to involvement of the skull base must be eliminated. It is generally out of the range of therapeutic action, although x-ray therapy may relieve it to some degree.

Pain sometimes will be produced by acute otitis in the course of evolutive cancer of the cavum. In such a case I have seen paracentesis of the drum bring relief.

Lastly, when continuous pain is localized to the trigeminal nerve and the cervical plexus, direct operations on these nerves should be preferred.

Besides these two syndromes there are others in which the influence of the sympathetic nerve is less obvious. For instance, brachial pain in the course of carcinoma of the breast is relieved in 50% of cases by routine infiltration of the cervico-dorsal chain. Oedema of the arm and hand is frequent. A phlebogram is not easily obtained in such cases. Nevertheless, when these symptoms seem to be produced by chronic phlebitis, infiltration is usually successful. Similarly, a patient had a cancerous node closely connected with the lower portion of the axillary artery, together with radial paralysis. Cervico-dorsal trunk infiltration resulted in the pain being relieved and the paralysis attenuated. This procedure, repeated every two months, was successful for a year and a half. In refractory cases I believe that a high posterior myelotomy, as advocated by Putnam, may give satisfactory results.

Intolerable pain in cancer of the stomach did not appear to be relieved by infiltration of the splanchnic nerve, except for a few hours. Pain in bladder and rectum in evolutive cancer of the cervix is not always abolished by section of the presacral nerve (Cotte, 1932) or by infiltration of the lower lumbar sympathetic trunk. Of three presacral sections one was a failure, one a three-weeks success, and in the other relief lasted one year. In the last case resection of both the fifth and fourth sympathetic ganglia of the lumbar trunk was performed simultaneously by transperitoneal approach.

I have noted that some accompanying symptoms may be relieved by infiltration of the cervical sympathetic trunk:

- (1) a few days' attenuation of dysphagia is obtained in upper pharynx carcinoma in 50% of the cases;
- (2) dyspnoea in some laryngeal cancers is seen to disappear after infiltration of the middle cervical ganglion;
- (3) in the case of trismus due to inflammatory lesions associated with cancer infiltration of the upper cervical ganglion will cause it to yield noticeably.

Selecting the Sympathetic Operation

Most of the patients have already experienced drugs: they have got used to them, especially in the case of opium. A careful study should first be made of the actual characteristics of the pain in order to avoid misapplication of treatment. The general condition, cancerous extension, and the migratory nature of pain (as in diffuse cancerous osteosis) should be considered. The psychological condition of the patient must also be taken into account. At all events, infiltration of sympathetic trunks is an easy and harmless test. If successful, and the general condition is fairly good, these infiltrations may be repeated over a long period of time.

Should sympathetic operations be recommended in patients whose general condition is very good? I feel less and less convinced that they should. In spite of two

satisfactory results, extending over two years, of lumbar sympathectomy in patients with slowly evolutive cancer of the cervix, I have witnessed recurrence of pain after three weeks and two months respectively. It seems that the stumps of sympathetic trunks that have undergone section soon get irritated by the progressive involvement of lymph nodes and thus bring about recurrence of pain; besides, infiltration on a higher segment may yet be successful, so that operation may well be deemed useless. I still perform it, however, under the following circumstances: (1) In the case of left colostomy for very extensive and painful pelvic cancer. Before opening the peritoneum I explore the left sympathetic trunk by subperitoneal approach, and when accessible I remove it. (2) When haemorrhages render operation in the neck necessary I remove the external carotid, together with a considerable portion of the upper thyroid, facial, and occipital arteries—the most sensitive arteries in this area. In addition, I resect the upper cervical sympathetic ganglion.

Summary

Lesions of the sympathetic ganglia and arterial walls are encountered in cancerous patients undergoing pain.

There are in the lumbar region and in the neck well-defined types of sympathetic pain. These are greatly relieved by cocaine infiltrations of the sympathetic trunks. This procedure, which is simple, should be preferred to operations on the sympathetic nerve, which are difficult and which often lead to recurrences.

I am grateful to Prof. J. F. Martin, pathologist, and Mr. Delaunay, medical photographer, for the photomicrographs reproduced on the photogravure plate.

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Many of the functions previously exercised by the Ministry of Health under the Food and Drugs Acts have been transferred to the Ministry of Food in consequence of an Order in Council entitled the Transfer of Functions (Food and Drugs) Order, 1948, made under the Ministers of the Crown (Transfer of Functions) Act, 1946. Broadly, the effect of the transfer is that the Ministry of Food is concerned with the composition, description, and inspection of foods, while the Ministry of Health continues to be concerned in measures for dealing with infected food or food poisoning. These changes affect only departmental functions. The duties of enforcement and execution placed by the Acts and regulations upon local authorities are not affected. The Ministry of Food becomes the department concerned with the Preservatives and the Condensed and Dried Milk Regulations and other matters relating to the composition and description of food; with the Meat and Imported Food Regulations and other matters relating to food inspection and food hygiene generally; and with the Milk and Dairies and Milk (Special Designations) Regulations so far as they concern dealers and distributors. The Ministry will also become responsible for approval of terms of appointment of public analysts. The Ministry of Health remains the department primarily concerned with drugs and with matters directly related to the protection of the public from infected food—for example, food poisoning and regulations relating to ice-cream, shell fish, and the stoppage of the sale of infected milk. All regulations under the Food and Drugs Act, 1938, which are at present made by the Minister of Health, will in future be made jointly by the Ministers of Food and Health. None of the changes involved in this transfer of functions affects the position in Scotland.

ASEPTIC NECROSIS OF PANCREAS DUE TO ARTERIAL THROMBOSIS IN MALIGNANT HYPERTENSION

BY

WALTER PAGEL, M.D.

AND

A. L. WOOLF, M.B., B.S.

(From the Central Middlesex County Hospital)

[WITH PHOTOGRAVURE PLATE]

The possibility of a vascular factor in the production of acute pancreatitis has long been suspected, yet no conclusive evidence has so far been adduced. Gerlei (1930) described two cases of embolic occlusion without any tissue damage. Two other cases with disseminated necroses were observed, but all were incidental findings due to multiple small emboli and were visible only under the microscope: none showed evidence of fat necrosis or haemorrhagic pancreatitis. Lynch (1940) mentioned a case of embolic infarction, the embolus originating in an atheromatous aortic patch. Here "massive haemorrhagic necrosis of the tail of the pancreas" is claimed, but no more exact description of the findings is given. By experimental injection of the pancreatic arteries of dogs with mercury pellets, Smyth (1940) produced anaemic infarcts localized to the infarcted areas in contrast with the spreading tendency of clinically observed acute haemorrhagic pancreatitis.

Of the older cases, those by Chiari (1900) and Rössle (1921) should be mentioned; in these arterial thrombosis was followed by anaemic infarction of considerable extent, but no appreciable fat necrosis or haemorrhagic pancreatitis was observed. Brentano's (1900) case, which is sometimes quoted in this connexion, is actually not concerned with primary vascular changes in the pancreas.

It is therefore still undecided whether multiple small or gross vascular changes and infarction of the pancreas can lead in themselves to acute pancreatitis, and a supplementation of the scarce material available appears to be imperative.

The following is a report of a case recently admitted to the Central Middlesex County Hospital, with the findings at necropsy.

Case Report

The patient, a builder aged 45, was admitted on Aug. 29, 1947, on account of a dull aching pain for two to three weeks in the epigastrium, radiating around the sides of the chest to the shoulder-blades and also over the front of the chest. He had had a similar attack of pain twelve months before, and bouts at intervals in the intervening periods. There was nausea but no vomiting.

Examination revealed several areas of petechiae on the skin, particularly around the shoulders and upper chest posteriorly. He was not apparently in severe pain, but had pain localized to the midline of the epigastrium. The abdomen was semi-rigid, and thus there was indefinite tenderness; the percussion note was tympanitic all over. The pulse was 100, and a regular apical systolic murmur was heard. The fundus oculi showed bilateral papilloedema (doubtful in the left eye) and haemorrhages, with exudates in the right eye. Blood count: white cells amounted to 18,400 per c.mm. (neutrophils 86%, lymphocytes 8%, monocytes 6%), with a marked shift to the left.

A clinical diagnosis of malignant hypertension with uraemia was made. The uraemia increased, ending in coma (blood urea, 275 mg. per 100 ml.), with evidence of pericarditis.

Necropsy.—The body was that of a thin man, with petechiae on shoulders, chest, and thighs. Brain: no changes. Uraemic pleurisy and pericarditis with subserous petechiae. Heart: left ventricular hypertrophy. No parietal or valvular thrombus

HYPERTENSION—AETIOLOGY AND SURGICAL TREATMENT : GEOFFREY BOURNE

FIG. 1.—Right eye before sympathectomy.

FIG. 3.—Renal retinopathy pre-sympathectomy.

FIG. 2.—Same eye after sympathectomy.

FIG. 4.—Same eye after sympathectomy.

ROLE OF SYMPATHETIC NERVE IN CANCEROUS PAIN : MARCEL DARGENT

FIG. 1.—Cluster of lymphocytes around sympathetic ganglion cells.

FIG. 2.—Alterations of protoplasm in ganglion cells. Pyknosis of nuclei.

FIG. 3.—Carcinoma tongue. Metastatic node in sympathetic ganglion.

FIG. 4.—Relation between the metastatic node and arteriolar wall.