Etiology of Decubitus Ulcers

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Eighty separate experiments were performed in an attempt to accurately determine the effect of both constant and alternating localized pressure on normal and denervated muscle. Localized pressures were applied over muscular tissue and the relationship between microscopic changes in the muscle and time and intensity of pressure was noted. Data compiled demonstrated the marked susceptibility of tissue to relatively low constant pressures for short periods of time and the somewhat greater resistance to change following the application of equal amounts of intermittent pressure. This was true of both normal and denervated tissue. A critical time interval at which pathologic change occurs in both normal and denervated skeletal muscle following the application of pressure was noted.

Decubitus ulcers are one of the major problems confronting any physician who is called upon to supervise the care of the severely disabled or debilitated patient. Every clinician is well aware of the complications which often manifest themselves following the occurrence of ulceration in the chair- or bed-ridden patient. Decubitus ulcerations not only prolong the morbidity and interfere with the rehabilitation and maintenance of these people but they also may frequently be implicated as a major contributing factor leading to the patient's demise.

Ulceration of the skin especially over bony prominences has undoubtedly plagued the disabled and debilitated patient since the beginning of man. Before the advent of antibiotic therapy, secondary infection of the ulcerations led to early death, whereas today the patients usually survive for prolonged periods of time in spite of the ulcerations. Improved medical, nutritional, and environmental factors have increased the life span of man with the result that there are more persons than ever before living to a relatively old age. This presents a problem in that a greater number of patients with cerebral vascular disease, malignancies and neurologic disorders are being cared for in our hospitals and nursing homes. With the increase in the average age of the population, as well as the improvement in medical facilities, the medical profession is being faced with the problem of maintaining and rehabilitating the elderly and severely disabled person.

In spite of the relatively widespread occurrence of ulcerations in the general hospital population and the almost inevitable occurrence in the patient with spinal cord injury, no agreement exists as to the basic underlying cause of the ulceration. This is undoubtedly due to the fact that very little basic research has been done regarding the etiology of decubital ulcers. Most of the prevailing evidence has been derived from clinical observations.

Decubital ulcerations are localized areas of cellular necrosis. Normal cell metabolism is dependent on the receipt of nutrients and the elimination of metabolites. Any condition which interferes with these exchanges will affect the function of the cell. The circulating peripheral blood fulfills the metabolic needs of the cell so that any alteration in the circulation is reflected in cellular changes. Severe or prolonged circulatory interference ultimately leads to death of the cell.

Because ulcerations occur almost exclusively over bony prominences which have been subjected to excessive pressures for varying lengths of time and because ulcerations almost inevitably will heal when pressure is removed, it would appear that ischemia caused by supra-capillary pressures is one of the primary factors in the production of decubital ulcers.

Review of the Literature

To effectively evaluate the physiologic changes which occur as a result of the application of pressure it would appear that the three basic problems which must be investigated are: (1) pressure, (2) tissue ischemia, and (3) capillary changes.

1. Pressure. It is difficult to evaluate

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the effect of pressure per se on the physiologic function of the living cell without involving the circulation to the cell. Cattell carried out experiments on isolated tissues, enzymes, and unicellular organisms in an attempt to determine the physiologic effects of pressure on tissue under conditions in which the effect produced could be attributed only to the pressure and not to the interference with receipt of nutrients or the elimination of waste products of cell metabolism. The pressures were applied through a fluid medium. Pressures in excess of 250,000 pounds/square inch were necessary at times to produce significant changes in cellular function. However, pressures as low as 260 mm. Hg were observed to stop nerve conduction in a few minutes.

2. Acute Ischemia. Early impetus for the investigation of pathologic changes arising from ischemia of voluntary muscle was provided by Volkmann, who described the necrosis of muscle due to ischemia induced by compression of the arteries with constrictive dressing. However, early workers, because of the interest in the pathogenesis of Volkmann's contractures, devoted most of their attention to the chronic lesions arising from ischemia of voluntary muscle and gave little attention to the initial phases or changes that occurred in the first 24 hours.

Brooks noted that the application of 130 mm. Hg pressure by means of a plethysmograph to the tail of a rat for approximately 18 hours produced massive necrosis in all instances while a pressure of 130 mm. Hg for 17 hours produced gangrene in only seven of nine cases. However, when pressures of 100 mm. Hg were applied for 48 hours, gangrene of the entire tail was again noted. Ulceration generally was first noted two or three days after the application of pressure. Microscopically, there was a thickening of the epithelium and the muscle showed evidence of degeneration, myositis, and fibrous replacement. Harman reported that ischemia of two to four hours duration produced by ligation of the major arteries to the extremity of a rat resulted in microscopic pathologic changes which readily were recognized.

The alteration in structure was first observed in muscles of animals subjected to ischemia for at least four hours. This was characterized by individualization or separation of fibers, regression of longitudinal striations and enhancement of cross-striations. Muscles of the extremities were exposed and tested in situ for contractility with a Faradic current applied directly to the muscles through metal electrodes and the contractions were graded relative to those in the normal limb. Weakness or absence of contractility generally preceded and accompanied the pathologic changes. Harman concluded that this physiologic change confirmed the pathologic phenomena which was present.

In an attempt to determine the difference between arterial and venous occlusion, Brooks isolated the rectus femoris muscle of dogs and then ligated the single artery, vein or nerve which supplied the muscle. Microscopic examination of tissue taken from dogs in which the muscle was completely separated from arterial supply for periods of seven to 60 days showed slight degenerative changes and in no instance was there a marked inflammatory reaction of fibrous tissue in the muscle. Because of the appearance of hemorrhage, edema, degeneration of muscle fibers and acute inflammatory process following the ligation of the vein, the author concluded that the changes noted were initiated by capillary damage produced by greatly increased capillary pressure.

Harman more recently noted that complete arterial ischemia of the extremity of a rat for periods of four to four and one-half hours was followed by dilatation of the arteries in the ischemic limb and patency of the veins following the removal of constriction. This led the author to believe that degenerative muscular changes were probably due to severe capillary damage. Because of this capillary damage, stasis and alteration of the normal permeability, there was a decrease in the inflow of blood to the cellular units and a considerable depression of the rate of exchange of metabolites.

Husain recently noted microscopic changes in the muscles of a rat when
pressures as low as 100 mm. Hg were applied for as little as two hours. While no gross changes were noted, 24 hours after pressure was applied, there was microscopic evidence of cellular infiltration, interstitial capillary hemorrhage, and various stages of cellular degeneration. Pressures of 100 mm. Hg for six hours produced similar but more severe changes. They have recently reported that microscopic examination of tissue obtained 24 hours after the application of only 60 mm. Hg for one hour showed cellular infiltration, extravasation, and hyaline degeneration. Tissue subjected to higher pressures for longer periods of time showed muscular necrosis, hyaline degeneration and venous thrombosis as well as cellular infiltration and extravasation.

3. Capillary Changes. With this implication of the minute vasculature of the tissue, it would seem that some discussion and review of the circulatory bed is indicated.

Zweifach and Metz reported observations on the skeletal muscle of the rat. They noted arterial arcades from which arterioles branched at right angles and these in turn divided into capillaries which lay on the surface of the small bundles of muscle fibers. The capillaries usually lay along the axis of the muscle fibers and were 40 to 50 microns apart.

Most authors making direct observations on minute vessels report a phenomenon which has been designated as "active vasomotion." This is an intermittent ebb and flow through the network because of the opening and closing of the arterioles and precapillary sphincters. Nicol and Webb expressed the view that the slow vasomotor changes were due mainly to local changes in tissue and that faster vasomotor changes were probably due to neural influences since they were abolished by denervation. They suggested that active vasomotion may be the main determinant of capillary pressure.

Burton and Jamada demonstrated that the rate of flow through minute vessels was related to the perfusing pressure. They found the relationship between the blood flow and the transmural pressure to be approximately linear through most of the pressure range. However, as the transmural pressure was reduced, there was a rapidly progressive decrease in blood flow and the flow stopped while the transmural pressure was still at 20 to 40 mm. Hg. The level of transmural pressure at which the blood flow stopped was called the "critical closing" pressure. This "critical closing" pressure could be produced either by an increase in externally applied pressure or a decrease in intravascular hydrostatic pressure.

Nicholls has demonstrated remarkable instability in capillaries at low perfusion pressures with cessation or temporary reversal of flow at a low positive pressure. This closing pressure was found to range from three to six centimeters of water in the hind leg of a frog. Burton noted complete cessation of arterial flow in the forearm of man at times when the external pressure to the forearm by means of a water plethysmograph was 70 mm. Hg less than the subject's mean arterial pressure.

Landis, using the microinjection method for determining blood pressure in single capillaries, found the average pressure in the arteriole limb to be 32 mm. Hg. He noted increases in maximum capillary pressures to 60 mm. Hg during hyperemia and 50 mm. Hg during histamine flare.

Much information exists in the literature regarding the phenomenon of reactive hyperemia which manifests itself following several types of stimuli. This hyperemia is generally regarded as a normal protective response and is noted routinely following arterial occlusion.

Much of the early work regarding reactive hyperemia was carried out by Lewis and Grant as well as by Goldblatt who did their work at approximately the same time. They showed that occluding a portion of an extremity for five seconds or more generally produces a reaction. The reaction is proportional to the duration of occlusion and to the temperature of the limb. The duration of the reaction generally increases with the time of occlusion up to one hour and generally lasts one-half to three-fourths
as long as the occlusion. They also demonstrated that hyperemia was not dependent on central innervation of the blood vessels since it would occur in tissue which was completely denervated. It would therefore appear that reactive hyperemia is not due to changes in intravascular pressure but to accumulation of some products of metabolism during the periods of circulatory disturbance.

Recent work by Landis and Henry would tend to implicate anoxemia as the primary reason for reactive hyperemia. Landis showed that a complete ischemic anoxia of three minutes duration would cause temporary damage to the capillary of frog's mesentery and produce a movement of fluid through the capillary wall which was four times the normal rate.

Purpose of Study

This study was undertaken in an attempt to accurately determine the effect of both constant and alternating localized pressure on normal and denervated muscle. Localized pressures were applied over muscular tissue and the relationship between microscopic changes in the muscle and time and intensity of pressure was noted.

Methods

Forty albino rats ranging in weight from 300 to 400 grams were subjected to localized pressures ranging from 35 to 240 mm. Hg for periods of one to four hours. All animals were anesthetized with pentobarbital (Nembutal, 30 mgm./kgr. body weight) during a test period. The animals were placed in a prone position with the hind extremities secured in a relaxed abducted position.

Constant pressures were applied to the hamstring group of muscles of 12 normal rats for a predetermined length of time. Eight normal rats were subjected to alternating pressures for equal periods of time with the pressure being relieved every five minutes for a period of five minutes.

Mid-thoracic section of the spinal cord was performed on a group of 20 animals. Twelve animals in this group were subjected to constant pressures while alternate pressures, at five minute intervals, were applied to the other eight animals.

All animals were returned to their cages following completion of the test. Twenty-four hours later the animals were sacrificed and the belly of the lateral hamstring muscle was removed. The tissue was fixed in Bouin's solution for a period of six hours, sectioned to a thickness of five microns and stained with hematoxylin and eosin as well as trichrome stain.

Pressures were applied by an air-driven piston consisting of a 20 cc. hypodermic syringe which was inverted and stabilized over the test area as described in a previous study.

Tissue pressures were measured by means of a Statham P23A physiologic transducer which was connected to a 20 gauge needle inserted into the muscle. The needle had five openings bored into the lateral surface within a distance of one centimeter from the tip. To assure contiguity between the fluid being tested and the fluid within the system saline was infused at the rate of 4.6 cc. per hour from a constant injection pump. It was thought that this low rate of flow would not influence the tissue pressure being measured. Pressures were measured with the needle horizontal to the plunger head and all values were recorded on a Sanborn polyviso recorder (fig. 1).

Results

Eighty separate experiments demonstrated a marked susceptibility of tissue to single applications of moderate pres-
sure for relatively short periods of time (table 1). Microscopic examination of tissue 24 hours after the application of pressure demonstrated varying degrees of involvement in both the normal and paraplegic rats. Characteristic pathologic changes noted in individual muscle fibers consisted of decrease or loss of crossstriations and myofibrils, hyalinization of fibers, neutrophilic infiltration as well as floccular changes with phagocytosis by neutrophils and macrophages (figs. 2 and 3). Isolated muscle fiber involvement was designated as a minimal change. Moderate change indicated involvement of up to 10 per cent of the muscle fibers and marked change referred to involvement of more than 10 per cent of the fibers examined with the presence of edema and inflammatory changes.

No changes were noted in the specimens which were subjected to pressures of 35 mm. Hg for periods of time up to four hours. This was true of both the normal and paraplegic rats. The application of varying pressures up to 190 mm. Hg in the normal rat and 155 mm. Hg in the paraplegic rat for one hour did not produce any noticeable microscopic change in the tissue. However, the application of 70 mm. Hg pressure in both the normal and paraplegic rat produced changes after two hours. This is in complete agreement with the work of Husain. Working with dogs, we have shown that the application of 60 mm. Hg pressure for one hour produced edema, cellular infiltration and extravasation.

The application of alternating pressures, whereby the tissue was completely free of pressure for five minute intervals, showed consistently less change or no change when compared with tissue subjected to an equivalent amount of constant pressure. This was true even at pressures as high as 240 mm. Hg for three hours.

There appeared to be no consistent increase in susceptibility of the muscle in the paraplegic rats as compared to normal rats at all ranges of pressure. No apparent microscopic difference was

<table>
<thead>
<tr>
<th>Pressure Transmitted to Muscle</th>
<th>Time in Hours</th>
<th>Normal</th>
<th>Alternating Pressure — 3 min. intervals</th>
<th>Paraplegic</th>
<th>Alternating Pressure — 3 min. intervals</th>
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<tr>
<td>35 mm. Hg</td>
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<td>2</td>
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<td>3</td>
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<td>Marked</td>
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<td>4</td>
<td>Moderate</td>
<td>Minimal</td>
<td>Marked</td>
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</tbody>
</table>

None — No microscopic change.
Minimal — Involvement of isolated fibers.
Moderate — Involvement of up to 10 per cent of muscle examined.
Marked — Involvement of more than 10 per cent of muscle examined.
tion of constant pressure slightly greater than capillary pressure would tend to support this reasoning. The presence of edema and cellular infiltration 24 hours after the application of moderate pressure would indicate moderate changes in capillary permeability probably due to the capillary membrane ischemia. Increasing the degree or duration of ischemia not only increases the changes in membrane permeability but interferes with cellular metabolism to such a degree as to produce cellular necrosis and inflammatory reaction in the muscle tissue.

Husain\textsuperscript{12} has demonstrated that microscopic changes produced after the application of localized pressure were due primarily to ischemia. In a group of rats in which the femoral artery had been ligated, microscopic changes were noted after a single application of pressure of only 50 mm. Hg for a period of only one hour. These changes were similar to those noted in rats with normal circulation following the application of 100 mm. Hg pressure for a period of two hours. Production of generalized ischemia in the entire extremity tended to increase the degree of ischemia produced by the local application of pressure.

If any variation existed in the pathologic changes found in the normal rats as compared to those with sectioned spinal cords, the pattern was not consistent. Individual variations were probably due to the lack of sensation and general decrease in muscle circulation.

Regarding the importance of a neurotrophic factor as a primary cause of ulceration, there is very little basic evidence to lend any support to this theory. The fact that ulcerations occur more frequently in patients with spinal cord injury or peripheral nerve involvement, cannot be denied. However, without implicating a neurotrophic factor, it would seem that the simplest explanation for this occurrence is the fact that sensory function is interfered with so that the patient does not experience pressure and the general circulation to the denervated area is somewhat decreased making the tissue more susceptible to ischemia. The fact that ulceration frequently occurs in a normally innervated area subjected to pressure and that ulcerations in extremities divorced from any neurologic control invariably heal when maintained free of pressure tends to relegate the neurotrophic theory to a secondary if not completely insignificant factor in the production of ulcerations.

The metabolic deficits which manifest themselves following trauma or prolonged immobilization have been well documented by several groups of investigators.\textsuperscript{26-27} Though the effects of general metabolic changes on the production and healing of ulcerations have not been demonstrated experimentally, it would seem that healthy, well-nourished tissue not only can survive an insult of any type more readily, but is better able to recover from this insult.
Other contributing factors in the production of ulcerations are edema and anemia. Since the rate of diffusion of oxygen and metabolites from the capillary to the cell decreases in proportion to the distance from the capillary to the cell, it is clear that edema has profound influence on the survival of the ischemic cell. If ischemia is accompanied by anemia and decreased oxygen content in the blood, cellular metabolism is further restricted and the tissue becomes more susceptible to the ischemia.

Because of microscopic degenerative changes which result from the application of only relatively low pressures for short periods of time, it becomes apparent that degenerative reaction and recovery from these changes is probably taking place simultaneously. Where tissue is subjected to pressures for only short periods of time, the normal reactive hypemic response partially compensates for the temporary ischemia with the result that the tissue does not undergo mor phologic degeneration. Even when excessive pressures are applied for a sufficient period of time to result in early degenerative changes, it would appear that complete relief of pressure may often permit restoration of circulation and cellular metabolism without ulceration.

Clinically, even when adequate nursing care is available the incapacitated person is rarely turned oftener than once every two hours; thus, each trochanter, the sacrum or the iliac spine is subjected to suprapacillary pressures for two hour intervals at least three times each day. Many bed-ridden patients develop ischemic ulcers on such a regimen. This would indicate that the damage produced during the time that the pressure was being exerted was not completely repaired during the intervals when the area was free of pressure. More frequent turning of the patient would result in more frequent periods of complete relief of pressure during which restoration of cellular function could occur.

Though no measurements of pressure under the sacrum or trochanters while the patient is in the lying position have been reported, the superficial covering is so limited that almost all pressure applied must be transmitted to all tissue depths. Trumble has calculated that if a person’s weight were equally distributed over the entire surface available for weight bearing when in the recumbent position, it would amount to less than one-third pound/square inch (17 mm. Hg). However, in an ordinary bed, the weight of the body is borne primarily over certain bony prominences whose combined area is very small with the result that the pressures over these areas undoubtedly exceed capillary pressure.

The weight bearing area available to the patient is considerably less when sitting than when supine; it depends primarily on the sitting posture itself, and to a lesser degree, on the sitting surface available. If the intertrochanteric distance is assumed to be approximately 32 cm. and the anteroposterior sitting surface is the same, the available sitting area is approximately 150 square inches. Since approximately 75 per cent of a subject’s total body weight when he is sitting is exerted over this limited area, the pressure would exceed 26 mm. Hg even if it were evenly distributed. But, the brunt of the pressure is borne by a rather limited area immediately under the ischial tuberosities. We have shown that even with a two inch foam rubber cushion, average pressures under the ischial tuberosities and surrounding area generally exceed 150 mm. Hg. If only 50 per cent of this pressure were transmitted to the ischial tuberosity, there would be complete cellular ischemia of all tissue over the bone and ultimate ulceration would only be a matter of time.

Cut-out areas intended to decrease or eliminate pressures over the bony tuberosities only tend to divert more of the weight bearing to the surrounding area. Increasing the thickness of the cushioning to as much as six inches of foam rubber appears to have had little effect on the occurrence of ulceration in the wheelchair patient. Conversely, the more sophisticated, well-informed paraplegic with good upper extremities can remain relatively free of ischemic ulcers by conscientious weight shifting several times each hour regardless of the seat padding which is used. Since it is impossible to
completely eliminate all pressure for a long period of time, it becomes imperative that the pressure be completely eliminated at frequent intervals in order to allow circulation to the ischemic tissues.

Summary

1. Skeletal muscle from both normal and paraplegic rats exhibited a high degree of susceptibility to low constant pressures for relatively short periods of time.

2. Microscopic pathologic changes in muscle were absent or less prominent following the application of equal amounts of alternating pressures in both the normal and paraplegic rats.

3. There are no detectable microscopic differences between normal or denervated muscle following the application of either constant or alternating pressure.

4. A critical time interval at which pathologic change occurs in both normal and denervated skeletal muscle following the application of pressure was noted. This critical period was between one and two hours.

5. Microscopic pathologic changes due to the application of pressure consist of edema, loss of cross-striations and myofibrils, hyalinization of fibers, neutrophilic infiltration and phagocytosis by neutrophils and macrophages.

References


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Information relative to securing reprints of this study may be had by checking the Reader Service column on page iv of this issue.

**VERY IMPORTANT**

The next examinations, written and oral, of the American Board of Physical Medicine and Rehabilitation will be held in New York City, June 24 and 25, 1961. The final date for submitting application is February 15, 1961. Write to the Secretary, Dr. Earl C. Elkins, 200 First Street, S.W., Rochester, Minnesota, for application.