INTRAMEDULLARY PRESSURE WITH PARTICULAR REFERENCE TO MASSIVE DIAPHYSEAL BONE NECROSIS

EXPERIMENTAL OBSERVATIONS

RALPH M. LARSEN, M.D.

NASHVILLE, TENN.

FROM THE DEPARTMENT OF SURGERY OF VANDERBILT UNIVERSITY, NASHVILLE, TENN.

As a result of Lexer's[1] experimental studies, the anatomic distribution of blood vessels in long bones is now clearly understood. But there has been so little concrete experimental study of the function of these vessels, in the voluminous literature dealing with growth, repair, regeneration, atrophy, necrosis and other disorders of bone, that their fundamental physiologic reactions remain, with few exceptions, unknown.

Axhausen[2] found focal epiphyseal bone necroses associated with resorption and incomplete repair in embolism of epiphyseal vessels. Although Streptococci were cultivated from these lesions he attributed the degenerative change to ischemia rather than bacteria because of the absence of inflammation.

Nussbaum[3] experimentally verified the ischemic nature of the lesions described by Axhausen. Nussbaum's work is of particular interest because it is one of the few dealing with experimental vascular insufficiency of epiphyseal bones.

Müller[4] observed focal necrosis of compact human bone in advanced arterial sclerosis due, he believed, to infarction. He attributed the brittleness of senile bone to these lesions and emphasized the difficulty of producing prolonged bone ischemia by simple arterial occlusion. In no instance did he encounter medullary necrosis.

The experiments of Johnson[5] constitute the first fundamental contribution to our knowledge of the rôle played by each of the three components of the blood vascular system of long bones in bone repair. Johnson concluded that outer cortical bone is supplied and its viability maintained by periosteal vessels; whereas the internal portion of the shaft and metaphyses is supplied and kept viable by the nutrient and metaphyseal vessels.

Brunschwig[6] produced extensive bone and marrow necrosis in experimental animals by actually destroying most of the periosteal, metaphyseal and nutrient vascular connections. In some of his experiments the necrosis involved almost the entire shaft and marrow. Infarction occurred only in animals with unclosed epiphyseal lines, and in no instance was there sequestration.

While Brunschwig had shown that bone and marrow could be killed by extensive interference with their blood supply, Drinker and Drinker[7] first studied blood flow and cytology of living marrow vessels perfused with dif-

Submitted for publication January 17, 1938.

ferent substances at different pressures. They demonstrated the effect of stimulation and interruption of the nerve accompanying the nutrient vessels and the effect of asphyxia on volume flow of blood. Their experiments were conducted, however, under conditions in which collateral circulation of the periosteum and metaphyses was uncontrolled and the state of the epiphyseal cartilages in these experiments is not clearly described.

In 1928, Axhausen[8] and his collaborators advanced the hypothesis that massive necrosis in acute suppurative osteomyelitis is due to septic infarction of bone.

Phemister[9] pointed out that the experimental findings of Johnson and Brunschwig are contrary to this assumption because complete ischemia of a massive segment of diaphyseal cortex would require obstruction of at least two independent vascular networks.

We would suggest, however, that the rigidity of the walls of medullary cavities in long bone, and the close interdependence of volume blood flow and pressure which this anatomic characteristic implies, indicates that massive necrosis of acute suppurative osteomyelitis may be due to ischemia caused by increased intramedullary pressure, which may produce its effect independent of the course and origin of the vessels involved. Studies of the effect of pressure exerted in and upon long bones are infrequently recorded in literature.

Bergman,[10] attempting to ascertain the mechanism by which the pressure of expansile tumors produced its changes, drove expanding pins into the medullary cavities of long bones. Spiral fractures always followed. Employing pegs of diameter slightly less than the medullary cavity, he found extensive, painless lacunar resorption, never involving the whole thickness of the shaft, associated with both periosteal and endosteal proliferation, and concluded that continuously acting pressure from inside the medullary canal produces greater proliferation than absorption. One must credit him with clearly emphasizing the importance of distinguishing changes in growing and adult bone, differentiating between directly and indirectly applied pressure, and indicating the importance of the axis of the bone in which pressure is applied. It is almost paradoxical that this investigator, studying pressure which produces its effect so frequently by disturbances in circulation, should have overlooked the importance of the tremendous damage to medullary circulation which his experimental methods induced.

Robl,[11] studying the effect of externally applied pressure, wrapped the long bones of rabbits with elastic bands and springs, and produced resorption of a thin layer of underlying cortex, greatest at the site of greatest pressure. He did not ascertain to what extent these changes were due to the immediate injury of the periosteal circulation or its subsequent exclusion.

Burkhardt,[12] applying pressure to the whole extremity by wrapping the legs of rabbits and dogs with elastic bands, found that extensive bone necrosis accompanied soft tissue necrosis, that bone is especially susceptible to disturbances in circulation, that the marrow withstands ischemia better than

the compact bone itself, and that bone proliferation occurs only when the damage has been great enough to involve the marrow. While the degree and duration of circulatory exclusion is not quite clear in his paper, it constitutes one of the first purely physiologic studies of the bone blood vascular system. The simplicity of the experimental method is worthy of mention.

It is the purpose of this paper to record experimental results obtained in the study of intramedullary pressure with particular reference to massive diaphyseal bone necrosis.

Part I. Studies of Intramedullary Vascular Pressure

Animals.—Ten dogs, young and old adults, were employed. Some of these were street dogs, other had been fed on regular balanced diets with adequate proteins, salts and vitamins for a period of several weeks before being studied.

Preparation.—The animals in good health were anesthetized with 0.03 Gm. of barbital per kilo intravenously. They were then given 200 mg. Toronto heparin intravenously. The right common carotid was cannulated low in the neck and after shaving and preparing the left thigh, the distal one-eighth of the femoral shaft was exposed without otherwise disturbing the periosteum or its adjacent and contiguous structures.

Procedure.—The periosteum over the anterior surface of the femur was then incised vertically for approximately 2.5 cm., the central portion of the incised periosteum stripped laterally about 0.5 cm. on each side, and the cortex of the femur was then perforated approximately 2 cm. proximal to its distal epiphysis by a 0.75 cm. drill. The marrow was punctured by the perforating drill as it penetrated the cortex. A tapered threaded steel cannula was then turned into the cortical perforation, immediately connected to a mercury manometer; and the pressure, thus obtained, recorded simultaneously with the right carotid arterial pressure on a common base line.

Results.—In eight dogs the marrow cannula pressure obtained in this manner rapidly rose to 30 to 40 Mm. of mercury. Pressure variations in the medullary system occurred simultaneously with carotid arterial pressure variations but were of less magnitude. Even Traube Herring type variations in pressure could be clearly seen in the medullary cannula system. These pressure relationships persisted for the duration of the life of the animal if anticoagulants were repeatedly administered.

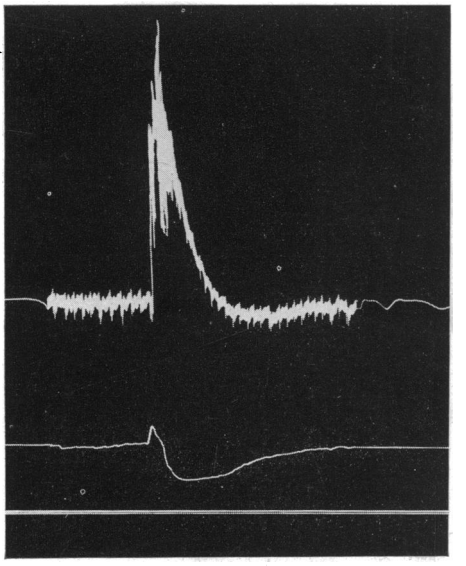
In two dogs the medullary pressure did not rise. In one a clot was found about the bur-hole. In the other the cannula had probably been screwed against the opposite wall.

Conclusions. Part I.—When dogs anesthetized with barbital are heparinized and the marrow cavity cannulated in the manner described, the average relationship of arterial to intramedullary cannula pressure is approximately 3:1 and the intramedullary cannula pressure changes parallel the arterial pressure variations.

Part II. Studies of the Effects of Adrenalin, Ephedrine, Pituitrin and Histamine on Intramedullary Pressure

Adrenalin Hydrochloride.—Experiment. Eight animals, prepared and anesthetized as in Part I, were each given one-half minim of $\frac{1}{1000}$ adrenalin hydrochloride per kilo intravenously.

Results.—In all experiments performed, the following of which is illustrative (Graph 1), essentially the same results were obtained. Synchronous with the rise in arterial tension to 200 plus Mm. mercury, there was a rise of 4 to 6 Mm. of mercury in the intramedullary cannula pressure of only a few seconds' duration, after which the intramedullary cannula pressure precipitously fell from 38 Mm. of mercury to 12 to 14 Mm. mercury where it remained during the period of elevated carotid arterial pressure. Thereafter as the arterial tension fell from 180 to 200 Mm. mercury toward normal, the intramedullary cannula pressure gradually rose so that both the arterial and intramedullary pressures returned to their respective levels which they maintained prior to the administration of adrenalin at the same time. There was no tendency to a delayed over-rise in the intramedullary cannula pressure.



GRAPH 1.—Adrenalin: The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the mercury manometer medullary cavity pressure. The lowest tracing is the base line. Initial arterial pressure 104, initial intramedullary cannula pressure 34 Mm. mercury. Ten seconds before the point of the abrupt rise in arterial pressure one-half minims per kilo, 1/1000 adrenalin chloride was given intravenously left jugular. Duration of this experiment approximately 20 minutes. Note the abrupt and marked divergence of arterial and intramedullary cannula pressure.

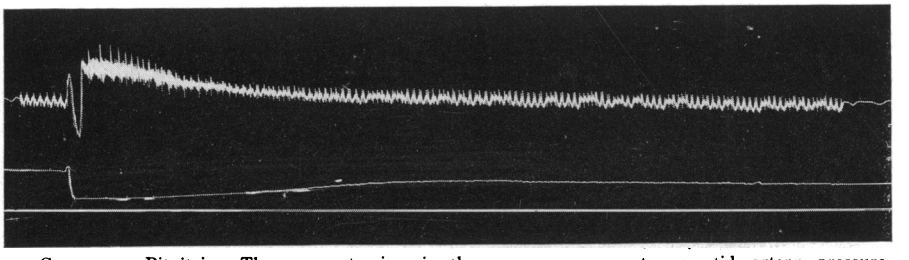
Pituitrin (Surgical).—Experiment. Eight animals, prepared and anesthetized as in Part I, were each given one unit per kilo pituitrin S, intravenously.

Results.—In all of our experiments we obtained essentially the same results as in the following graphically illustrated experiment (Graph 2). Synchronous with the rise in arterial tension from 110–120 to 160 Mm. mercury, there was a very brief rise in intramedullary pressure of 2 to 4 Mm. of mercury followed by an almost instantaneous drop from 36 to 8–10 Mm. mercury. Coincident with the gradual fall in arterial pressure toward normal there was a slow proportionate recovery rise in intramedullary cannula pressure, both arterial and intramedullary cannula pressure arriving simultaneously at the level maintained prior to the administration of pituitrin.

Ephedrine Hydrochloride.—Experiment. Four animals, prepared and

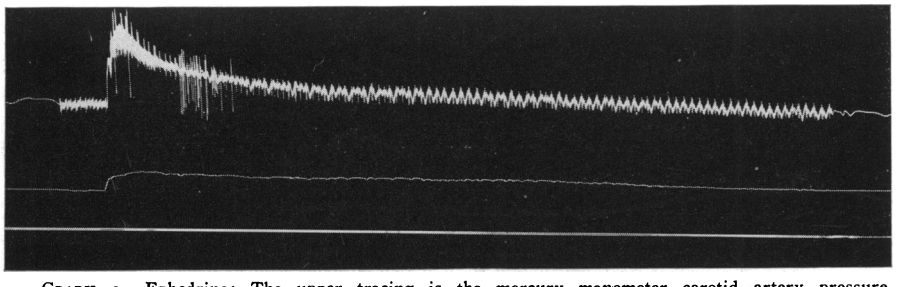
anesthetized as in Part I, were each given 2.5 mg. per kilo ephedrine hydrochloride intravenously.

Results.—The following graphically illustrated experiment (Graph 3) is typical of the results obtained in all dogs studied. Synchronous with the rise in arterial tension from 110–120 to 180 Mm. mercury there was a rise in intramedullary pressure from 34–36 to 52–54 Mm. mercury. This relationship persisted throughout the effective period of the drug so that both the arterial and intramedullary cannula pressure reached the level sustained prior to the administration of ephedrine simultaneously.



GRAPH 2.—Pituitrin: The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the medullary cavity pressure. The lowest tracing is the base line. Initial arterial pressure 104. Initial intramedullary cannula pressure 36. Ten seconds before the primary rise in arterial pressure one unit per kilo, pituitrin S, was administered intravenously left jugular. The transitory rise in intramedullary cannula pressure followed by the precipitous fall sustained throughout the period of hypertension is apparent. Duration of recorded experiment approximately one hour.

Histamine.—Experiment. Four animals, prepared and anesthetized as in Part I, were each given 0.05 mg. per kilo histamine hydrochloride intravenously.

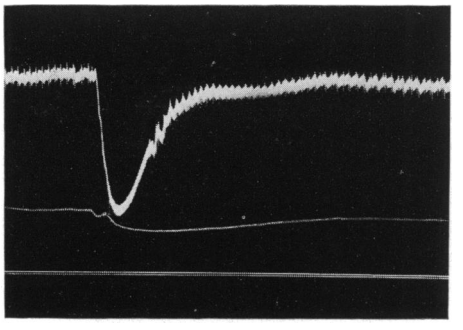


GRAPH 3.—Ephedrine: The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the mercury manometer intramedullary cannula pressure. The lowest tracing is the base line. Initial arterial pressure 100. Initial intramedullary cannula pressure 38. Ten seconds before the abrupt rise in arterial pressure dog was given 2.5 mg. per kilo ephedrine hydrochloride intravenous left jugular. The precipitous sustained rise in intramedullary cannula pressure throughout the period of hypertension is apparent. Duration of recorded experiment approximately one hour.

Results.—The results in all dogs studied were almost identical with the following graphically illustrated experiment (Graph 4). Coincident with the abrupt fall of arterial pressure from 120 to 30 Mm. mercury there was an abrupt fall in intramedullary pressure from 34 to 24 Mm. mercury, widely disproportionate to the fall in arterial tension. Inconstantly present was a short lived secondary rise in intramedullary pressure after the initial decline.

Comparison of the Pressure Effects of Adrenalin, Ephedrine and Pituitrin S.—Graph 5 is an illustration of the divergent effect of both adrenalin and pituitrin between carotid arterial and intramedullary cannula pressure, contrasted with the parallel effect of both ephedrine and histamine on these pressures.

Conclusions. Part II.—In animals prepared as described in these experiments, the clear-cut, constant divergent effect produced by both adrenalin and pituitrin between arterial and intramedullary cannula pressure and the parallel effect of ephedrine on these pressures are clearly established.



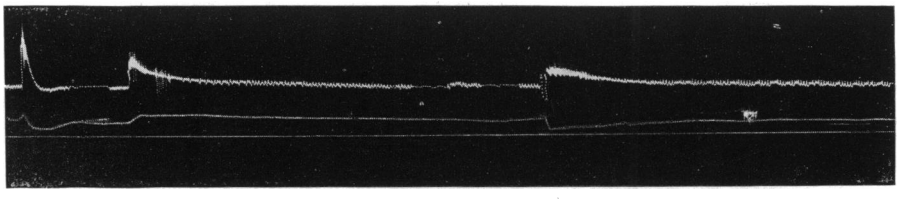
GRAPH 4.—Histamine: The upper tracing is the mercury manometer carotid artery pressure. The middle tracing is the mercury manometer intramedullary cannula pressure. The lowest tracing is the base line. Initial arterial pressure 106. Initial intramedullary cannula pressure 38. Eight seconds before precipitous fall in arterial pressure, dog was given 0.05 mg. kilo histamine hydrochloride intravenous left jugular. The precipitous fall in intramedullary cannula pressure and its gradual recovery are apparent. Duration experiment approximately 25 minutes.

It is not within the scope of this paper to investigate the minute physiologic and pharmacologic reactions which underlie these clear-cut results.

We are well aware that the pressures developed in the intramedullary cannula may not be the exact intramedullary pressure in these experiments. Certainly, however, the fluid in the intramedullary cannula space was in direct pressure continuity with the intramedullary vascular pressure, and the results obtained are in accord with what one would anticipate when dealing with a vascular network enclosed in rigid walls.

Part III. Studies of Degenerative Changes Occurring in Long Bone Following Elevation of Intramedullary Pressure by Physiologic Saline Solution

Experimental Procedure.—Part A: Dogs and pups ranging from 7 to 14 kilos were deeply anesthetized with barbital 25 mg. per kilo, and the anesthesia maintained by repetition of one-half the above dosage of barbital



GRAPH 5.—Shows the results of a composite experiment in which drugs were given in sequence—producing their characteristic change in intramedullary cannula pressure. The precipitous fall and slow rise with adrenalin and pituitrin is in interesting contrast to the sustained rise produced with ephedrine. (a) Adrenalin. (b) Ephedrine. (c) Pituitrin S.

supported by ¼ Gr. morphia whenever the animals reacted sufficiently to whine or move.

TABLE I

GROUP I—BUR-HOLE IN SHAFT OF BONE

Hydrostatic Pressure of 65 to 75 Cm.

Dog No.	Hydrostatic Pressure in Cm.	Length of Time Pressure Was Applied	Number of Cc. Infused	Interval before Dog's Death	Condition of Bone after Death. Other Remarks
4	65	22 hrs.	15 (clot in cannula)	24 hrs.	Dog did not recover from anesthetic. There was no edema or separation of periosteum
2	65	22 hrs.	400 (clot in cannula)	36 hrs.	Dog did not recover from anesthetic. There was no edema or separation of the periosteum
15	65	24 hrs.	400	19 days	On fifth postoperative day wound spontaneously partially disrupted, drained sanguinoseropurulent material 4 days, then gradually healed over. Killed on nineteenth day. There was an irregular thin layer of periosteal new bone deposited over distal half of shaft, the underlying cortical bone was grossly normal and the marrow in the distal half was gray. Epiphyseal cartilages grossly normal
14	65	48 hrs.	2,000	23 days	On sixth postoperative day wound spontaneously disrupted, discharged serosanguineous material for 6 days, then gradually closed. Killed on twenty-third day. There was slight thickening of periosteum around bur-hole. Cortical bone grossly normal. Marrow in immediate vicinity of bur-hole grayish, amorphous, surrounded by plug of granulation tissue. Epiphyseal cartilages normal
101	70	20 hrs.	2,650	7 days	No separation of wound although on third day considerable swelling of soft tissues of entire thigh. Killed on seventh day. Periosteum slightly thickened, easily stripped. No gross defect in cortical bone. Bur-hole marrow defect filled with vascular granulation tissue. Epiphyseal lines closed. Epiphyses normal

Operative Procedure.—The animals were well padded and their restraints loosely applied. The entire thigh and leg were shaved and cleaned and a lateral vertical incision made over the lateral intermuscular septum, the muscles were separated at the septum and two inches of the distal femur

exposed. The lateral periosteum was then incised vertically 3 cm., stripped laterally 0.5 cm. at the midpart of the incision and the underlying cortex was then perforated by a 0.75 cm. drill. The underlying marrow was penetrated as the drill slipped through the cortical bone. A phlanged screw cannula was then turned into the medullary cavity. A pressure apparatus supplying sterile salt solution, 0.9 per cent, was then coupled to the cannula and the wound in muscle, fascia and skin closed with interrupted silk. No attempt was made to close the periosteum.

At the termination of the experiment, the pressure for the first time was lowered or discontinued and the cannula removed. A single skin suture previously placed at the site of the emergence of the cannula was then tied. Collodion dressing was applied and the dog allowed up without splints.

TABLE II

Hydrostatic Pressure of 105 to 135 Cm.

Dog No.	Hydrostatic Pressure in Cm.	Length of Time Pressure Was Applied	Number of Cc. Infused	Interval before Dog's Death	Condition of Bone after Death. Other Remarks
30	105	24 hrs.	350	10 days	No separation of wound although from third to seventh day thigh was extremely swollen. Killed on tenth day. There was diffuse thickening of very vascular, normally adherent periosteum, beneath which there was widespread deposit of new bone intimately adherent to old shaft which when separated from the subperiosteal bone was irregular and motheaten on the opposing surface. There was an area of white bare bone about 2 cm. long on each side of the bur-hole. Marrow irregularly soft, homogeneous, yellow throughout canal. Epiphysis closed, no gross abnormality.
34	135	23 hrs.	6,600	10 days	On fifth postoperative day wound opened spontaneously, drained large amount of purulent material and was granulating. Draining when animal was killed on tenth day. There was diffuse thickening of very vascular periosteum which formed part of the wall of a large extraperiosteal abscess. Diffuse deposit of large amount of subperiosteal new bone intimately continuous with bone of old shaft from which it could be peeled leaving rough mottled surface. Small area bare yellow bone immediate vicinity bur-hole. Marrow irregularly necrotic. Epiphysis closed, no gross abnormality

TABLE III

Hydrostatic Pressure of 180 Cm.

Dog No.	Hydrostatic Pressure in Cm.	Length of Time Pressure Was Applied	Number of Cc. Infused	Interval before Dog's Death	Condition of Bone after Death. Other Remarks
80*	180	12 hrs.	400	14 days	Wound did not disrupt. On fourteenth day when killed there was massive sequestration of distal one-third of shaft, from which the periosteum was separated by a large amount of thin purulent fluid, complete separation from the distal epiphysis and diffuse deposit of new bone over cortex of upper two thirds of shaft, beneath which old cortex was rough but in intimate continuity with newly deposited bone. Marrow totally necrotic in distal one-third, irregularly necrotic mid shaft, and red near upper metaphysis
117*	180	22 hrs.	2,100	16 days	Wound remained closed. Marked swelling and redness until sixth postoperative day. Killed on sixteenth day. Distal one-third of shaft except in immediate vicinity of epiphysis bare and white. Periosteum elevated and separated from dead bone by pus. Epiphyseal line closed. No separation. General deposit new firmly adherent subperiosteal bone remainder of shaft. Marrow necrotic except in spongy bone adjacent to epiphysis
114*	180	20 hrs.	3,400	12 days	Wound healed without disruption. Killed twelfth day. Complete sequestration shaft with separation of periosteum by subperiosteal pus and separation distal epiphysis
47	180	24 hrs.	No appreciable infusion	18 days	Wound infected. Drained very little. Killed on eighteenth day. No bare bone save in immediate vicinity of bur-hole, filled with granulation extending into marrow which was widely necrotic and amorphous. Extensive thinning of old cortical bone by granulation tissue in marrow and deposit of new layer of subperiosteal bone thicker than the original diaphysis. Epiphyseal lines closed and there was marked absorption of end of shaft adjacent, which was replaced by cancellous bone from the epiphysis partly obliterating the distal marrow space

* Mixed flora including *Staphylococcus aureus* obtained from subperiosteal fluid of animals 80, 117 and 114.

TABLE IV

Hydrostatic Pressure of 240 to 265 Cm.

Dog No.	Hydrostatic Pressure in Cm.	Length of Time Pressure Was Applied	Number of Cc. Infused	Interval before Dog's Death	Condition of Bone after Death. Other Remarks
46	256	24 hrs.	? but infusion took place	8 days	Died. Extensive necrosis of bone with separation of both epiphyses and denuded lower one-third of shaft. *Grossly infected.* During 8 of the 24 hours of pressure, tap water was used
37A	240	20 hrs.	1,500	12 days	Marked swelling of thigh from second to sixth day when wound broke open and drained small amount for 3 days. Killed on twelfth day. Entire shaft bare except small area of attachment (?) at linea aspera and at metaphyses, where the periosteum for approximately 1 cm. was adherent to the underlying epiphysis and resorbing shaft through a layer of new bone 0.5 cm. thick. A clear-cut line of separation between the shaft and epiphysis was clearly demonstrable at the cortex but the medulla for approximately 2 cm. was replaced by dense cancellous bone continuous with the epiphyseal bone and new subperiosteal bone deposits. The periosteum itself was greatly thickened and extremely vascular. It contained new bone only where directly approximated to dead shaft near the metaphyses and along the linea aspera
6	265	8 hrs.	?	37 days	Killed on thirty-seventh day. There is tremendous enlargement of the entire shaft. When bisected the thickening is found due to tremendous, diffuse deposit of new, dense subperiosteal bone. The outline of the old shaft is very irregular both on periosteal and endosteal sides. It, in places almost invisible, is still present at the midshaft but near the epiphysis is obliterated by new bone. The marrow cavity is entirely filled with dense spongy bone directly continuous with epiphyseal bone and subperiosteal new bone
73	180	12 hrs.	2,900	11 days	Wound grossly infected from onset. Killed eleventh postoperative day. Large abscess involving deep tissues and communicating with separated periosteum. Distal one-half of shaft bare. Distal epiphysis separated at epiphyseal line

Part B: In this series the same anesthetic and preparation were employed as in animals in Part A. The marrow was cannulated by exposing the femoral condyles and perforating the epiphysis and metaphysis. Pressure was applied as in Part A, and at the termination of the experiment the cannula was removed and the drill hole plugged with wax and fascia. The joint capsule and skin were then closed with interrupted silk.

TABLE V

GROUP 2.—BUR-HOLE IN INTERCONDYLAR REGION

Hydrostatic Pressure of 180 Cm.

Dog No.	Hydrostatic Pressure in Cm.	Length of Time Pressure Was Applied	Number of Cc. Infused	Interval before Dog's Death	Condition of Bone after Death Other Remarks
3	180	24 hrs.	4,000	7 days	Killed. Extensive necrosis of entire shaft. Complete separation periosteum from shaft
6	180	32 hrs.	? but infusion took place	9 days	Died. Extensive necrosis of left femur. Separation of epiphyses and periosteum. Large accumulation of subperiosteal pus
17	180	24 hrs.	? but infusion took place	5 days	Killed. Specimen discarded. No bone necrosis or periosteal change. Bur against opposite wall?
37B	180	24 hrs.	Only small amount	10 days	Killed. Periosteal thickening. No resorption. No separation of epiphysis. Plug of compressed marrow and blood at midpart of marrow canal. This may have occluded the cannula
2	180	24 hrs.	? but infusion took place	7 days	Killed. Extensive separation periosteum from distal one-half of shaft. No separaration epiphysis. Marrow widely destroyed by cannula

Summary. Part III.—When the femoral marrow cavity is infused with physiologic salt solution:

(A) At pressures from 65 to 75 cm. of salt solution for 20 to 24 hours (Table I):

(1) The amount infused ranges from 400 to 2,650 cc.

(2) There is no edema or elevation of periosteum during period of infusion and for 24 hours afterward.

(3) The marrow is killed irregularly distal and adjacent to the site of infusion.

(4) Sequestration of bone does not occur although the wounds are grossly infected.

(5) There occurs a small amount of periosteal new bone especially distal to the site of infusion.

(B) At pressures from 105 to 135 cm. salt solution for 23 to 24 hours (Table II):

(1) The amount infused ranges from 350 to 6,600 cc.

(2) The marrow is killed irregularly throughout most of the cavity.

(3) Sequestration of bone occurs only in the immediate vicinity of the site of infusion even though the wound be grossly infected.

(4) Periosteal new bone is deposited throughout the extent of the shaft, and there is resorption of the underlying cortical bone.

(C) At pressures of 180 cm. or greater salt solution for 12 hours or more (Table III):

(1) The amount of salt solution infused ranges from 400 to 3,000 cc. (Table V).

(2) The marrow becomes completely necrotic.

(3) Massive necrosis of bone with subsequent separation of periosteum and one or both epiphyses occurs. Because of spontaneous reopening of wounds, as subperiosteal fluid accumulated, all wounds studied ultimately became infected in this series. Mixed flora including *Staphylococcus aureus* were recovered from all wounds studied.

(4) Typical involucrum may be formed where sequestration occurs. In two instances (Dogs 6 and 37A, Table IV) sequestration did not occur but a massive segment of old shaft was undergoing substitution when animals were killed.

Conclusions. Part III.—(1) The medullary infusion of 0.9 per cent salt solution at pressures below 75 cm. for 24 to 48 hours does not lead to bone necrosis even though the wounds are grossly infected.

(2) The medullary infusion of 0.9 per cent salt solution at pressures of 180 cm. or greater for as short a period as 12 hours, independent of the amount infused, leads to massive bone necrosis, followed by massive sequestration in bones whose epiphyseal cartilage existed at the time of the experiment, and widespread resorption in bones where epiphyseal lines had closed prior to the experiment. All wounds studied bacteriologically in this series ultimately became infected.

(3) The continued infusion of salt solution, the absence of necrosis or substitution in bones exposed to (55 Mm. mercury) 75 cm. salt solution pressure for 24 hours even when infection follows, and the constant bone substitution or sequestration incurred by application of pressures of (77 Mm. mercury) 105 cm. salt solution or greater leads us to the conclusion that increased intramedullary pressure may be of extreme importance in the production of massive bone necrosis.

(4) In these experiments "stripping" of the periosteum was not a factor in the production of bone necrosis since the periosteum was incised at operation widely enough to allow of decompression throughout the period required for periosteal detachment to occur. Detachment of periosteum is, therefore, secondary to necrosis of the shaft in these experiments and represents the reaction of the living periosteum to the dead infected bone, rather than a primary factor in the production of massive necrosis.

(5) Our experiments suggest that sequestration of dead bone occurs only when there has been complete destruction and long continued exclusion of the vascular connections between bone and surrounding vascular tissue.

DISCUSSION

We are aware that in the experiments cited the marrow cannula fluid was often in continuity with the open marrow vascular system. However, the rapidity with which marrow cannula pressure changes were induced by the drugs administered in Part II as well as the marked variation of fluid infused

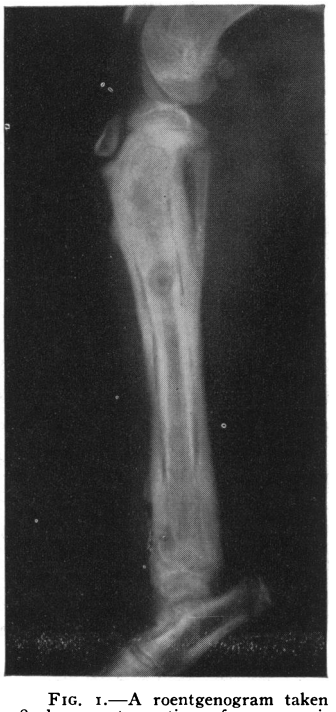


FIG. 1.—A roentgenogram taken 18 days postoperative of an experimental animal whose tibia had been subjected to 160 cm. salt solution for 24 hours. (For the sake of clearer roentgenographic reproduction, the tibia above, not included in the foregoing experiments, was used rather than the femur.)

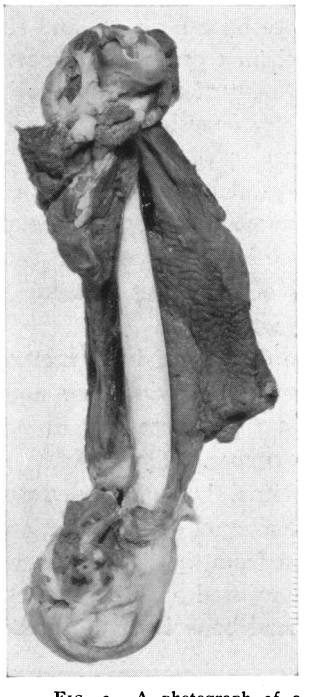


FIG. 2.—A photograph of a typical specimen of massive necrosis produced by high intramedullary pressure (240 cm.) which was removed from Dog 37A, Table IV.

in Part III suggest that the degree of open communication between marrow vessels and cannula fluid in these experiments was relatively insignificant.

In long bones the total medullary capacity in a given bone is fixed by the inexpansile cortex forming its walls except as it is modified by growth or disease. Moreover, excluding the marrow vessels the medullary cavity is occupied by relatively incompressible material. Intramedullary tension must, therefore, be normally dependent upon intravascular tension. Likewise any increase in the relative volume of extravascular tissue can occur only at the expense of the volume of blood in the vascular bed.

In our pressure experiments, therefore, it would seem that whether the circulation in bone and marrow was excluded by compression of vessels or

by substitution of salt solution by infusion is insignificant. And, while part of the exclusion of the circulatory bed in acute suppurative osteomyelitis is probably due to the accumulation of inflammatory exudate in extravascular tissues of bone and marrow, this process is probably of greater importance in zoning pressure heads within the marrow cavity than in the production of absolute ischemia as indicated by the results of Johnson's[6] experiments.

In our opinion the results of the foregoing experiments have an extremely important clinical application in the treatment of acute suppurative osteomyelitis.

Since massive sequestration of diaphyseal bone can occur only secondary to massive bone necrosis, and since massive diaphyseal bone necrosis results from ischemia produced primarily by pressure, the fundamental principle in the treatment of acute suppurative osteomyelitis is *the release of pressure in the infected bone* before the bone is killed.

Failure to clearly distinguish between massive necrosis and sequestration of diaphyseal bone, pointed out years ago by Axhausen,[2] and so important in our present concept of the pathogenesis of sequestration in suppurative osteomyelitis, is responsible for much of the current disagreement as to methods of treatment of acute suppurative osteomyelitis and infected compound fractures.

Once diaphyseal bone necrosis has occurred in the presence of infection, the surrounding living bone and periosteum detach themselves, and depending upon the degree and duration of vascular exclusion, sequestration inevitably ensues. The problem then becomes one not of dealing with acute osteomyelitis, but of sequestration and chronic osteomyelitis. Obviously, since the amount of sequestration parallels the degree and duration of vascular exclusion from the dead bone, preservation of maximum vascular connection with the injured bone and the earliest possible reapposition of vascular tissue to the dead bone is of the greatest importance in treating this phase of the disease.

In acute suppurative osteomyelitis, it is, therefore, necessary that the involved metaphysis be opened early if massive necrosis and subsequent sequestration are to be avoided.

REFERENCES

[1] Lexer: Arch. f. klin. Chir., **71**, 1, 1903; Deutsch. Ztschr. f. Chir., **133**, 170, 1915; Arch. f. klin. Chir., **119**, 520, 1922.
[2] Axhausen: Deutsch. med. Wchnschr., **40**, 1, 111, 1914; Arch. f. klin. Chir., **151**, 72, 1928.
[3] Nussbaum: Bruns. Beiträge z. klin. Chir., **130**, 495, 1923–1924.
[4] Müller: Arch. f. klin. Chir., **142**, 610–612, 1926; Beitr. z. klin. Chir., **138**, 614–624, 1926.
[5] Johnson, J.: Bone and Joint Surg., **9**, 153–184, 1927.
[6] Brunschwig: Proc. Soc. Exper. Biol. and Med., **27**, 1049, 1930.
[7] Drinker, *et al.*: Am. Jour. Physiol., **40**, 514, 1916; Am. Jour. Physiol., **62**, 1, 1922.
[8] Axhausen: Arch. f. klin. Chir., **151**, 72, 1928.
[9] Phemister: Jour. Bone and Joint Surg., **12**, 769, 1930.
[10] Bergman: Arch. f. klin. Chir., **145**, 568–579, 1927.
[11] Robl: Arch. f. klin. Chir., **145**, 515–526, 1927.
[12] Burkhardt: Beitr. z. klin. Chir., **138**, 625, 1927.