COMPLICATIONS OF INTRA-OSSEOUS THERAPY

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IN 1940, WHEN the technic for infusing blood or other fluids into the circulation *via* the bone marrow was discussed, the following points were stressed: (a) The method is indicated only when intravenous injections or infusions are needed and the peripheral veins are not available for one reason or another (poor development; delirious or uncoöperative patients; extensive burns; shock). (b) The operator should familiarize himself with the anatomic landmarks in adults (sternum) and infants (tibia and femur), and practice the technical steps on the cadaver before attempting to carry out the procedure in a patient. (c) No irritating substances should be introduced by this route. (d) In the presence of extensive infection, with or without bacteriemia, the use of this route is not advisable except for the introduction of bacteriostatic drugs (sulfonamides, penicillin).[1, 2, 3]

There has been wide application of this method and the reports thus far published have, on the whole, been favorable.[4–19] The feeling may grow, however, that infusion by this method may be undertaken by any one, without previous training and in disregard of the points enumerated above. Lest this happen, attention is hereby drawn to certain serious complications which have resulted from trials at the performance of this technic.

The outstanding example of the consequences of flagrant disregard of simple precautions is that reported by Ravitch,[20] in September, 1943: Seventy-five cubic centimeters of *seven-day-old blood,* removed from a flask *opened two days previously,* were given in the *sternum of an eight-month-old infant.* The child developed a mediastinal abscess requiring drainage, which was followed by recovery. In October, 1941, the anatomic features of the bone marrow in the sternum, femur and tibia of infants were reviewed, and attention was drawn to the fact that in infants under three years of age, the sternum should not be used for this purpose because of its small size and somewhat irregular distribution of its marrow deposits.[3] Use of either femur or tibia was recommended in such patients.

Papper[7] has recorded a death presumably resulting from the administration of 5 per cent glucose solution *via* the marrow of the corpus sterni in a 20-year-old woman, with acute thrombopenic purpura. The infusion needle was inserted into the sternum while a splenectomy was in progress and, because of the necessity of not interfering with the operative field, the needle was pointed caudad. A small amount of marrow was obtained before the

infusion was carried out. The patient died 12 hours postoperatively, and postmortem aspiration of the pleural spaces yielded about two liters of fluid containing glucose in almost 5 per cent concentration. Autopsy was not completed. Whether the insertion of the needle in the caudad direction affected the technic is uncertain.

Elsewhere[21] we have described a similar complication which, however, did not end fatally. In attempting to enter the sternal marrow, two orifices had been made. At the first trial the posterior plate of the sternum had apparently been penetrated. The needle had been withdrawn and the second insertion made, slightly below the first one, but in the same segment of bone. Some of the fluid infused through the point of the second insertion, apparently found its way into the chest through the orifice made on the posterior plate during the first trial (Fig. 6).

Two instances of supposed osteomyelitis have been called to our attention, following attempts at infusion *via* the tibial marrow. In both instances, in spite of the fact that no marrow was removed, an attempt had been made to inject blood forcibly. Each patient received between two and five cubic centimeters of blood. Roentgenograms disclosed elevation of the periosteum and some resorption of the nearby bone in each patient. It is likely that in each of these instances the blood was injected not into the marrow cavity but subperiosteally. The bone resorption changes usually demonstrated roentgenologically[4] in these and similar instances probably result from pressure necrosis rather than from true osteomyelitis. A severe osteomyelitis did follow the use of this route in an infant with *Staphylococcus aureus* abscesses throughout the body, and a probable bacteriemia (ref. 22, footnote). Blood had been injected through the tibia during the height of the acute septic process, not far from an area where there were several subcutaneous abscesses.

Behr[23] gave 60 infusions to infants, and had two complications. In one child the needle-guard pressed against the leg and caused necrosis of the skin. In another child the needle was left in place for about three days, resulting in leakage of fluid around the needle into the subcutaneous space. An osteomyelitis developed which cleared up after surgical treatment. Maintenance of a needle in the bone of infants for prolonged periods of time (over 12 hours) seems inadvisable. It is perhaps preferable to use another bone if the infusion must be repeated every other day. The devices introduced by Gimson,[11] and Behr,[23] to prevent undue motion of the infant's leg while the infusion is in progress and to guard against a too deep penetration of the needle into the bone, are useful additions to the technic.

Meola[12] describes the occurrence of black discoloration of the foot and leg of a six-week-old female child, within one-half hour after 50 cc. of plasma and 50 cc. of 10 per cent glucose solution had been given without difficulty into the right tibia. The discoloration extended one-third of the way up the leg to a point two inches distal to the site of the needle puncture, and was followed by loss of the great and middle toes on the involved foot. The cause

of the reaction was not clear; it was felt that arterial thrombosis might have occurred. Dickins and Richmond[24] have recently reported gangrene of toes associated with a "thrombophlebitis" in a premature infant, and possibly related to the hypodermic injection of a vitamin K preparation into the thigh. This incident, in which the injection was not intra-osseous, and not so intended, necessitated disarticulation of all the metatarsal bones in the involved foot.

The following complication arose after infusions into the sternum of an adult: A 25-year-old woman was hospitalized because of intestinal obstruction. She had had diabetes mellitus for 14 years, and had had her right kidney

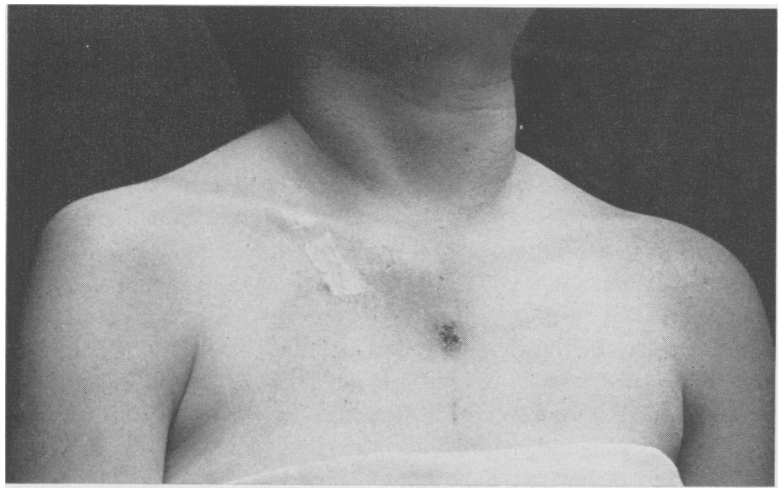


FIG. 1.—Appearance of lesion before incision and drainage.

removed in April, 1943, because of abscesses and pyelonephritis. She later became pregnant and, because of poor renal function and almost unmanageable diabetes, a therapeutic abortion and fundectomy were performed in March, 1944. In June, 1944, she suffered an attack of amebic colitis which responded promptly to therapy.

The intestinal obstruction failed to be relieved by conservative therapy and celiotomy was performed on August 4, 1944, revealing organic, sigmoidal obstruction due to old diffuse pelvic inflammation, with matting together of intestinal loops. The involved loops were freed, cecostomy was performed, and the abdomen closed. Postoperatively, it was difficult to control her fluid balance and diabetes. Feeding during the first few days had to be entirely parenteral. Her veins were extremely small and efforts were made to preserve the few which were available as sources of blood samples needed for biochemical determinations. She received infusions of blood, plasma, 0.85 per cent NaCl, and 10 per cent glucose in saline by the intravenous and intramedullary routes. On August 4 and 5, 1944, the patient received 1,500 cc. of 10 per cent dextrose, 500 cc. of whole blood and 500 cc. of 0.85 per cent NaCl *via* the

marrow of the corpus sterni. On August 12, 1944, while receiving whole blood *via* the marrow of the manubrium, the needle worked loose and before its malposition was discovered, a fairly large amount of blood had escaped into the subcutaneous tissues of the upper anterior chest wall. Her postoperative course was further complicated by wound disruption and a fecal fistula. The wound was resutured and the fistula gradually closed. Because

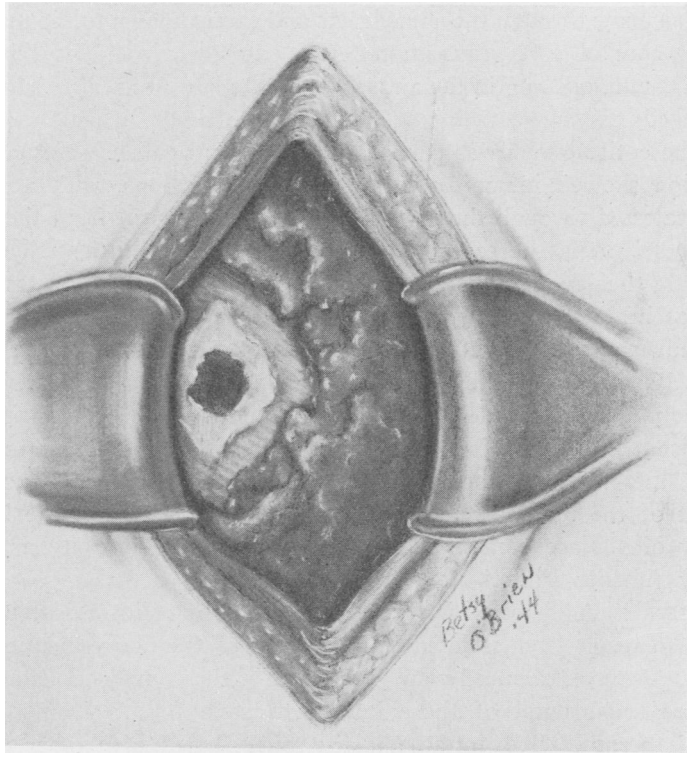


FIG. 2.—Operative exposure of the site of the infusion into the sternum.

of the deposition of blood in the subcutaneous tissues, the area over the manubrium sterni was diffusely swollen and discolored. This reaction gradually decreased, leaving a 4-cm. zone of induration, which was elevated 0.5 cm. above the surrounding skin. This area remained slightly tender, and at irregular intervals the patient complained of pain in her right shoulder top. Clinical and roentgenologic search failed to disclose any intrathoracic or subphrenic lesion.

The patient was discharged, September 30, 1944, and five days later the area over the manubrium gradually began to increase in size and in tenderness. At the same time the dull pain in her right shoulder grew worse. The swollen zone pointed and opened spontaneously, draining thick yellow pus. She was treated by her local physician and returned to the clinic for reexamination one month later. At that time the two sinuses were draining purulent

material and the surrounding zone was slightly swollen and tender (Fig. 1). Culture of the exudate yielded *Staphylococcus albus*. Roentgenologic examination of the sternum disclosed slight irregularity about the right lateral margin of the manubrium near the sternoclavicular articulation, with localized areas of decalcification and irregularity of the cortex, due probably to osteomyelitis.

On November 9, 1944, under cyclopropane-oxygen anesthesia, a vertical incision was made through the sinus tracts and carried down to the manubrium sterni. A core of soft granulation tissue extended from the skin sinuses down to a 4-mm. opening in the anterior sternal plate (Fig. 2). The opening was enlarged, exposing an area of seminecrotic tissue, which was curetted away. The entire cavity was packed with iodoform gauze. Tissue removed at operation showed inflammatory and fibrotic reactions, with a few bony spicules scattered through the sections. When discharged from the hospital, November 15, 1944, the cavity was clean and draining little. She is being cared for by her family doctor and his last communication states that the wound was healing well.

The advanced deterioration of the patient's metabolic status probably contributed somewhat to the local changes at the point of the infusion. The same reason, however, made it imperative, originally, to use the intra-osseous route, since peripheral veins were unavailable. In this group of patients one must, therefore, take special precautions to avoid mishaps such as dislodgement of the needle, long maintenance of the needle in the bone, and possibility of surface contamination. A similar complication has been recorded by Jimenez Pinto.[4]

COMMENT: A distorted impression of the risks of intra-osseous therapy is certain to result from isolated consideration of the above-mentioned complications. A more balanced view is obtained if the complications are viewed against the background of those known to have followed other types of parenteral therapy. The intramedullary route shares with other parenteral routes the fundamental risks and complications surrounding the introduction of a hollow needle into the body. In addition, it has a few risks of its own. In many respects, the present status of intramedullary injections is analogous to that of intravenous, intramuscular and subcutaneous injections during the second and third decades of the present century. The medical literature of that period contains numerous references to the complications and difficulties experienced at a time when certain parenteral routes were becoming popular, but were still under trial. No figures are available for the average incidence of complications which occurred either during or after such injection therapy and whether they resulted from action of the substance injected, faulty technic, or both. Local suppuration as well as aseptic necrosis following parenteral injection (intravenous, intramuscular or subcutaneous) was reported by various authors.[25-28] Gas gangrene following injections was discussed by Junghanns,[29] and Harney.[30] The latter author reported 86 instances of gas gangrene following various parenteral injections; the mortality

for this group was 88 per cent. Reports of venous thrombosis and thrombo phlebitis following injection therapy, leading at times to fatal pulmonary emboli and pulmonary infarctions, were not uncommon.[31–36] Systemic infection, including septicemia and metastatic osteomyelitis, was reported by Gants.[32] Various types of nerve injury followed injection therapy.[37–40] Payenneville and Castagnol[41] recorded an instance of intramuscular injection in the gluteal region producing gangrenous changes and destruction of the

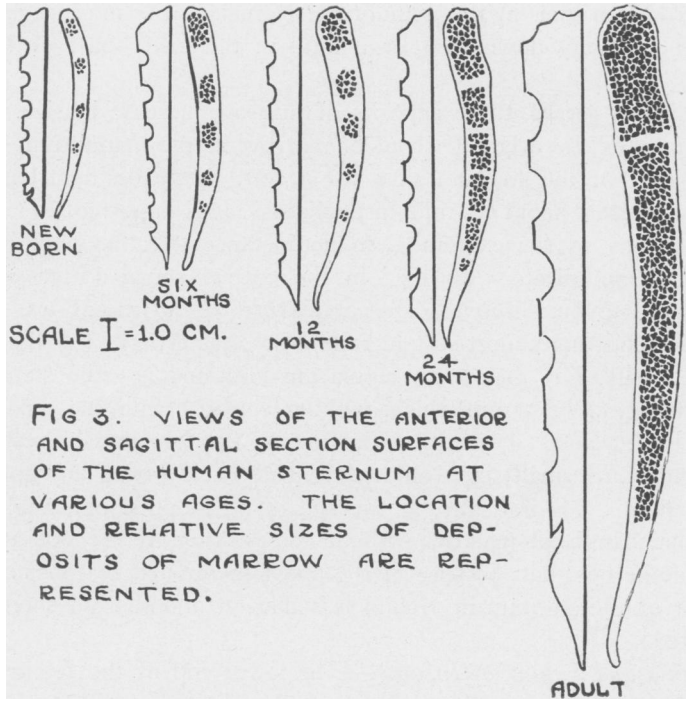


FIG. 3.—Diagrammatic representation of the relative sizes of human sternal plates, showing the development of marrow deposits.

anastomosis of the gluteal and internal pudendal arteries, with necrosis and gangrene of the rectum, bladder, genitalia and thigh. Arterial embolism has followed the intramuscular injection of iodobismotol into the buttock.[42] Complications, both local and general, have followed intra-arterial injections for roentgenographic visualization of the vessels.[43]

Therefore, when assessing the dangers of intra-osseous therapy, one must keep in mind the risks inherent in the parenteral administration of any substance, in addition to those that may be peculiar to intra-osseous therapy. Our own experience with over 400 intra-osseous infusions, and the experience of others, [1–23] have not caused us to modify our feeling that, if the method is employed only when indicated, by those who are familiar with the technic, and who observe the known contraindications, the risks involved do not appear to be any greater than those carried by other forms of parenteral therapy.

SUGGESTIONS FOR THE PREVENTION OF COMPLICATIONS

Aside from complications caused by bacterial contamination, most difficulties seem to originate from failure to consider anatomic details, and how they govern the fate of fluid injected into various bone marrow deposits.

The Sternum in Infants.—At birth, the sternum is a cartilaginous plate 5 to 7 cm. long, from 1.0 to 1.5 cm. broad, and from 1.0 to 3.0 mm. thick. There are usually three deposits of marrow in its substance, varying in diameter from 5.0 mm. in the manubrium (which is the most constant one in size and location) down to 1 or 2 mm. in the lower part of the body (Fig. 3).

As the infant grows, these deposits of marrow increase in size. By the age of 24 months the original island of marrow in the manubrium occupies all of that part of the sternum save for a soft, partly ossified, but mainly cartilaginous cortex, about 0.5 mm. in thickness. It is important to note, that, in the specimens so far examined, in no instance did the marrow in the manubrium communicate with that in the corpus sterni (Fig. 3). Any attempt to infuse fluid into the sternal marrow of an infant less than 24 months old is courting almost certain failure or disaster, for: (a) the marrow islands are small; (b) they are irregular in location; (c) the sternal plate is soft and only 2 or 3 mm. thick, making entrance into the mediastinum highly probable; and (d) even if the needle tip fortuitously rested in a marrow deposit, its small size would prevent its transporting any appreciable amount of fluid. Theoretically, at the age of 24 months, one might infuse fluid *via* the manubrial marrow without complication if the operator were unusually dexterous, but, because of the above-mentioned reasons, injections in any part of the sternum in a child less than 36 months old should never be attempted.

The Tibia and Femur of Infants.—The lower end of the femur and the upper end of the tibia are the sites of election for the infusion of fluid in infants up to four, and probably up to five years of age. The marrow deposit in the distal end of the femur is approximately 1.8 cm. broad at its widest point, and 6 to 10 mm. deep, while that in the proximal tibia is usually 6 to 8 mm. in any diameter. At birth, the distal 1.0 to 1.5 cm. of the femur and the proximal 1.0 to 1.5 cm. of the tibia are cartilaginous, and each contains a single center of ossification. These centers appear at about the time of birth, and join their respective shafts at about the twentieth year.

In infancy the patella is cartilaginous and ossifies from a single center, which appears at the third year and is completely ossified at puberty. When inserting a needle into the marrow cavity of the lower end of the femur in an infant, the operator must avoid the patella, and he must recall that the needle will traverse the upper extension of the synovial cavity beneath the quadriceps tendon anterior to the femur (Fig. 4). Careless technic may result in injury to the epiphyseal line or causing fluid to enter the knee joint.

The marrow cavity of the upper end of the tibia must be entered, not

directly anteriorly, but on the anteromedial surface of the bone, with the needle pointed away from the knee joint, in order to avoid injury to the epiphyseal line, which lies 1 to 1.5 cm. distal to the distal edge of the patella when the knee joint is extended (Fig. 4).

When inserting a needle into either tibia or femur, it is possible to drive the point through both anterior and posterior cortical plates, with resulting deposition of fluid into the popliteal space. This area is enclosed by fascia

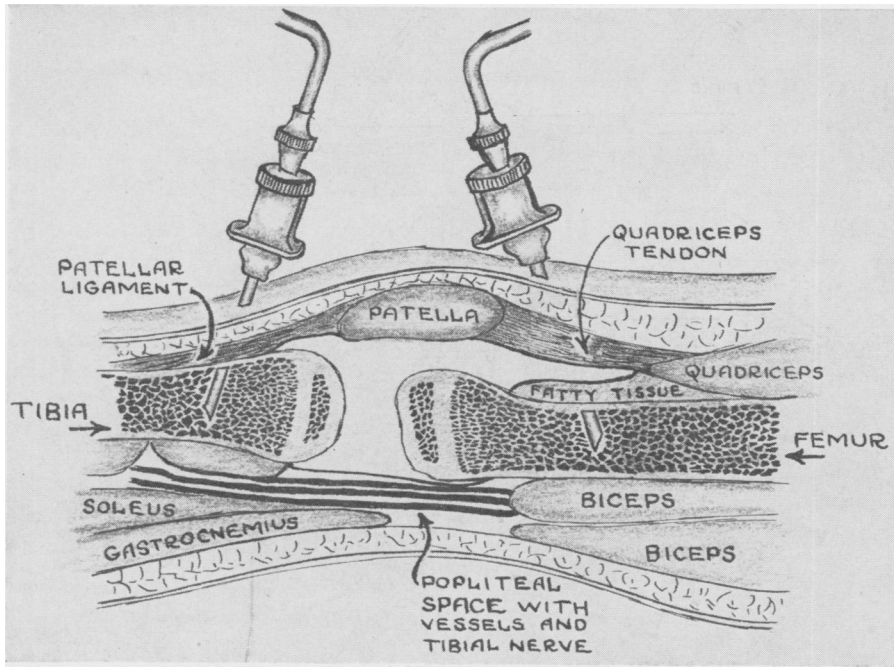


FIG. 4.—Diagram of a longitudinal section of the knee joint area in a full-term, newborn infant, showing the important anatomic relations and the correct position of needles for infusion. In the diagram the size of the joint cavity proper is purposely exaggerated.

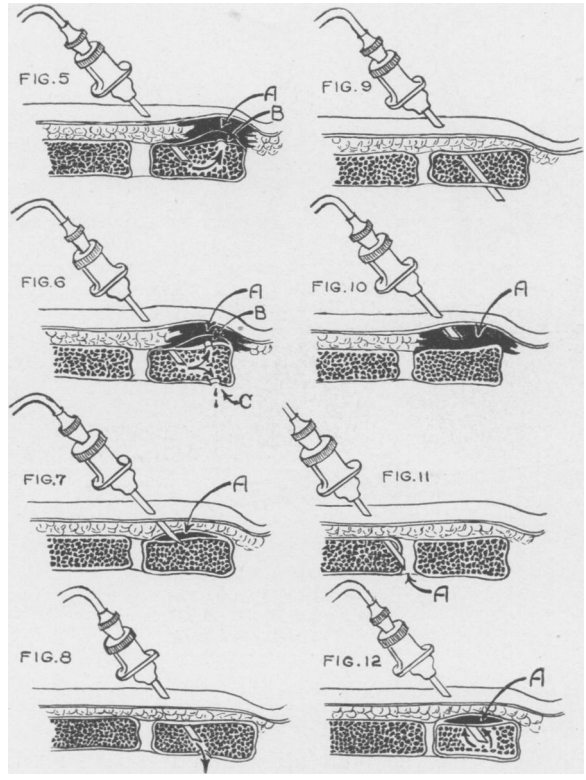
and sufficient pressure may be built up within it (particularly if the substance is injected rather than administered by gravity flow) that the popliteal vessels may be shut off and the tibial nerve damaged. The needle-guard and precautions advocated by Gimson[11] should help in preventing this mishap.

The red marrow in the tibia and femur begins to change into fatty marrow between the fifth and seventh year. Theoretically, therefore, the tibia or femur should not be used for infusion after the age of five.

The Adult Sternum.—If a needle is inserted into either the manubrium or the corpus sterni and, for any reason, the infusion attempt is unsuccessful, under no circumstances should the needle be removed and reinserted close by the first puncture site within 12 hours. This is most important when any suspicion exists that the posterior plate might have been punctured. If this precaution is overlooked and a second puncture is made soon after, near to the preceding orifice, part of the fluid infused *via* the second orifice will

leak out through the first one, resulting in a collection of fluid either beneath the skin, beneath the periosteum (Figs. 5 and 6-A, B) or in the mediastinum (Fig. 6-C).

A similar word of caution applies to infusing fluid through a needle which has been deeply inserted, and then partially withdrawn after the operator was unable to aspirate marrow. This maneuver may leave a hole in the posterior surface of the sternum, and fluid infused will leak into the



FIGS. 5 to 12, incl.—Mechanism of complications resulting from various errors in the technic of inserting a needle into the sternal marrow. Each drawing represents a sagittal section of the manubrium and upper portion of the body of the sternum of adult man.

mediastinal space (Fig. 8). If the needle tip perforates the posterior sternal plate the operator will not be able to aspirate marrow (Fig. 9).

When, for any reason, a needle is withdrawn from one compartment of the sternum, and must be reinserted soon thereafter, it should be placed in a separate portion of the sternum. Thus, if the first attempt was in the manubrium, the second should be made in the corpus, or *vice versa*. It is probably safe, when the need is imperative, to make more than one puncture in the body of the sternum within a short time (two to three hours), provided the orifices are at least six or seven centimeters apart.

If sufficient time has elapsed for previously made orifices to become occluded by firm clots, a second puncture can apparently be made nearby with safety. It is assumed that 12 hours is sufficient time for a firm clot to form unless a disorder of the blood is present. This time-interval will also vary with the amount of pressure applied to the fluid infused through the second orifice.

If a long-bevelled needle is used, it is possible for some of the infused fluid to enter the marrow cavity and some to leak out subperiosteally (Fig. 7). A similar difficulty arises if the needle works loose, and fluid leaks out around

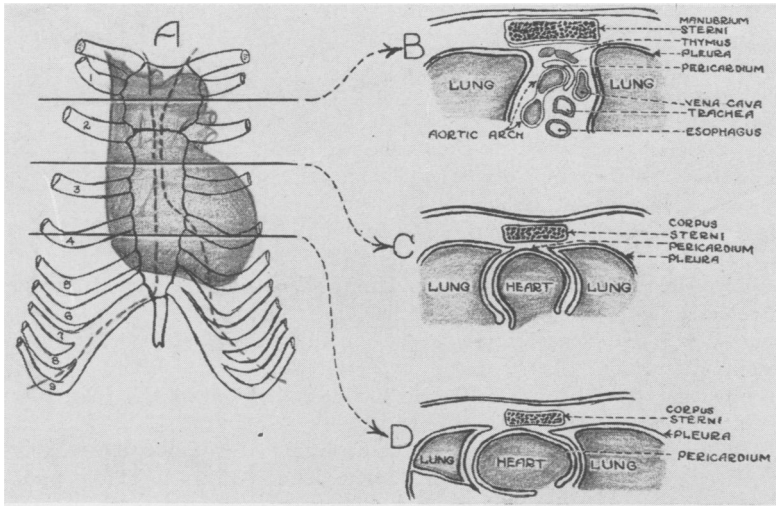


FIG. 13.—Diagrammatic representation of cross-sections of the sternum and thoracic viscera made at the three levels at which intra-osseous infusions are usually given. In "A" the solid dark shadow represents the outline of the heart and great vessels; the solid black lines represent the outlines of the sternum and adjacent parts of the clavicles and costal cartilages; the dotted lines represent the reflections of the pleura. From the cross-section diagrams, "B", "C", and "D", it may be seen how faulty technic might result in damage to the intrathoracic viscera.

it (Fig. 12). A needle may become dislodged completely from the bone, and a quantity of fluid may be deposited in the subcutaneous tissues (Fig. 10). This occurred in the patient whose case was related above. If a needle is inserted too high in the corpus sterni, or at too oblique an angle, its point may come to rest in the cartilage of the superior intersternal articulation. In such an instance, no marrow would be aspirated, and, therefore, an infusion should not be attempted (Fig. 11).

From a consideration of the cross-sectional anatomy of the sternum and thoracic viscera, as diagrammed in Figure 13, it is obvious that faulty technic may result in instillation of fluid into the pleural, pericardial or mediastinal spaces, with sequelae depending on the amount and type of fluid infused.

SUMMARY

To avoid needless complications, the intra-osseous route for the infusion of fluids should be employed only when indicated, by those acquainted with

the technic and the existing contraindications. The risks involved in intraosseous therapy do not appear to be any greater than those inherent in other forms of parenteral therapy. A complication is reported following infusion *via* the sternal marrow of a diabetic. The relevant anatomy, as well as certain actual and possible technical mishaps, are reviewed.

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