Experimental production of subdural hematomas

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Experimental evidence is offered to refute the hypothesis that cerebrospinal fluid alters blood coagulation or clots to favor the formation of chronic subdural hematomas. Rather, the envelopment of preformed blood clots in membranes containing neovascular sinusoidal channels and their subsequent regression from the subdural space are seen as a normal biological process analogous to that occurring elsewhere in the body. The presence of fibrin and its contact with the dura have been found to be essential precursors to membrane formation. Histological evidence of bleeding into both blood and fibrin subdural clots is presented, and theoretical considerations are discussed to explain possible mechanisms of enlargement and chronicity of subdural hematomas as well as repeated failures to obtain an experimental small animal model.

KEY WORDS • subdural hematoma • fibrin • neovascular sinusoids • subdural membranes

THE importance of trauma in the etiology of chronic subdural hematoma was recognized in 1914 by Trotter,\textsuperscript{16} who conjectured that episodes of clinical deterioration were due to renewed hemorrhage from the torn veins that produced the hematoma. Putnam and Cush\textsuperscript{ing\textsuperscript{11} in 1925 agreed that rebleeding correlated with clinical deterioration, but thought it came from thin-walled sinusoidal blood vessels in the outer (dural) surface of the encapsulating membrane. This explanation was generally accepted until Gardner\textsuperscript{4} in 1932 suggested that, following encapsulation of the original hematoma and breakdown of its cellular constituents, an osmotic gradient was created that led to the transport of fluid into the subdural sac from the cerebrospinal fluid (CSF). When the pressures on either side of the walls of the sac were equal, the sac stopped enlarging and the subdural fluid was slowly reabsorbed. Gardner supported this thesis by publishing serial measurements of the protein concentration of the fluid that showed a progressive decrease, and demonstrating that a cellophane bag containing subdural fluid increased 59% in volume when immersed in a container of CSF for 18 hours. However, when he repeated the experiment with human subdural membrane as the container, the results were less convincing, the increase in volume amounting to only 2.9%.

Gardner's hypothesis has been vulnerable to criticism on four grounds. First, there was
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little increase in fluid volume in his model when actual subdural membranes were used. Second, fresh red blood cells were always found in encapsulated subdural effusions when these were tapped on account of clinical deterioration, a phenomenon Gardner himself noted as being unexplained and at variance with his theory. Third, there was no attempt to demonstrate that the arachnoid, which intervenes between the CSF and the fluid inside an encapsulated subdural hematoma is permeable. Fourth, it has been shown that albumin, the protein in greatest concentration in the subdural fluid as well as the one most osmotically active, is derived from plasma and cannot result from destruction of red blood cells. Thus, albumin molecules moving from the bloodstream to the subdural space are doing so against the osmotic gradient postulated by Gardner. Weir recently has published additional evidence refuting Gardner's osmotic hypothesis when he found no osmotic gradients between the CSF, blood, and subdural fluid on direct measurement.

To date, a new hypothesis has not been substituted because of the lack of a suitable animal model. Previous models have produced subdural clots that formed membranes, but the clots always were reabsorbed without evidence of secondary expansion. However, Watanabe, et al., have recently reported that they have reproduced expansion of chronic subdural hematomas in dogs and monkeys, attributing their success to certain special properties of clots formed from mixtures of blood and CSF.

We have repeated their experiments in cats, and are presenting our findings and hypothesis.

Material and Methods

In Vitro Studies: Effect of CSF on Blood Clotting

Four 5-ml samples of fresh human venous blood were drawn; aliquots of one were mixed with fresh CSF of normal chemical and cytological composition at dilutions of 1:20, 1:10, 1:5, 1:1, 2.5:1 and 5:1. Similar dilutions were made with artificial CSF and normal saline, and one sample was left undiluted. All specimens were transferred to clean, sterile test tubes, capped, and incubated for 24 hours at 37°C. The resulting clots were inspected at 1, 2, 6, 12, and 24 hours to determine if their properties had been modified by the predilution of the unclotted blood.

Additional experiments were carried out to identify some factor in the CSF, possibly an enzyme in the protein fraction or an ionic peculiarity, that might modify the blood clot. Solutions were made by dissolving human or bovine fibrinogen (0.04 mg/ml) in human and artificial CSF, human serum, normal saline, and 5% glucose. To each sample were added 10 units of thrombin. The solutions were rapidly mixed and allowed to stand at 37°C until clotted. The same experiments were performed with pretreatment of the natural and artificial CSF with sodium oxalate to remove calcium ions and with calcium chloride added to the saline and glucose solutions. When all the mixtures were completely clotted, samples of each were treated with either saturated urea solution or monochloracetic acid. These were examined as to the differences in the coagula.

In Vivo Studies: Effect of CSF on Blood Clotting

Forty healthy adult cats of either sex weighing 2.0 to 3.5 kg were lightly anesthetized with nembutal, and 22 ml of blood were removed from the most prominent vein of one or, if necessary, both forelimbs, and 1.5 ml of CSF through a cisternal puncture. The animals were then left to regain consciousness.

The freshly withdrawn blood was divided into four 4 ml portions in clean sterile test tubes and diluted with 1.0 ml of CSF, artificial CSF, saline, or left undiluted; these were thoroughly mixed and incubated at 37°C for 24 hours. The additional 2 ml of blood was either left undiluted or mixed with 0.5 ml of CSF, artificial CSF, or saline and similarly treated.

Subdural Implants. On the following day the animals were reanesthetized and a standard operative procedure followed: through a midline incision the soft tissues were removed from one half of the cranial vault as far as possible into the temporal fossa and a 2 cm trephine disc removed. The

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dura was opened by a horizontal incision, and a small rubber balloon attached to a fine catheter was introduced into the subdural space. The balloon was then inflated slowly with 2 ml of water for 20 to 30 minutes to avoid too sudden compression of the cranial contents; it was left in place for 1 hour, then emptied and withdrawn. (In a few experiments the brain was sufficiently slack for balloon withdrawal after 30 minutes). The preformed clot was gently manipulated from its test tube into the subdural space and the dura sutured over it with 6/0 nylon in an atraumatic needle. The trephine disc was replaced and fixed in position with dental cement, after which the scalp was sutured in two layers. (In three early experiments an attempt at bilateral implantation was attempted but the animals died during surgery from brain compression).

One animal was sacrificed on the 8th, 10th, 13th, and 21st day respectively from each group of subdural implantations (i.e., implants of clotted blood alone, or CSF, artificial CSF, or saline mixed with blood). Two animals with CSF/blood subdural implantations were permitted to survive until the 29th and 30th days and one saline/blood preparation until the 27th day. Following sacrifice, the calvarium was exposed, the trephine disc removed, and the vault of the skull rongeured away, preserving the dura down to the olfactory grooves anteriorly and to the tentorium. The dura was then stripped inward to the margin of the tentorium where it was incised and the brain stem transected. After examination for evidence of residual hematoma or membrane formation, the specimen was fixed in buffered formalin solution. Following fixation, blocks of dura and brain were cut so as to include the entire implanted areas, and these in turn were sectioned, stained with hematoxylin and eosin, and examined.

Subcutaneous Implants. Immediately after craniotomy, the anesthetized animal was turned to the supine position, and four pockets dissected in the subcutaneous tissues on either side of the abdomen. The four preformed clots were inserted into these pockets, the skin sutured, and a prophylactic injection of long-acting penicillin given. Thereafter the animal received normal care until sacrificed. Following sacrifice, the abdominal skin and subcutaneous tissues were removed in one piece so that the hematomas that were encapsulated were undisturbed. Following fixation in formalin, blocks of abdominal skin were cut to include the entire implanted area, and these were sectioned, stained with hematoxylin and eosin, and examined.

Two dogs were similarly treated, save that the volume of blood used for the subdural implant was 5 ml; it was mixed with 1 ml of CSF in one dog and left undiluted in the other. The subcutaneous implants were made as in the cat. Both dogs were sacrificed on the 13th day.

In Vivo Studies: Factors Inducing Membrane Formation in Experimental Hematomas

To attempt to identify factors essential for membrane formation, experiments were conducted with human or bovine fibrinogen, prepared as described in the in vitro study. These coagula were introduced into the subdural space in 10 cats as described in the in vivo study above.

In two additional cats gelatin sponge approximately the same size as the fibrin clots were implanted subdurally; one of these was first impregnated with defibrinated blood. In another four cats whole blood clot was implanted as before but insulated from contact with the dura by a thin sheet of polyethylene. Finally, in two animals a circular incision was made in the dura over an area larger than the surface of the clot so as to interrupt the blood supply. It was then sutured back in place. These preparations were all examined after 10 days except one on the 11th day.

Results

In Vitro Study

We were unable to confirm that any special characteristics could be seen on inspecting the coagula formed in blood/CSF mixtures as compared with those resulting from the clotting of blood alone, blood mixed with CSF, or blood mixed with normal saline. Only the shape of the fully retracted clot varied a little from time to time.
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As to the differences between the coagula formed by the addition of thrombin to human or bovine fibrinogen solutions, we found, as did Watanabe, et al., that those formed in CSF were translucent and those formed in saline or glucose were opaque. But the clots formed in serum and in artificial CSF proved to be translucent also. Furthermore, the effect could be completely reversed by the oxalation of normal and artificial CSF respectively and the addition of ionic calcium to the saline and glucose solutions (Fig. 1).

On saturating the solutions with urea or adding monochloracetic acid, all the opaque clots (those formed in the absence of calcium ions) dissolved, whereas the translucent clots were unchanged.

In Vivo Studies

Subdural Implants. All the subdural implants, regardless of whether CSF or control substances had been added to the hematomas, showed a uniform pattern of evolution. By the 8th day a neomembrane had formed and enclosed both the outer and inner aspects of the hematoma. Erythrocytes could still be seen within the hematoma, which remained solid in most cases. Specimens on the 10th day showed considerably more proliferation of fibroblasts around the clot, which had begun to liquefy, and growth of new blood vessels into the parietal (outer) layer of the membrane (Fig. 2). By the 13th day the membranes seemed to have attained their maximum thickness, and again the outer layer showed many newly formed vascular sinusoidal channels, essentially similar but smaller than those seen in the human subject. By contrast, the inner membranes were much thinner and less vascular. Remarkably, fresh red blood cells could be seen in various stages of passage from the engorged vascular channels into the hematoma (Fig. 3 left). A progression from obviously fresh red blood cells to fragmented disintegrating cells, to amorphous material, could be seen evolving from the outer membranes inward to the center of the hematoma. By the 21st day the hematoma had largely disappeared, its site being marked by an area of modest thickening on the inner surface of the dura (Fig. 3 right). Specimens from animals sacrificed on or after the 27th day showed either a little fibrosis on the inner layer of the dura or a complete return to normal.

Both dogs were sacrificed on the 13th day after implantation, this being approximately the time of maximum reaction in the cat. In these animals the subdural hematomas also were surrounded by well-developed membranes with some evidence of recent hemorrhage from the parietal layer.

The subdural implants of fibrin all became encapsulated, the formation of membranes occurring at about the same speed as with clotted blood. Remarkably, in several instances hemorrhage occurred from the sinusoidal vascular channels in the outer membrane into the fragmenting coagulum just as had occurred with the blood clots (Fig. 4). After 10 days neither the simple gelatin sponge preparation nor the gelatin...
FIG. 2. Photomicrographs of the outer subdural membrane. Note the connective tissue proliferation under the dura with multiple neovascular sinusoidal channels overlying fresh red blood cells at the periphery of the hematoma. D = dura, S = neovascular sinusoidal layer, H = hematoma, R = red blood cells. H & E, X 40.

A sponge soaked in defibrinated blood showed membrane formation, and the material had begun to disappear from the subdural space. The factor common to all the successful instances of membrane formation was the presence of fibrin. This agrees at least partially with Watanabe, et al., for they noticed that clotted CSF/blood mixture pretreated with plasmin provoked no neomembrane formation.

None of the four animals in which a subdural implant was insulated from the dura with plastic showed any sign of neomembrane formation, nor of absorption of the clot except one in which, by a technical error, a small area at the edge of the hematoma was left covered with dura. Membrane formation was limited to this area. Both the devascularized dura preparations developed membranes, but in slightly

FIG. 3. Left: Photomicrograph showing fresh red blood cells entering hematoma from the vascular layer of outer membrane. H & E, X 40. Right: Photomicrograph showing older resolving hematoma composed now of fibrotic areas with only scattered vascular islands and some amorphous debris. B = brain, S = neovascular sinusoidal layer, R = red blood cells. H & E, X 52.
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Fig. 4. Photomicrographs of the fibrin clots. Upper Left: Neovascular sinusoidal layer (S) around the disintegrating clot showing some extravasation of red blood cells (R) into the fibrin (F). H & E, × 40. Upper Right: Higher power view showing extensive bleeding from the neovascular sinusoids into the fibrin coagulum. H & E, × 64. Lower Right: Islands of red blood cells are seen which have extravasated into the degenerating fibrin clot. H & E, × 52.

delayed timing. Membrane formation occurred best at the edges of the lesion and where the clot had contact with un uninterrupt ed dura.

In none of our animals did any late neurological phenomena develop comparable with those of chronic subdural hematoma in the human subject. In two animals an epidural abscess developed, resulting in their being discarded from the study.

Subcutaneous Implants. A similar pattern of evolution was seen with the subcutaneous implants. Hematomas formed from blood alone did not differ from those to which CSF and saline had been added. At 8 days the blood clot remained mostly solid, surrounded by a thin membrane. Two days later, liquefaction had advanced and the membrane showed increasing fibroblastic proliferation with invasion by vascular sinusoidal channels, a process again appearing maximal by the 13th day. By the 21st day little trace remained of the subcutaneous hematomas, save for a slight fibrotic reaction and a little hemosiderin staining in and around the implantation site. The same was true of the later specimens.

In both dogs 13 days after implantation, the abdominal hematomas were surrounded by well-developed membranes with some evidence of recent hemorrhage. We thought that in a few of our animals there was a modest swelling (1 ± 2 times its original size) of a few of the subcutaneous hematomas during the second week after implantation, but this was not related to any particular type of implant nor did it ever approach the size claimed in the dog by Watanabe, et al.

Discussion

Watanabe, et al.,17,18 reported their studies of clots formed in both blood alone and in blood/CSF solutions as well as with fibrinogen clots. They noted that clot retraction proceeded differently in the CSF-containing clots and demonstrated that this was due to an ultrastructural modification of the fibrin. Thus, translucent clots formed in the fibrinogen-treated CSF samples whereas opaque clots formed in the control solutions (5% glucose and normal saline). They felt this modification of the fibrin molecule was
due to pretreatment of fibrinogen with CSF before the addition of thrombin.

They also found that blood clots implanted within the subdural space of dogs and monkeys became encapsulated only when they had been premixed with CSF in a blood/CSF proportion of 20:1 to 1:5. Specifically, they stated that these hematomas formed from blood/CSF mixtures became encapsulated in a membrane containing neovascular channels, that they progressively enlarged, and occasionally caused neurological deficit after a few days. Thus, after 7 to 14 days, they were said to show the characteristics of chronic subdural hematoma. In the absence of CSF, however, the clots rapidly disappeared, with little or no trace remaining.

They also implanted similar clots within the abdominal subcutaneous tissues of their animals. Those containing CSF were said to swell up to 30 times their original volume within 10 to 15 days and become lined with a membrane similar to that of a chronic subdural hematoma. They claimed that this effect could, however, be abolished by pretreatment of the clots with plasmin, thus destroying the fibrin membrane surrounding them. The whole-blood clots they reported were reabsorbed completely in 5 days, leaving only a small area of induration.

We attempted to reproduce the results of Watanabe, et al., in 40 cats and two dogs, but in both our in vitro and in vivo studies we felt it desirable to control the experiments more extensively, using not only whole blood but also mixtures of artificial CSF and saline with blood. In other respects we adhered as closely as possible to their techniques. Similar considerations determined our choice of diluent under "Materials and Methods." We have not been able to confirm Watanabe, et al.'s statement that special features can be detected on inspecting the coagulum formed in blood/CSF mixtures as compared with that from blood alone or blood mixed with artificial CSF or saline. It is known that the phenomena of clot retraction are affected by many variables, among them the age of the blood, the exact way in which it is handled, temperature, pH, and so on. Several of our preparations were made in the presence of two experienced hematologists, who confirmed our findings.

We have confirmed Watanabe, et al.'s observations on the properties of coagula formed by the addition of thrombin to solutions of fibrinogen in CSF and in saline or 5% glucose respectively. However, the difference is attributable to the presence of fibrin in the double-bonded form in the first experiment, and in the single-bonded form in the other two. This is shown by their behavior in the presence of saturated urea solutions or monochloracetic acid, and by the fact that the effect is reversed by removing calcium from the CSF solution and adding calcium to the others. Since, in normal human or mammalian tissues, calcium ions are available, the fibrin of any clot formed either in the subdural space or elsewhere will be present in the double-bonded form, and the differences noted are irrelevant.

Failure to confirm Watanabe, et al.'s conclusion that the presence of CSF modifies the clot so formed would not, in itself, disprove their thesis that CSF is essential for the production of chronic subdural hematoma, but it does negate their contention that mixtures of CSF and blood clotting within the subdural space must have some special characteristics.

Our findings yield no support, however, for their contention that CSF is necessary for the formation of membranes around a subdural hematoma, or that it causes blood clots in the subdural space or the subcutaneous tissues to be absorbed less rapidly and to increase in size more readily. We
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have been unable to reproduce and cannot explain the growth to several times their original size of the subcutaneous implants of blood and CSF mixtures that Watanabe, et al., reported. In our cats we saw only a modest increase in the size of a few of the subcutaneous implants, and this did not correlate with their composition. This is in keeping with the results of Wilkins, et al., who found that CSF did not influence the blood coagulation system or chick fibroblast growth, nor have fibrinolytic activity.

In our animal models, at least, and presumably in man, also, encapsulation of a subdural hematoma results from an interaction between the fibrin of the hematoma and the inner surface of the dura mater. Putnam and Cushing in 1925 theorized that “...the presence of fibrin, alone or in blood or in an inflammatory exudate, causes proliferation of granulation tissue” (from the internal surface of the dura). Putnam and Putnam implanted fibrin subdurally in 1927 and noted the typical reaction with membrane formation that we have described. The presence of fresh red blood cells issuing from the neovascular sinusoidal channels in our fibrin clots is, we feel, a significant finding. This explains why fresh-looking red blood cells are found clinically in subdural hematomas and the probable mechanism of expansion.

The dura is essential to the encapsulation process. When we effectively isolated the subdural clot from the dura by a thin plastic sheet, no neomembrane formed, and when the dura was devascularized, formation was delayed. As has been the almost universal experience, we found no adherence to the arachnoid and no neovascular channels in the arachnoidal surface of the clot membrane in any of our preparations. Histologically it has been recognized that, while the dura contains an extensive thin-walled capillary network on its inner surface, the arachnoid is without any capillary bed. Leary has pointed out the impervious nature of the arachnoid, it being the only serous membrane in the body that can hold back an infection or invasion by meningiomas, so it is not surprising that it similarly is uninvolved with subdural hematomas.

The isolation and removal of a collection of clotted blood by encapsulation is not a phenomenon unique to the dura. It is the body's normal method of disposal of a hematoma and is described in standard pathology textbooks. The tendency of a chronic subdural hematoma to expand or refill after tapping is also not unique, although when this occurs within the rigid confines of the skull it can be especially dangerous. It is not uncommon to see a large hematoma in the soft tissue of the thigh or back which increases in size and which may refill after aspiration. On the rare occasions where these need to be excised one finds the central cavity surrounded by a smooth membrane stained with hemosiderin which is similar to the outer layer of the membrane surrounding a chronic subdural hematoma.

Hypothetical Considerations

Previous investigators have attempted to reproduce in small animals the spontaneous enlargement of a chronic subdural hematoma, without success. The belief that any subdural hematoma should be subject to expansion, regardless of the species of mammal in which it occurs, was implicit in Gardner's osmotic hypothesis as well as in Zollinger and Gross' parallel suggestion that extra fluid is osmotically drawn from the circulating blood plasma and in Munro and Merritt's concept that dissolution of the subdural blood induces transport of fluid across the arachnoid, acting as a dialysing membrane. As we have already pointed out, Gardner's experimental proof of his hypothesis was open to criticism. Our experiments have shown that contact between the coagulum and the dura is necessary for the production of a true subdural hematoma, a fact recognized by Putnam and Cushing. Rabe, et al., found that the osmolarity of subdural fluid removed from an infant whose acute clinical symptoms indicated expansion of a subdural hematoma was equal to that of plasma, and Weir confirmed this in 23 cases. We also have measured the osmolarity of subdural fluid in two clinical cases and found it to be the same as that for plasma. We feel that Gardner's hypothesis is inadequate to explain the facts and should be abandoned.
Two alternatives have been proposed: 1) Trotter's\textsuperscript{16} view as modified by Putnam and Cushing\textsuperscript{11} and shared by Watanabe, \textit{et al.}\textsuperscript{17,18} that repeated hemorrhages occur from the subdural membrane itself; and 2) Gitlin's\textsuperscript{5} suggestion that fluid high in albumin and low in globulin content effuses from damaged capillary walls in the subdural membrane, a view shared by Rabe, \textit{et al.}\textsuperscript{13}

Both explanations require that a membrane must be formed before expansion occurs (except insofar as the original source of the bleeding remains active), and imply that the rate of change of the volume of the subdural hematoma as a result of either "absorptive" or "expansive" forces is related to the surface area of the surrounding membrane. We have given some consideration to this possibility. Subdural hematomas are, in fact, irregularly-shaped lesions conforming to the geometry of the skull and to a lesser extent to that of the underlying brain. They resemble to a considerable degree oblate spheroids whose volume and surface area can be calculated.*

For a first approximation, however, it is not unreasonable to consider the lesions as spherical,\textsuperscript{†} recognizing that a sphere is the most efficient volume-containing geometric form with minimal surface area per unit volume. Therefore we will be underestimating the surface area of the actual lesion.

The rate of absorption of a subdural hematoma should be directly related to its surface area or at least that part of which is in contact with the dura. If surface area is compared to volume, it is quickly evident that since the volume of a sphere varies by the cube of the radius and the surface area by the square, the volume will increase exponentially faster than the surface area for any given increment in overall size. Conversely therefore, the smaller lesion has proportionately greater surface area per unit volume and hence a greater propensity for absorption.

It is conceivable that clinical hematomas must achieve a critical size if they are to become chronic lesions. Due to the above mentioned surface area/volume relationship, lesions smaller than this critical size would be within the biological capability for absorption and hence be removed. Such a concept would explain the failure of animal models as well as the clinical observation that small postoperative clots rarely if ever progress to become chronic subdural hematomas.

Factors other than surface area must come into play influencing the growth of these lesions. We have already dealt with the evidence for rebleeding as at least a partial explanation. The sinusoidal neovascular channels within the outer layer of membranes can be seen discharging fresh red blood cells into our experimental hematomas. For this to occur, the pressure within the subdural hematoma must drop below the venous or capillary pressure. Several factors would favor such a state: for example, a disproportion between brain and skull, such as exists with cerebral atrophy in the elderly or in infants before maturation of the cortex, coupled with a soft calvarium prior to union of the sutures. These obviously are clinical situations in which one sees chronic subdural hematomas.

It is noteworthy that in adults subdural hematomas are often found in low-pressure conditions. Papilledema is uncommon, the lumbar puncture pressure is usually normal or low, and when the subdural space is opened and drained the brain often shows little or no tendency to re-expand to fill it. Because the cavity remains, many surgeons have felt it necessary to inject fluid into the lumbar theca either during or after the operation, whereas this is rarely thought necessary after removal of other intracranial space-occupying lesions. Similarly, subdural hematomas have been described after the lowering of intracranial pressure by ventriculoatrial and other shunting procedures, and they were particularly common before the use of pressure-regulated valves. These features all support the idea that low pressure is of importance and that active rebleeding explains the postulated delayed

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*Volume is \( \frac{4}{3} \pi a^2b \), and surface area is 
\[ 2\pi a^2 + \pi b^2 \log \frac{1 + e}{1 - e}, \]
where \( a \) and \( b \) are the major and minor semi-axes and \( e \) the eccentricity.

†For a sphere, the volume is \( \frac{4}{3} \pi r^3 \), and surface area is \( 4 \pi r^2 \).
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expansion of subdural hematomas. Goodell and Mealey's failure to reproduce these phenomena to a degree analogous to the human clinical situation, despite the use of urea to diminish cerebral volume and pressure in some of their animals, is explained by the prior considerations of size and speed of reabsorption which we have already indicated above.

The variations in man's intracranial pressure are presumably much greater than in the experimental animal. This is due to several reasons. Man's upright posture partially is responsible. In addition, there is a time phase lag between pressures recorded cisternally and in the lumbar canal associated with coughing and crying. Initially, this results in a higher pressure below the foramen magnum which should displace the CSF upward into the cranial cavity. This pressure gradient, however, will be quickly compensated by a decrease in volume of the venous vascular system. As the intraspinal pressure falls, the direction of the gradient is reversed. The CSF will then be displaced downward, allowing the intracranial pressure to briefly drop below normal before stabilizing as the intracranial vascular system refills. The human intracranial blood volume has been estimated at about 10% whereas in the dog it is about 3%, so that large volume shifts and hence greater pressure changes should occur in the human, resulting in more time when the intracranial pressure is low enough to allow bleeding from the sinusoidal channels, than in smaller animals.

Thus, the tendency toward increased bleeding time combined with less effective absorption, superimposed upon low intracranial pressure clinical states, may explain the clinical features of chronic subdural hematoma formation in man and the failure to achieve these in experimental animals.

Conclusions

In the cat model one can reproduce the main histological features of the evolution of a subdural hematoma, although these are not accompanied, as in man, by clinical correlates. This evolution is a normal process involving the removal of a collection of blood from any space or tissue. The stimulus to membrane formation is contact between the fibrin of the blood and the inner surface of the dura. Gelatin sponge soaked in defibrinated blood does not precipitate it, nor does the reaction occur when hematoma and dura are separated by a layer of inert material. On the other hand, a bolus of fibrin placed in the subdural space provokes encapsulation and even hemorrhage into the liquefying material.

Summary

Experimental evidence has been presented to refute the contention that special properties in CSF enhance formation of subdural hematomas. Rather, it has been shown that the body reacts in a well-defined manner to handle blood clots intracranially as it does anywhere else in the body. Specifically, a fibroblastic reaction, stimulated by fibrin within the blood, arises from the inner layer of the dura and envelopes the hematoma as neovascular sinusoidal channels develop in this membrane. That some of these lesions in humans clinically enlarge and become chronic is well known. We have reviewed the evidence favoring recurrent hemorrhage as one mechanism for this enlargement and demonstrated fresh red blood cells entering experimental lesions from the neovascular channels. It would thus appear that on rare occasions the normal body reaction to an intracranial clot fails due to abnormal circumstances and rather contributes to its enlargement and chronicity.

Factors influencing absorption and accumulation have been suggested. Analysis of these factors also suggests an explanation for the failure of repeated attempts to produce an animal model.

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