Experimental missile wound to the brain

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Among civilians in the United States, 33,000 gunshot wound deaths occur each year; probably half of these involve the head. In combat, head wounds account for approximately half of the immediate mortality when death can be attributed to a single wound. No significant reduction in the neurological mortality associated with these wounds has occurred between World War II and the Vietnam conflict, and very little research into missile wounds of the brain has been undertaken. An experimental model has been developed in the anesthetized cat whereby a ballistic injury to the brain may be painlessly reproduced in order that the pathophysiological effects of brain wounding may be studied and better treatments may be designed to lower the mortality and morbidity rates associated with gunshot wounds.

Prominent among physiological effects observed in this model was respiratory arrest even though the missile did not injure the brain stem directly. The incidence of prolonged respiratory arrest increased with increasing missile energy, but arrest was often reversible provided respiratory support was given. It is possible that humans who receive a brain wound die from missile-induced apnea instead of brain damage per se. The mortality rate in humans with brain wounding might be reduced by prompt respiratory support. Brain wounding was associated with persistently increased intracranial pressure and reduced cerebral perfusion pressure not entirely attributable to intracranial bleeding. The magnitude of these derangements appeared to be missile energy-dependent and approached dangerous levels in higher-energy wounds.

All wounded cats exhibited postwounding increases in blood glucose concentrations consistent with a generalized stress reaction. A transient rise in hematocrit also occurred immediately after wounding. Both of these phenomena could prove deleterious to optimal brain function after injury.

KEY WORDS: penetrating head injury • brain injury • missile wound • apnea • intracranial pressure • emergency care

In combat, the head receives about 20% of all "hits" and head wounds account for approximately half of all single missile deaths. The most comprehensive data on the surgical treatment of missile wounds to the brain come from neurosurgical series reported from various wars of the 20th century. Review of these neurosurgical statistics reveals no significant reduction in the neurosurgical mortality rate from wounds inflicted in World War II through the Vietnam experience: during World War II, the neurosurgical mortality rate for United States Army soldiers in Europe was 14% while in the Korea and Vietnam conflicts it was 10% to 12%. Among civilians in the United States, approximately 33,000 deaths each year are caused by bullet wounds. Assuming that no difference exists between civilian and military wounds in their potential lethality to specific body regions, one may infer that missile wounds to the brain account for approximately 16,500 civilian deaths from gunshot wounds each year in the United States. Despite the serious problem of brain wounds for military personnel and for civilians, very little experimental research into brain wounding has been undertaken.

We have developed an experimental model to realistically simulate a missile wound to the brain which would not necessarily result in death. It is hoped that a better knowledge of the pathophysiology of brain wounding may lead to correction of specific derangements contributing to mortality and morbidity. The present communication gives technical details of the laboratory gun, delineates the "standard brain wound," provides an analysis of acute breathing abnormalities seen with brain wounding in this model, and presents some central and peripheral pathophysiological effects caused by a nonfatal missile wound to the brain.
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Materials and Methods

Laboratory Gun

The laboratory gun* consists of a precision-made steel tube seated inside a 69-cm hollow steel bar. The inside diameter of the steel tube just accommodates the test missile, a 2.0-mm 31.7-mg steel sphere. The breech-loaded barrel is coupled to a solenoid valve which controls the release of pressurized helium propellant. Missile velocity is a function of helium pressure. The triggering mechanism provides a direct current power source supplying a solenoid valve. The time required for the missile to pass between two electronic break switches set exactly 50 cm apart is determined by an electronic time base. Missile energy (E, in joules) is calculated by: E = 1/2 mv², where m represents mass (in kg) and v represents velocity (in m/sec).

Surgical Procedures

Unselected, unfasted mongrel cats, each weighing 3 to 5 kg, were used in this study. After induction of pentobarbital anesthesia (40 mg/kg intraperitoneally), unilateral or bilateral groin incisions were made for femoral artery or vein cannulations. One femoral arterial line was connected to a transducer physiograph for blood pressure recording while the other femoral artery catheter was used for blood sampling as needed.† All groin incisions were closed. An endotracheal tube was then placed and end-expiratory CO₂ was continuously recorded.‡ Each cat was placed prone in a stereotactic frame 80 cm from the muzzle of the helium gun.§ In order to prevent the missile from ricocheting off the sloped anterior wall of the cat’s frontal sinus, the anterior wall of the right frontal sinus was removed. The posterior sinus wall, which remained intact, was vertical to the missile trajectory and was readily penetrated by the wounding sphere.

Experimental Procedures

In conducting the research described in this report, the investigators adhered to the “Guide for the Care and Use of Laboratory Animals,” prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council. At the start of each experiment baseline recordings were made of physiological variables including mean arterial blood pressure (MABP), end-tidal CO₂, and respiratory frequency. Arterial blood gas analyses and intracranial pressure (ICP) measurements were made in selected experiments. After check-

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1. Laboratory gun designed and constructed by Mr. Robert Carpenter, formerly with the Edgewood Arsenal, Aberdeen, Maryland.
3. End-tidal CO₂ monitor, Model IL-200, manufactured by Instrumentation Laboratory, Lexington, Massachusetts.
4. Stereotactic frame manufactured by David Kopf Instruments, Tujunga, California.

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Results presented in this report were derived from two series of cats. In the first series the effects of missile wounding upon breathing were obtained from a retrospective analysis of 83 cats studied primarily for the evaluation of postwounding brain edema and/or behavior. These cats were wounded through a completely intact skull. If a cat became apneic following wounding and if spontaneous breathing did not resume within 1 minute, the animal was ventilated until spontaneous breathing resumed, or for a maximum of 2 hours. Return of respirations in apneic cats was evident from the end-tidal CO₂ trace. The ability to breathe spontaneously was also tested by the periodic brief removal of the ventilator. In cats allowed to recover from anesthesia and wounding, local antibiotic ointment and topical anesthetic were applied to all sutured skin incisions. They were given penicillin G (50,000 U intramuscularly), carefully nursed, and observed in the animal care facility until they had fully recovered. If necessary, hydration was supplied by normal saline solution given intraperitoneally for the first few days after wounding. During the recovery period no cat appeared in any pain. At the appropriate times the cats were sacrificed with intravenous pentobarbital and exsanguinated, and their brains were removed.

In the second series of 20 cats the effect of missile wounding upon several physiological variables, including ICP, was determined after an epidural pressure balloon had been inserted through a left parietal craniectomy prior to wounding.¶ The craniectomy was then sealed with methyl methacrylate. Four groups of five cats each (both sexes) were used in this series of experiments. Group 1 consisted of unwounded cats (control group), while cats in Groups 2 through 4 were wounded by a missile having a mean energy of 0.90, 1.40, or 2.50 J. In all groups MABP, ICP, cerebral perfusion pressure (CPP; CPP = MABP − ICP), heart rate, respiratory frequency, and end-tidal CO₂ were monitored continuously for 6½ hours. Arterial blood was sampled (1.5 ml each) before injury, at 1, 3, 5, 10, 20, 30, and 60 minutes, and at 2, 3, 4, 5, and 6 hours after wounding. Blood samples were analyzed for pCO₂, pO₂, pH, blood glucose concentration, and hematocrit.* All of the cats were painlessly sacrificed by intravenous pentobarbital at the end of the experimental period.

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* Blood gas and pH analyzer manufactured by Instrumentation Laboratory, Lexington, Massachusetts; Dextrometer; Model 5570, manufactured by Ames Division, Miles Laboratory, Inc., Elkhart, Indiana.

† Epidural pressure balloon, Model ICT/b, manufactured by MMI-Gaeltic, Hackensack, New Jersey.

¶ Epidural pressure balloon, Model ICT/b, manufactured by MMI-Gaeltic, Hackensack, New Jersey.
In this group only the data obtained during the first hour postwounding were analyzed because these data best demonstrated the effect of brain wounding alone in the pentobarbital-anesthetized cat. After this time, anesthesia lessened. All results are given as the mean ± standard deviation. The data were initially analyzed by analysis of variance for repeated measures. Individual comparisons were made using Student-Newman-Keuls' test. Results were considered significant at p < 0.05.

Results

Ballistic Considerations and the Brain Wound

Missile Velocity and Energy. For any given shot the velocity error was less than 2.5% and the energy error less than 4.5% compared with that intended. A missile velocity of 178 to 210 m/sec (0.50 to 0.70 J) was required to penetrate the posterior wall of the right frontal sinus which is about 1 mm thick. Consistent bone penetration was achieved with a sphere velocity of 238 m/sec (0.90 J) and this determined the lower ballistic limit of the model. When missile velocity was increased to 389 m/sec (2.50 J) and the sphere was fired through the completely intact skull into the right cerebral hemisphere, the wound was fatal in two-thirds of instances owing to immediate respiratory arrest. This velocity and energy represented the upper ballistic limit permissible in our model. A missile velocity of 297 m/sec (1.4 J) produced a fatality from apnea in about 40% of all cats. Because our interest was in the pathophysiology of nonfatal brain wounds, most experiments were carried out with missile velocities from 238 to 297 m/sec (0.90 to 1.40 J).

Assuming a skull 1 mm thick (approximately the thickness of the posterior frontal sinus wall through which the test missile enters), a skull strength of 100 megapascals, and a breaking strain of 1%, our test missile loses only about 20 m/sec (0.09 J) velocity with skull penetration. (M Iremonger, personal communication, 1987). This small loss of velocity and energy from frontal bone penetration will not be considered further in discussing wound velocities and energies in this experimental model.

Missile Trajectory and Wound Characteristics. The animals' occiputs were rotated 20° to the left in the stereotactic frame. The missile invariably entered the brain at the right frontal tip through the cruciate sensorimotor cortex which was hemorrhagic and contused from 2 to 4 mm around the missile entry site. Tiny flakes of frontal bone were sometimes seen near the entrance of the brain wound track. In most instances after skull penetration the missile continued into the right lateral parieto-occipital region away from the lateral ventricle and brain stem. This trajectory minimized as far as possible the physiological brain-stem effects that would have been accentuated by missile impact directly over the medulla (Fig. 1).

Most missiles traversed the superior half of the right cerebral hemisphere above and lateral to the lateral ventricle (Fig. 2). The missile usually struck the inside of the skull posteriorly. It might then ricochet to the tentorium and bounce back into the brain for several millimeters. Hence, the right occipital pole often received more extensive damage than the right frontal tip. The missile track itself was filled with varying amounts of blood ranging from very little to obvious major clots. Some subarachnoid bleeding occurred in all cases over the wounded hemisphere; a small amount of blood was frequently found in the area of the brain stem and was rarely seen over the contralateral cerebral hemisphere. The anterior surfaces of the right cerebellum and the right inferior colliculus lying under the tentorium were often slightly contused.

Effects of Wounding on Breathing

Table 1 summarizes the effect of brain wounds caused by missiles of different energies upon breathing and the duration of brain wound-induced apnea.
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approximately the same percentage of cats in the 0.90-J and the 2.50-J energy groups never experienced post-wounding apnea. Among all cats experiencing apnea, however, those with milder wounds (0.90 and 1.40 J) were much more likely to have shorter periods of apnea (up to 1 minute) than were those receiving the most severe wound (2.50 J). Increasing wound energy significantly increased the likelihood of prolonged apnea of 6 minutes or longer.

Table 2 shows the effect of early respiratory support for cats that became apneic for 6 minutes or longer. For data analysis, animals that did not resume spontaneous breathing within 6 minutes were considered to be "dead" even though they may have subsequently recovered ventilatory function owing to respiratory support. This end-point was chosen because anesthetized uninjured cats develop fatal cardiac failure and permanent loss of electroencephalographic recording if apnea lasts longer than 5 or 6 minutes (D Torbati, D Awashi, ME Carey, unpublished data).

Early respiratory support was beneficial but became less so when brain wounds were caused by high-energy (2.50-J) missiles. Nevertheless, 15 (60%) of 25 cats rendered apneic for 6 minutes or longer were saved by means of prompt respiratory support. Twenty minutes was the median ventilatory support time but one animal required 80 minutes. Fourteen of 36 cats wounded at 1.40 J became apneic for 6 minutes or longer. All were ventilated following 1 minute of postwounding respiratory arrest, and 10 subsequently resumed spontaneous breathing. The beneficial effect of respiratory support in this group was highly significant (p < 0.005, McNemar's test). Eight of the 10 resuscitated cats from this group lived from 24 hours to 38 months after wounding, at which time they were sacrificed. After resumption of spontaneous breathing, these cats were behaviorally indistinguishable from cats that had never become apneic following wounding.

Selected Physiological Effects of Brain Wounding

Data on selected central and peripheral physiological effects of brain wounding were obtained from the second series of cats into which an ICP monitor had been placed prior to wounding.

Changes in MABP, ICP, and CPP

Among the five animals in the control group, MABP showed a significant rise from 97.0 ± 10 mm Hg when first observed to 120 ± 15.0 mm Hg at 1 hour (Fig. 3). Thirteen of the 15 wounded cats had a sharp rise in MABP which began a few seconds after wounding, peaked at approximately 1 minute, and at 4 minutes returned to control levels where it remained for the remainder of the experiment. Two cats showed a slight fall in MABP 1 minute after wounding. The transient, postwounding hypertension was significant for all three wounded groups but the transient MABP rises after wounding did not correspond with missile energy.

The ICP in control cats ranged from 6.7 ± 2.5 to 7.2 ± 3.3 mm Hg for the 1st hour of observation, then gradually rose throughout the remaining 5 hours (Fig. 4). Immediately after wounding, all 15 cats exhibited an abrupt large rise in ICP; pressure then fell over many minutes to a still-elevated but lower level that was sustained. Both the immediate and long-lasting ICP elevations were proportional to wound energy. Increases of ICP in the 2.50- and 1.40-J wounded groups were significant.

The CPP of unwounded cats tended to rise throughout the 1st hour of observation because of rising MABP; this increase became significant at 20 minutes (Fig. 5). In the wounded groups, CPP was uniformly elevated 1 minute after wounding due to the markedly elevated

<table>
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<tr>
<th>TABLE 1</th>
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<tr>
<td><strong>Effect of brain missile wounds upon breathing and duration of wound-induced apnea</strong></td>
</tr>
<tr>
<td>Missile Energy (J)</td>
</tr>
<tr>
<td>0.90</td>
</tr>
<tr>
<td>1.40</td>
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<tr>
<td>2.50</td>
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<th>TABLE 2</th>
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<tr>
<td><strong>Efficacy of respiratory support for apneic brain-wounded cats</strong></td>
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<tr>
<td>Effect of Respiratory Support</td>
</tr>
<tr>
<td></td>
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<tr>
<td>total apneic ≥ 6 min (&quot;dead&quot;)</td>
</tr>
<tr>
<td>did not resume breathing</td>
</tr>
<tr>
<td>resumed spontaneous breathing</td>
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</table>

* Values are number of cats.

![Fig. 3. Graph showing mean arterial blood pressure (MABP) in control and brain-wounded cats. The control group of unwounded cats showed a gradual rise in MABP during 1st hour of observation presumably because anesthesia lessened. All wounded groups showed a significant transient rise of MABP, commencing within several seconds of wounding. Animals were wounded at time 0.](image-url)
MABP. Since MABP returned to baseline within 5 minutes of injury, subsequent CPP reductions were caused by persistent ICP elevations. Cerebral perfusion pressure was reduced 5% in the 0.90-J injured cats, fell 23% after a 1.40-J injury, and was significantly decreased by 46% following a 2.50-J wound.

Changes in Heart Rate and Respiratory Frequency

The heart rate for all unwounded cats varied between 161 ± 11 and 195 ± 28 beats/min for the 1st hour of observation. Ten of 15 wounded cats exhibited transient bradycardia of 10% to 15% which began at times ranging from 1½ seconds after wounding and lasted 3 to 30 minutes. Following this, the heart rate tended to return to control levels. One cat developed transient tachycardia after wounding, and two had transient tachycardia followed by bradycardia. These variable effects of wounding precluded the almost universally seen postwounding bradycardia from reaching statistical significance.

Respiratory frequency in all unwounded cats ranged from 13 to 15 breaths/min during the 1st hour of observation. Ten of 15 wounded animals exhibited reduced respiratory frequency immediately after wounding; six became entirely apneic during the 1st minute postwounding. In seven of the 10 cats that exhibited a reduced respiratory rate after wounding a normal breathing pattern returned within 3 minutes. Neither the occurrence rate nor the degree of respiratory depression (as reflected by changes in respiratory frequency) after wounding could be related to a specific missile energy; three cats wounded at 0.90 J exhibited respiratory depression, as did three wounded at 2.50 J. Three cats had increased respiratory frequency after injury.

Arterial Blood Gases and pH

In the control group, the initial PaO₂ averaged 88.8 ± 15.8 mm Hg, the PaCO₂ was 40.7 ± 5.5 mm Hg, and the pH was 7.34 ± 0.05. Twenty minutes after observations began, the PaO₂ had risen significantly to 99 ± 17.2 mm Hg, and by 60 minutes it was 105.0 ± 18.3 mm Hg. This reflects improved respirations consequent to decreasing anesthesia. No significant changes in PaCO₂ or pH occurred among cats in the control group during the 1st hour of observation.

In the three experimental groups before injury, PaO₂ ranged from 89.9 ± 10.6 to 102.1 ± 16.2 mm Hg and the PaCO₂ from 38.4 ± 5.0 to 41.0 ± 4.9 mm Hg. Plasma pH varied from 7.35 ± 0.04 to 7.37 ± 0.07. No significant postinjury changes in arterial blood gas pressures or pH occurred in the group with 0.90-J wounds, but three cats showed decreased plasma PaO₂ and two had increased PaCO₂ during the 1st minute postwounding. Animals wounded at 1.40 J showed the most consistent and significant mean arterial blood gas and pH alterations 1 minute after wounding: the PaO₂ decreased to 55.7 ± 12.7 mm Hg, the PaCO₂ increased to 46.6 ± 4.9 mm Hg, and the pH fell to 7.30 ± 0.05. The decreased plasma PaO₂ level rose by 3 minutes postwounding, and by 10 minutes was no different from the control PaO₂ value. Plasma PaCO₂ remained elevated for 20 minutes after wounding, but the pH was reduced for 10 minutes. In cats wounded at 2.50 J, blood PaO₂ showed a significant reduction to 69.9 ± 29.7 mm Hg at 1 minute, after which it increased to control levels. Although the postwounding plasma PaCO₂ rose and the pH fell in this group, large standard deviations precluded determination of a statistical significance for these altered variables. Postwounding changes in arterial blood gases and pH could not be correlated with missile energy.
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**TABLE 3**

<table>
<thead>
<tr>
<th>Missile Energy (J)</th>
<th>No. of Cats</th>
<th>Prewounding</th>
<th>1 Min Postwounding</th>
<th>20 Min Postwounding</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.90</td>
<td>4</td>
<td>31.6 ± 4.9</td>
<td>38.9 ± 6.9†</td>
<td>34.4 ± 2.8</td>
</tr>
<tr>
<td>1.40</td>
<td>5</td>
<td>32.3 ± 3.6</td>
<td>40.8 ± 5.0</td>
<td>33.1 ± 4.2</td>
</tr>
<tr>
<td>2.50</td>
<td>5</td>
<td>32.8 ± 2.9</td>
<td>40.5 ± 4.9†</td>
<td>33.8 ± 4.3</td>
</tr>
<tr>
<td>3.50</td>
<td>3</td>
<td>27.3 ± 4.3</td>
<td>27.9 ± 3.1</td>
<td>27.5 ± 3.5</td>
</tr>
</tbody>
</table>

*Values are means ± standard deviations.
†Significant difference compared with prewound hematocrit (p < 0.05).

**Changes in Blood Glucose Concentration**

In the control group, the blood glucose concentration became significantly (p < 0.05) elevated (89 ± 19 mg/dl to 112 ± 27 mg/dl) after only 60 minutes of observation, whereas all wounded groups showed a rise within 3 minutes of injury. This rise became significant 10 minutes after wounding in the group with a 0.90-J wound (88 ± 31 mg/dl to 138 ± 46 mg/dl). Among cats wounded by a 2.50-J missile, the postwounding hyperglycemic increase was significant at 20 minutes (86 ± 21 mg/dl to 141 ± 61 mg/dl). Postwounding hyperglycemia occurred in the group with a 1.4-J wound, but was not significant. Although 14 of the 15 wounded cats exhibited postwounding hyperglycemia, the variability of control and postwounding blood glucose levels in these unfasteded animals reduced the number of "significant" rises in blood glucose concentrations among the wounded groups. No correlation between missile energy and subsequent blood glucose levels was apparent.

**Changes in Hematocrit**

In all three groups of wounded animals arterial hematocrit showed a significant rise within 1 minute of injury but then returned to prewounding levels 5 to 20 minutes after injury (Table 3). Splenectomy abolished this effect. In normal cats the hematocrit varies from 24% to 55%, accounting for the wide variation in prewounding findings.15

**Discussion**

**Ballistic Considerations**

**Physical Correlates of Missile Wounding in General.** Missile wounding can only be understood in terms of the physical interactions between the missile and the tissue through which it passes. The primary destructive effect of a missile interacting with tissue is caused by the crushing action of the missile itself.14,15,23,25,29 Besides this direct action, however, a missile moving in a water or tissue medium generates three distinct types of pressure within the medium which it transits:26,21,25

1. Juxta-missile pressure. Extremely high pressures (thousands of atmospheres) are generated immediately in front of and at right angles to a moving missile owing to flow of the medium in which the missile is traveling around the missile.

2. Longitudinal, "strong" shock wave pressure. When a missile strikes an object, a high-pressure compression front or shock wave is formed which, in tissue, moves spherically away from the missile strike-point at approximately the velocity of sound in water (approximately 1460 m/sec). The longitudinal, "strong" shock wave initially has a very steep front but its shape and duration wave may be changed with propagation through a medium, particularly one that is not homogeneous, such as tissue. As it travels, therefore, the steep front of a "strong" shock wave will become less steep and, finally, will assume the characteristics of an "ordinary" pressure wave (see below). In water, the peak pressure of a "strong" shock wave may exceed 80 atm but the entire "strong" shock wave event lasts only about 10 μsec. Blunt missiles may cause "strong" shock waves with strike velocities as low as 60% of the velocity of sound in the medium. Some investigators24 have thought that, in the absence of fluid to air transfer, "strong" pressure waves do not cause tissue damage because their brief duration prevents transfer of sufficient energy to surrounding tissues to distort and tear them.

3. Pressure waves from kinetic energy transfer. When a missile passes through tissue, kinetic energy is transferred to nearby tissue elements which are propelled radially from the missile track, creating a large sub atmospheric temporary cavity directly behind the missile. When the elastic limit of this outwardly displaced tissue is reached, it falls inward whence it was displaced. This cycle may be repeated several times before the deranged tissue comes to rest around the permanent track created by the missile. The oscillating, outward and inward rush of tissue creates a long-lasting (milliseconds) lower amplitude (20- to 30-atm) pressure wave which propagates widely throughout the medium. It has been considered that these lower-amplitude, longer-duration pressure waves are the cause of damage to tissues at a distance from the site of actual missile injury.

The amount of tissue damage caused by a missile may be correlated with the amount of energy deposited within the tissue by the missile.24,30 This is expressed by the equation: 

\[ E_d = E_{on} - E_{ex} \]

where \( E_d \) = missile energy of deposit, \( E_{on} \) = energy of entry, and \( E_{ex} \) = energy of exit. If a missile is retained within the tissue, \( E_{ex} = 0 \) and all missile energy will be given to the tissue. If the missile exits, only part of its kinetic energy will be deposited within the tissue. The same amount of energy may be deposited by a small-mass missile with a large velocity or a greater-mass missile with a smaller velocity. Kinetic energy deposited by a missile is partitioned between that which directly crushes tissues in its path and that which displaces tissues adjacent to the missile track.14 The latter is less destructive than the former owing to the elastic properties of the displaced tissue.
which may be deformed without being irrevocably destroyed (L. Sturdivan, personal communication, 1988).

Physical Correlates of a Missile Wound to the Brain

Most wounds in combat are caused by small fragments.1 It was determined that 80% of all wounds sustained at Dunkirk were caused by “splinters” 5 mm or less in diameter.2 Fragments weighing 110 to 220 mg inflicted most fatal brain wounds in Vietnam (Carey ME: Unpublished data from analysis of casualties surveyed by the Wound Data and Munitions Effectiveness Team (WDMET) in Vietnam). For this reason our laboratory gun was designed to fire a very small (31.7-mg) missile instead of a larger (310- to 870-mg) projectile as used by prior investigators.6-11,16,30 Utilization of a smaller, high-velocity missile in our experiments may explain some of the physiological differences observed by us as compared to prior brain-wounding experiments which utilized larger missiles fired at lower velocities.6-10,16,30

The developed laboratory gun propels a small sphere with enough velocity to penetrate the intact skulls of laboratory animals avoiding the necessity of creating a brain wound by firing through a previously placed trephine.6-10,16,30 Creating a nonfatal brain wound by shooting a missile through the intact skull imposes specific velocity and energy limits. In our experimental model, the lower ballistic limit (238 m/sec, 0.90 J) was that required for consistent skull penetration while the upper limit (389 m/sec, 2.50 J) was that which produced a fatal apnea in the great majority of instances (even though the missile did not directly damage brain-stem respiratory centers). Thus, wounding the experimental animal through the intact skull greatly reduces the spectrum of realistic missile velocities and energies available for the creation of a nonfatal wound. In our model, the missile does not exit so that all missile energy is deposited within the brain.

Ballistics research on animals to simulate human wounds involves significant animal-human scaling problems.25 The cat provides a 25-gm brain for our 31.7 mg experimental missile. The combat soldier has a 1300-gm brain and is often wounded by shell fragments with a mass of 100 to 200 mg. Accordingly, our test missile has a mass seven to 15 times too large. We have chosen to accept this scaling factor because constructing a test system to fire a smaller missile would be technically very difficult and to increase the size of the laboratory animal would make the experiments cost-prohibitive. Use of smaller experimental animals such as rabbits with a 7-gm brain or rats with a 1-gm brain would grossly distort the brain-missile ratio, making experimental findings of questionable significance relative to humans. Furthermore, the cat’s brain is architecturally more akin to the human brain than that of either the rabbit or the rat.

In the present model, tissue damage can be expected to be caused by the direct action of the missile upon tissues which it encounters and by “ordinary” pressure waves caused by kinetic energy transfer from missile to brain. These pressure waves may be widely transmitted throughout the brain. Theoretically, “strong” shock waves would not be created in our model because missile velocities do not approach 870 m/sec.

Effect of Wounding on Breathing

The neuronal substrate for respiratory control is complex and extends from the cerebral cortex through the medulla from which emanates the primary inspiratory and expiratory rhythm.23,31 The basic oscillating respiratory rhythm produced by the medullary neuronal network may be modified by pontine, mesencephalic, diencephalic, limbic, and cortical influences.33 Stimulation of various cortical and subcortical areas may cause respiratory arrest.2,23,34,62,63 Increases in systemic arterial blood pressure, such as occur after brain wounding, also may lead to temporary apnea.26 The occurrence of postwounding respiratory arrest in 83 cats wounded through a completely intact skull became greater as missile energy increased (Table I). Other experimental studies on brain injury also found apnea to be a prominent feature. Nilsson, et al.,37 impacted the closed skull of rats with a 600-gm piston and observed the onset of apnea when piston velocity exceeded 9 m/sec. Fluid-percussion injury models in the rabbit17 and cat16 have shown the occurrence of permanent apnea with impact pressure peaks above 2.5 atm. Crockard, et al.,9 observed that a 0.5-J missile injury through a trephine opening into a monkey’s brain caused no respiratory dysfunction; a 1.3-J wound caused the respiratory rate to slow, and a 5.0-J missile wound produced immediate apnea in four of seven animals. Fluid-percussion models have shown that, upon impact, a marked pressure difference exists between the intracranial and spinal spaces, which promotes rostral-caudal displacement of the intracranial contents. This movement might distort the brain stem and lead to postpercussion apnea.31 Actual brain-stem displacement following percussive injury to the cerebrum has been documented with x-ray flash cinematography.18 In our model, we have shown that passage of the missile through the brain generates a high ICP (Fig. 4). This might cause transient herniation of cerebral tissue from the intracranial to the intraspinal space, distort the brain stem, and affect medullary respiratory centers.

Another mechanism to explain missile-induced apnea might be the effect of “ordinary” pressure waves caused by kinetic energy transfer from the missile to the surrounding brain. These pressure waves might propagate to the brain stem and impair medullary neural function in general and respiratory neurons specifically. Evidence for widespread medullary dysfunction in our model includes an almost universally observed bradycardia seen after wounding. Perhaps the close proximity of the medullary respiratory nuclei to the floor of the fourth ventricle somehow accounts for
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the particular vulnerability of these cells to the indirect effects of the missile wound.

Missile injury in the present model produced an ablative cortical lesion rather than a stimulatory one. Whereas stimulation of cortical regions may cause respirations to cease, we are unaware of experiments where cortical ablations alone cause cessation of breathing. The respiratory arrests observed after hemispheral brain wounding in our model, therefore, are most likely caused by a direct medullary effect. Because the apnea was often permanent, it was unlikely to have been caused solely by the transient postwounding hypertension which occurred a few seconds after missile passage.25

The present experiments were conducted with cats under pentobarbital anesthesia, a respiratory depressant, and with an anteroposterior missile trajectory offset 20° from the sagittal plane. Whether the observed apnea would be significantly modified by use of another anesthetic agent, a different missile trajectory, or a primate brain with its different configuration is unknown. Nevertheless, the present data indicate that missile-induced apnea in the cat was often prolonged but also frequently reversible if respiratory support were given soon after the onset of apnea.

These findings in cats, extrapolated to humans, suggest that following a lower-energy brain wound to a cerebral hemisphere, the integrity of medullary respiratory centers may be the predominant factor which determines whether an individual lives or dies, provided excessive intracranial bleeding does not occur. A lower-energy hemispherical wound may not appreciably affect respiration, a somewhat higher-energy wound may cause transient apnea, while a yet higher-energy wound might irreversibly damage the medullary respiratory centers and cause death from apnea. This mechanism may explain deaths from brain wounding where the missile does not directly injure a vital structure and where intracranial bleeding is not excessive. Possibly, some individuals who have sustained hemispherical brain wounds and who are thereby rendered apneic may be saved, provided that respiratory support (such as mouth-to-mouth breathing) is given within a few moments. If respiratory support is delayed, secondary hypoxic brain damage or death may ensue. It may be impossible to tell immediately after injury which person with a brain wound has reversible or irreversibly apneic. Therefore, all who sustain a penetrating missile wound to the brain should probably be provided immediate respiratory support if they have severely depressed respirations or are apneic. Our data suggest that respiratory support should be maintained for several hours unless other findings indicate brain death, because spontaneous respiration may resume after even a prolonged period of apnea.

**Selected Central and Peripheral Physiological Effects**

The data presented here were derived from 20 cats which had an ICP monitor inserted before wounding.

**MABP, ICP, and CPP Following Wounding.** The transient increase in MABP observed within seconds of brain wounding followed by return to baseline over the next several minutes presents a pattern similar to that observed in cerebral percussion models involving rabbits,43 cats,44 and rats,37 and is unlike that demonstrated by trephinated missile-wounded primates.45 In monkeys, a 1.3-J missile wound to the brain caused a triphasic blood pressure response: immediately after wounding MABP decreased, 5 to 15 minutes later it increased above control levels, and thereafter it decreased significantly below baseline values.

The brief postwounding hypertension observed in our model may have been incited by brain (probably medullary) mechanisms acting reflexly through the sympathetic nervous system because the hypertension response commenced several seconds after wounding. In percussion-injury experiments, postinjury hypertension could be abolished by cervical spinal cord transection implying that a descending spinal pathway mediated this response.45

Both mild and fatal percussion injuries to the brain may produce hypotension immediately after impact.58 Since only two of 15 cats in the present study became hypotensive, this effect was not a prominent feature in our model. The lowest missile energy of 0.90 J which we used probably did not create a “mild” brain injury. We have excluded high-energy, inherently lethal wounds from our study.

The immediate and sustained ICP elevations seen after brain wounding must not be confused with instantaneous intracranial overpressures generated by missile passage through the brain. Intracranial overpressures associated with the “ordinary” pressure waves of missile transit last about 10 msec and cannot be recorded on our physiograph.20 The observed elevations in ICP occurred over a much longer time period and were caused by intracranial physiological-anatomical events associated with brain wounding. The ICP increases could have come from several sources: 1) associated intracranial hemorrhage; 2) an increased rate of cerebrospinal fluid (CSF) formation or decreased rate of CSF absorption; 3) associated vasogenic brain edema; or 4) an increase in the intracerebral vascular volume.

Measuring the amount of intracranial bleeding associated with the brain wound is difficult. Our experience, however, indicates that higher-energy wounds were not necessarily associated with more intracranial bleeding; sometimes lower-energy wounds caused larger intracerebral clots than did higher-energy lesions. A lower-energy missile would be just as likely to sever a cerebral vessel as a higher-energy missile. Thus, if intracranial bleeding alone were responsible for the observed sustained increases in ICP one might expect a more random distribution of ICP elevations among groups instead of a stepwise increase in ICP change with each incremental increase in missile energy deposit (Fig. 4). We are, therefore, inclined to discount associated intracranial hemorrhage as being the sole factor accounting for postwounding ICP elevations.
Our experiments on postwounding vasogenic brain edema indicate that no significant brain edema occurs within 6 hours of wounding by either 0.90-J or 1.40-J missiles (unpublished data). Thus, increased brain water does not account for the immediate and early rise in ICP.

Missile wounding of the brain appears to excite a sympathetic response, manifest by transient hypertension and increasing peripheral blood glucose levels, and a parasympathetic effect, exemplified by bradycardia. Sympathetic stimulation has been shown to decrease the rate of CSF formation while parasympathetic stimulation may increase it. Whether parasympathetic (cholinergic) stimulation consequent to brain wounding might increase the rate of CSF formation in brainwounded cats or whether blood in the CSF might decrease its absorption is unknown. The latter mechanism, particularly, would tend to raise postwounding ICP.

Increased intracerebral vascular volume following wounding also may account for the stepwise increase in ICP with increasing wound energy. Cerebral hyperemia has been hypothesized following closed head injury and may occur as well after a missile wound to the brain. If the intracerebral vascular volume does increase after brain wounding, medical therapies which expand the intracerebral vascular space further may prove detrimental to the wounded brain because expanding the intravascular volume would elevate the ICP further.

Just as ICP values showed a stepwise increase with rising wound energy, the CPP's had a corresponding decrease. Long-lasting and serious metabolic derangements within the brain occur when CPP is reduced below 40 mm Hg. The 2.5-J missile injury reduced CPP's to about 50 mm Hg 3 to 20 minutes after injury. Higher-energy missile injuries to the brain, therefore, might be associated with severe CPP reductions where metabolic abnormalities may supervene and compound the effects of direct missile damage. Crockard, et al., also observed persistently elevated ICP's and reduced CPP's following brain wounding in primates; the initial ICP elevations appeared missile-energy dependent. Fluid-percussion injury of the brain produces only a brief increase in ICP consequent to the brief rise in MABP immediately after impact. This injury, therefore, differs greatly from a missile wound.

Changes in Cardiac Rate. Bradycardia beginning about 2 seconds after the event has been rather uniformly observed following brain injury, be it percutaneous or following missile trauma. This may result from stimulation of brain-stem parasympathetic centers due to brain-stem distortion or may reflect a reflex baroreceptor response from the injury-induced increase in MABP. Although we observed no relationship between the degree of bradycardia and wound energy, others have noted heart rate slowing to be greater the more severe the brain injury.

Changes in Arterial Blood Gases, pH, and Respiratory Frequency. Ten of the 15 wounded cats had a reduced respiratory rate after wounding, presumably from brain-stem effects resulting from high intracranial overpressures generated by the wounding missile. Violating the closed cranial vault to insert our chosen epidural pressure transducer, however, abolished prolonged (≥ 6-minute) postwounding apnea which was a prominent feature when cats were wounded through a completely intact skull (Table 1). Possible reasons for this include trephination (even though the cranial defect was sealed with acrylic) and the volume of the air-filled monitor itself. The small amount of air within the epidural pressure-sensing balloon may have been enough to absorb some of the missile energy and protect the brain stem.

Since brain wounding generally slowed the respiratory rate or caused apnea, it is not surprising that many of the brain-wounded cats had decreased PaO2 and pH and increased PaCO2 immediately after wounding. These results in cats differ from those reported for comparable wounded monkeys. Monkeys wounded at 1.3 J showed a diminished respiratory rate but an increased tidal volume without alterations in arterial blood gases or pH.

Changes in Blood Glucose Concentration. Cats in the control group showed a progressive rise in blood glucose values during the 1st hour after induction of anesthesia in the stereotactic frame, attributed to diminishing anesthetia and consequent stress, although all cats appeared asleep. All of the wounded groups showed a prompt rise in blood glucose concentration following the brain wound. Both stress and intracranial lesions are commonly associated with a rise in arterial blood glucose levels due to catecholamine release and gluconeogenesis. Theoretically, large postwounding elevations in blood glucose concentrations could prove detrimental to brain function if brain ischemia were caused by the missile wound. Elevations in blood glucose levels aggravate ischemic brain damage, presumably from increased lactic acid production in the damaged brain. Excessive lactic acid in the tissue adds to ischemic tissue damage.

Changes in Hematocrit. The transient increase in hematocrit following brain wounding was mediated by splenic contraction and injection of red blood cells from the spleen into the circulation, because this immediate postwounding response was abolished by splenectomy (Table 3). We infer that this splenic response was mediated by sympathetic stimulation following the brain wound. Arterial resistance and venous capacitance vessels in the splenic capsule have a dense sympathetic adrenergic innervation which, when excited, contract the vascular smooth muscle and expel blood from the spleen. In the cat, splenic nerve stimulation results in the discharge of large volumes of splenic blood with a hematocrit of 70% to 80%. Increased hematocrit slows blood flow; if the flow were reduced sufficiently, ischemic brain damage could theoretically be superimposed upon the mechanical damage associated with...
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missile passage. To our knowledge, this is the first demonstration of transiently increased arterial hematocrit following brain wounding. No information on this subject in man exists.

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