Pulmonary Damage and Head Injury* (33475)

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Experimental studies have shown that pronounced pulmonary pathology commonly attends the occurrence of severe epileptic seizures induced by exposure to OHP and by various chemical agents such as pentamethylenetetrazol (Metrazol) and picrotoxin, and further, that this pulmonary pathology is in large part of central rather than peripheral origin (1–3). The implication that the disruption of central nervous system function is an important factor in the causation of this pulmonary pathology finds support in earlier clinical reports of pulmonary edema and congestion in organic nervous disease (4), in spontaneous and traumatic intracranial hemorrhage (5), in experimental vagotomy (6), and in other conditions of CNS dysfunction including that of increased intracranial pressure (7–10). If, as it would appear, this pulmonary damage is of central origin, one might reasonably infer that similar pulmonary damage would occur in association with severe cerebral trauma resulting from head injury, but the literature provides relatively little experimental data on this phase of the subject.

The experiments herein reported were carried out, therefore, in an attempt to determine: (i) whether pulmonary damage can be consistently induced in association with the cerebral trauma experimentally produced by head injury in animals; if so, (ii) what is the basic mechanism of causation of this pulmonary pathology; (iii) what means might be suggested whereby this pulmonary pathology could be prevented or mitigated.

Methods. Forty-two young adult male rats (200–300 gm) were subjected to cerebral trauma induced by means of a captive bolt mechanism which has now gained acceptance as an effective and humane instrument for use in the abattoir industry. The spring-loaded, 0.15 oz bolt used in these experiments had a flat impact surface 0.5 in. in diameter, and was delivered with a velocity of 50 ft/sec at the point of impact. The kinetic energy at impact was calculated to be 1.1 ft-lbs. Adjustments were made so that this produced immediate unconsciousness without severely crushing the skull. Most rats died within a few minutes after impact without regaining consciousness. Those which showed any signs of returning consciousness were immediately given a lethal dose of sodium pentobarbital intraperitoneally. No survival experiments were carried out.

The unanesthetized rat was hand-held in a relaxed horizontal position, with its nose placed in the tip of a V-shaped wire frame. The lower jaw rested on a thin 0.5-in. layer of sponge rubber cemented to a heavy unyielding block of wood. The V-shaped frame insured accurate duplication of head position in each experiment, and the layer of sponge rubber prevented extracranial fractures as well as the occurrence of any attendant nasal hemorrhage. The bolt was fired from a gun firmly fixed to an adjustable vertical support above the rat so that the area of impact could be centered on the midsaggital line between the ears just anterior to the occipital protuberance.

Immediately after administering the blow, the EKG was recorded from limb leads and the duration of respiration noted. After complete cardiac arrest, as indicated by the EKG, body weight was determined, the lungs were carefully removed, rinsed in saline, lightly blotted, freed from excess fat tissue, weighed, and photographed. The trachea was examined, and an estimate of lung pathology was made by gross inspection. The meninges were exposed for visual inspection, and the brain was carefully removed and examined for gross damage and hemorrhage. Lung and brain tissue were fixed in formalin, and sub-

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TABLE I. Pulmonary Damage Induced by Cerebral Trauma.

No. of animals	Fatalities (%) (died of trauma)	Fatalities (%) showing gross lung damage	Survivors of trauma subsequently killed by anesthetic (%)	Survivors (%) showing gross lung damage	Rats killed by subsequent anesthesia (%)	Rats killed by anesthetic showing lung damage (%)
Controls (8)					100	0
Subjected to cerebral trauma (42)	64	92	36	40	36	40

sequently sectioned and mounted for histological examination.

Because of the remote possibility that the observed changes in the lungs may be due to hypoxia associated with circulatory or respiratory disfunction, additional rats (16) were exposed to a low oxygen (2–4%) nitrogen atmosphere until death to determine the effect that hypoxia alone would have on the lung tissue. Oxygen levels were monitored with a Beckman E-2 oxygen analyzer. Rats were dropped into a bell jar containing the low oxygen atmosphere and removed after termination of all respiratory movements. Postmortem gross and microscopic tissue examinations for these control animals were the same as those carried out for the test animals killed by the captive bolt.

Results. Sixty-four percent of the rats subjected to cerebral traumatization died as a result of this trauma without regaining consciousness, while 36% temporarily survived the trauma but were subsequently killed by a lethal dose of sodium pentobarbital administered at any signs of regaining consciousness (Table I). Lung damage was present in 92% of the rats which died as a result of traumatization, and in 40% of the rats which survived traumatization but were subsequently killed by the sodium pentobarbital. Since no lung damage was found in the nontraumatized controls killed by sodium pentobarbital, the lung damage found in 40% of the rats which were killed by sodium pentobarbital after surviving the cerebral traumatization must be attributed to the effects of the cerebral trauma per se rather than to the sodium pentobarbital. These results are more fully presented in Table II.

The extent of gross lung damage was expressed in arbitrary units from +1 to +4; +1 indicated minimal congestion and +4 complete involvement of the lung, with congestion and frothing from the cut surface and the trachea. No gross pathology was found in the control group; the lungs were pink and well aerated. Rats which died of trauma alone had a gross pulmonary involvement

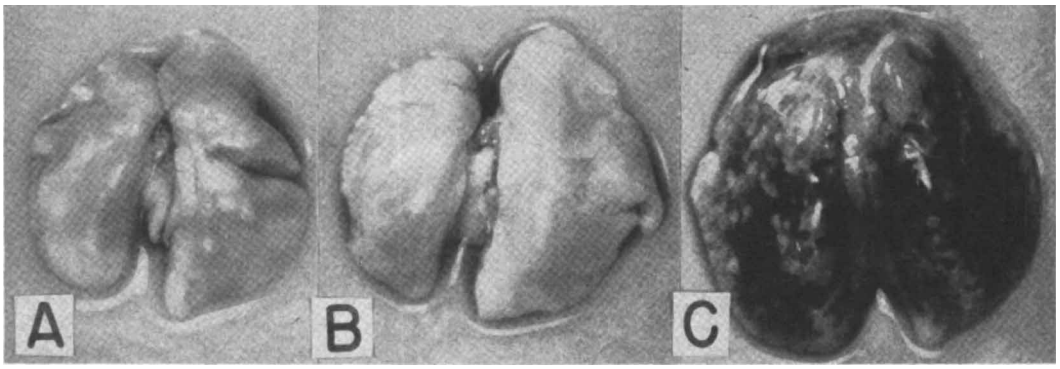

FIG. 1. Pulmonary pathology in a rat induced by cerebral traumatization in head injury, (A) Lung of control rat killed by sodium pentobarbital. (B) Lung of control rat killed by hypoxia. (C) Lung of traumatized rat killed by head injury induced by captive bolt.

TABLE II. Effects of Head Injury.[a]

Group	Lung gross damage (0 to +4)		Lung wt./Body wt. × 100		Brain gross damage (0 to +4)		EKG				Duration of respiration after trauma	
							Duration		Rate			
	No. of rats	Mean value	No. of rats	Mean value ± SE	No. of rats	Mean value	No. of rats	Mean value (min)	No. of rats	Mean value (rate/min)	No. of rats	Mean value (min)
Controls (killed by anesthesia)	(8)	0	(8)	0.61 ± 0.05	(8)	0	—		(8)	436		—
Traumatized (fatalities) died of trauma	(27)	+3	(27)	1.10 ± 0.05	(27)	+2	(27)	10.0	(27)	174	(27)	1.4
Traumatized survivors (given lethal dose anesthetic)	(15)	+2	(15)	0.60 ± 0.04	(15)	+1	(15)	17.0	(15)	309	(15)	8.0

[a] Heart rate approx 2 min after traumatization.

ranging +2 to +4 expressed in Table II as an average of +3, while the rats which survived traumatization (subsequently killed by sodium pentobarbital) showed a less severe gross lung damage of +2.

Lung wt./body wt. ratios for the control rats was 0.61. The group which died as a result of traumatization alone had a ratio of approximately double that of the controls (1.10), whereas those surviving traumatization (subsequently killed by anesthetic) had a lung wt./body wt. ratio about the same as the control value. Typical pulmonary changes in rats which succumbed to cerebral trauma are illustrated in Fig. 1.

The gross pathology of the brain was indicated primarily by the extent of subdural hemorrhage present on the dorsal surface, and by contusion of the parenchyma, and for controls is expressed as zero (Table II). Rats which died as a result of traumatization had a gross pathology of +2; this included the presence of considerable subdural and subarachnoid hemorrhage and suffused redness of the parenchyma of the brain itself, indicative of contusion. In the more severe cases where the skull was fractured, laceration of the brain tissue with rupture of the meninges was commonly present. In the rats which survived traumatization and were subsequently killed by anesthetic, the gross brain pathology was less severe and is expressed as +1.

Average duration of the heart beat (EKG) (Table II) for the rats which succumbed to traumatization was 10 min; for the rats which survived traumatization (subsequently killed by anesthetic), the heart beat was more persistent—the EKG continued for 17 min. But this, of course, was limited by the administration of sodium pentobarbital on signs of returning consciousness (about 6–8 min after the impact).

The average heart rate for normal rats (anesthetized controls), as given by the literature, is 352/min (11). In the present experiments the rats which were killed by trauma had a heart rate of 174/min approximately 2 min after impact, indicative of a pronounced slowing from the normal rate (probably of vagal origin). The rats which survived trauma

had a heart rate of 309/min (av) before they were killed by sodium pentobarbital.

Atrioventricular heart block, in most cases a 2:1 relationship was found in over 90% of those rats dying of impact, but in less than 10% of the survivors before the lethal anesthetic was given. Most of these developed a 2:1 heart block after the administration of the lethal dose of sodium pentobarbital.

The duration of respiration in those rats which died as the result of traumatization was 1.4 min. In those which survived traumatization and were subsequently killed by sodium pentobarbital 6–8 minutes after impact, respiration persisted for 8 min.

Pathologists' reports on rat brain tissue indicated brain damage of variable severity and commonly included subarachnoid hemorrhage, lacerations, and occasional hemorrhage in the choroid plexus, ventricles, cerebellum, and cerebrum. Reports on lung damage commonly indicated hemorrhage and congestion, atelectasis, and abnormal variation in alveolar size and shape. These reports are indicative of moderate to severe damage in both brain and lung tissues.

The additional experiments on low oxygen clearly ruled out the possibility that the damage induced by traumatization might have been due simply to low oxygen. The rats (16) which were exposed to a low oxygen (2–4%) high nitrogen atmosphere, ceased breathing in approximately 1 min. The gross lung appearance (Fig. 1) and lung weight body weight ratios of these control rats were essentially normal. Pathologists' reports indicated only moderate passive congestion in some cases.

Discussion. Clinical reports (4–6, 9, 10, 12) have indicated that pulmonary congestion, and other pathological changes were associated with serious disruption of cerebral function from a variety of causes. In a clinical study Swann showed that pulmonary edema was a marked feature of asphyxial deaths whereas hemorrhage was the outstanding feature of brain injury cases (13).

In addition, it has been reported that electrolytic lesions experimentally produced in the hypothalamus of the rat which left metallic deposits and frequent hemorrhage in the surrounding tissue resulted in extensive pulmonary edema whereas clean lesions produced by radio-frequency techniques resulted in very little pulmonary edema (14). Such pulmonary lesions might conceivably involve the sympathetics. Ivanhoe and Meyers have empirically divided such pulmonary edema into 2 groups: (i) "hyperactive-sympathetic," and (ii) "hypoactive-sympathetic or neuroparalytic." Cases of phosgene poisoning were classified in the hypoactive group (15).

The data from our experiments indicate that the most severe lung damage occurs in those rats having the shortest duration of the EKG. Rats with the most severe lung damage (those dying of trauma) breathed an average of only 1.4 min after impact as compared to the dyspneic breathing of the survivors (subsequently killed by anesthesic) which lasted for 8 min, usually following a brief initial apnea. Pulmonary edema and congestion thus developed in a very short time after impact. This is in accordance with the clinical reports (5) on cases coming to autopsy, which emphasized the rapid occurrence of edema in approximately 30–60 min following intracranial hemorrhage. However, the death of the rats which succumbed to the traumatization in our experiments, like those reported by Ommaya on monkeys (16), was apparently due to respiratory paralysis, (resulting from the impact) rather than to the pulmonary damage.

The pathology reports in our data indicate moderate to severe brain and lung damage, in the traumatized rats, but there is no positive correlation between the severity of brain injury and lung damage. However, they do show there is a pronounced positive correlation between the lung wt./body wt. ratios and the severity of the gross lung damage.

In several of the traumatized rats, blood was found in the external nasal orifices but careful examination of the trachea as carried out in all animals revealed the absence of aspirated blood. The pulmonary pathology cannot therefore be ascribed to the aspiration of blood. However, the presence of bloodless frothy fluid in the tracheas was indicative of pulmonary edema.

These experiments clearly demonstrate

that severe pulmonary pathology, primarily edema and congestion, can be regularly induced in the rat by cerebral trauma attending head injury under controlled experimental conditions. These studies indicate further that this pulmonary damage cannot be caused by hypoxia alone. The results lend support to the view that a dysfunction of the central nervous system and attendant "neurogenic" factors involving sympathetics and cardiovascular dynamics are important contributors to—if not the main causes of—the pulmonary pathology occurring in head injury as well as in some other conditions involving severe dysfunction of the CNS.

Summary. Experiments were carried out to investigate the effect of severe head injury on the lungs of 42 unanesthetized rats. Cerebral trauma was induced by means of a captive bolt mechanism producing sufficient force to cause immediate unconsciousness or death, apparently of respiratory origin, usually within a few minutes. Rats which showed any signs of regaining consciousness after trauma (36%) were immediately given a lethal dose of sodium pentobarbital. Gross pulmonary damage including edema and congestion and increased lung wt./body ratios were found in 92% of those rats dying from the impact and in 40% of the rats killed by the lethal dose of anesthetic given after impact. Pathology reports indicated the occurrence of moderate to severe brain and lung damage in traumatized rats. Control experiments in which animals succumbed during exposure to low oxygen have demonstrated that this pulmonary pathology cannot be attributed simply to low oxygen. Results indicate that hypoxia alone in rats does not induce the severe form of pulmonary damage resulting from cerebral trauma. It is tentatively concluded that these pulmonary changes are due in large part to nervous mechanisms of central origin. The data lend substantial support to the evidence previously reported that similar pathology which attends severe epileptiform convulsions induced by the toxic action of oxygen at high pressure and by chemical convulsants such as Metrazol and picrotoxin is in large part of CNS origin, and that this effect is mediated through the sympathetics and alterations in the cardiopulmonary hemodynamics and possibly also through changes in the pulmonary parenchyma itself.

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