

hemispheres, mid-brain, pons, medulla oblongata, and occasionally even the upper cervical cord, the impacts being constantly delivered on the occipito-parietal region.

In the Cajal stained preparations, thickening, spiroid course, and at times definite twisting of the axons of the cortical cells were already apparent in the animals killed at the 1st hour. The corresponding nerve cells in the Nissl stain showed obscuring of the cell outlines, tigrolysis, and huge peripheral vacuoli. These changes were not diffuse, as groups of damaged neurons alternated with others displaying normal patterns. The same type of focal change was displayed by the medullated axons which appeared poorly impregnated and swollen, with a corresponding moniliform swelling of the myelin sheaths in the Spielmeyer preparations.

More advanced myelin disintegration and neurolysis were found in the animals killed from the 4th to the 72nd hour, as shown by fragmentation of axis cylinders, with incip-

ient neurolysis and myelin reabsorption and resolution into round, oval or irregularly shaped fat globules.

Of 16 animals killed after 2 months observation, only 4 revealed a definite pathology characterized by focal areas of demyelination, and rarefaction of nerve cells in the cerebral cortex with obliteration of axis cylinders and glial proliferation in the most damaged areas.

Summary. Rats recovering from a temporary period of unconsciousness, varying from 10 seconds to 15 minutes, following a blunt impact on the head which had left skull and brain apparently intact, frequently revealed microscopic evidence of neuronal injury affecting, in multiple areas, nerve cells, axis cylinders, and myelin sheaths. Using a trauma of the same strength, no differences were seen, either in the immediate effects or in the type and extent of cerebral changes, when the impact was delivered on the stationary head or on the head in rapidly accelerated motion.

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Gastric Mucosal Lesions in Rats Submitted to Head Trauma.

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A relationship between cerebral birth injury and hemorrhagic erosions in the mucosa of the alimentary tract (stomach, esophagus, first portion of the duodenum) has been known to exist for many years; yet it was not until 1932 when Cushing¹ reported additional instances of ulcers developing in individuals submitted to surgical intervention in the brain that the conception of the neurogenic origin of mucosal lesions in the intestinal tract gained widespread interest (Oppper and Zim-

merman,² Vanzant and Brown,³ Ivy,⁴ Keller⁵). Although some observations on the experimental animal have shown that these mucosal defects have a tendency to heal promptly, yet in the opinion of others this does not seem to be invariably the case, leaving unsettled the problem of the relationship between head trauma and peptic ulcer.

Rats submitted for other investigative purposes to blunt impacts on the head, single or repeated, of different intensity, revealed evidence of gastric damage in a number of cases, 14 out of 183, or 7% approximately. Some of the rats had been struck by a moving object on the stationary head and others had

¹ Cushing, H., *Surg., Gynec. and Obst.*, 1932, **55**, 1.

² Oppper, L., and Zimmerman, H. M., *Yale J. Biol. and Med.*, 1938, **11**, 49.

³ Vanzant, F. R., and Brown, J. A., *Am. J. Digest. Dis.*, 1938, **5**, 11.

⁴ Ivy, A. C., *Arch. Int. Med.*, 1920, **25**, 6.

⁵ Keller, A. D., *Arch. Path.*, 1936, **21**, 137, 165.

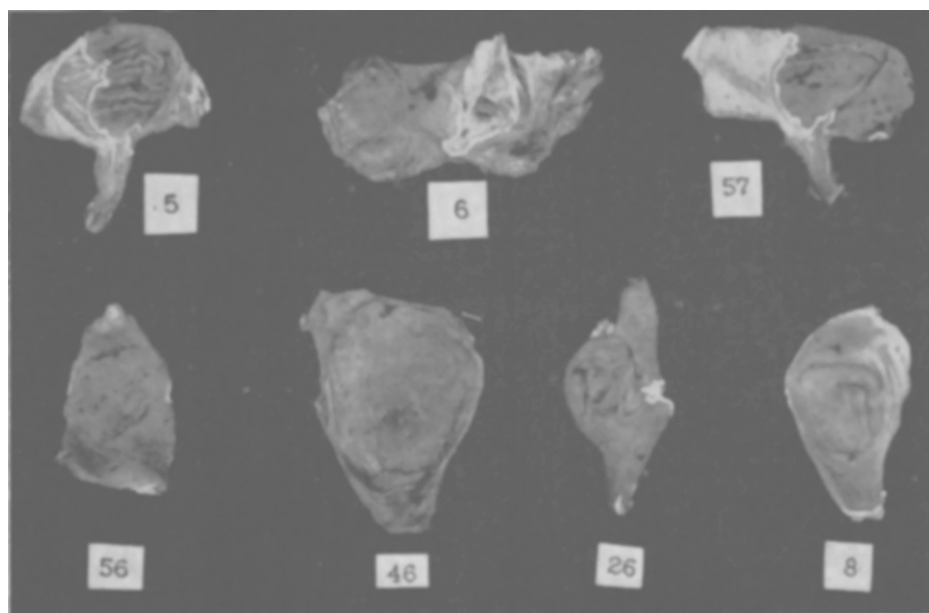


FIG. 1.

Photographs, nearly natural size, of the stomachs of rats submitted to head trauma, showing mucosal hemorrhagic erosions.

been made to strike the rapidly accelerated head against a stationary object, under controlled experimental conditions in both procedures. In 3 out of the 14 cases in which evidence of gastric damage was found the animals had received a single lethal impact; all others had been submitted to repeated "subconcussive blows" which were delivered either in close succession, 1 minute apart, or at intervals of from 2 to 6 days. By "subconcussive blow" is meant one the strength of which is insufficient to cause any apparent immediate or late ill effects in a normal animal. As is already described in another report, unconsciousness, at times followed by persistent changes in behavior or by death, was shown with a certain frequency as a cumulative effect of the repeated blows.

As displayed in the specimens shown in Fig. 1, the evidence of damage in the gastric mucosa consisted mostly of a dissemination of tiny hemorrhages which showed a tendency to align themselves along the crests of the gastric plicae. The hemorrhages were in general superficial, and as the mucosa was not depressed or otherwise altered, the resulting pattern, in most of the cases, was that of a simple

hemorrhagic change; definite erosions in the hemorrhagic areas were seen less frequently, and they did not seem to penetrate deeper than the mucosal layer. Formation of erosions without concomitant evidence of hemorrhage was found in one case only (Rat 46), but there were also tiny petechiae in between the erosions and 2 larger hemorrhages could be seen, one at the cardiac and the other at the pyloric region. With the exception of 2 cases (Rats 5 and 6), in which hemorrhages were found both in the stomach and in the prestomach, most of the animals showed the hemorrhages to be confined to the stomach proper, all portions of which seemed to be equally affected. The microscopic picture in the damaged areas was that of small foci of superficial necrobiosis, with obliteration of normal mucosal patterns and widespread infiltration of recently extravasated hematic cells. The blood capillaries, small arteries and veins all showed evidence of marked engorgement, but formation of thrombi was not noticed in any case. There was a certain correlation between the occurrence of the gastric changes on one side, the severity of the trauma and correspondingly of the cerebral damage on the

other. All the animals but 2 were made unconscious one or more times during the course of the experiments and died shortly after as an immediate consequence of the trauma. In one case, (rat 6), the brain damage consisted of extensive contused lacerations, in another (rat 8) a subarachnoidal hemorrhage was found, while in a third (rat 46) multiple petechiae of the ring type were seen irregularly scattered both in the cortex and in the subjacent white matter of the cerebral hemispheres. Various stages of a fundamentally identical neurolytic change affecting, in a disseminated fashion, both nerve cells and nerve fibers, were displayed in almost all of the remaining animals, by present histological methods. If it is true that vagal, sympathetic and parasympathetic stimuli of central origin, (Cushing¹), are responsible for the development of the gastric changes together with more striking disturbances in the circulatory system, the collateral findings of acute pulmonary edema and of petechiae in the serous membranes in 6 out of the 14 animals are significant, emphasizing the role of the neuro-circulatory disturbances elicited by mechanical brain injury. Of these 6 animals, one died 5 minutes after the trauma, another after

8 minutes. These were the earliest casualties showing evidence of gastric damage. Most of the animals displaying a similar finding died between the 1st and the 7th day, and no hemorrhages or erosions were found in the rats dying or killed beyond the 29th day (the majority of the animals). These observations, in agreement with the findings of others, support the opinion most generally accepted (Moritz⁶) that if recovery from the head injury occurs and the acute effects of the gastric changes are survived, the tendency of the latter is toward prompt and complete healing.

Summary. Hemorrhagic changes, less often erosions, in the gastric mucosa were found in a number of rats submitted to blunt impacts on the head, single or repeated, of different intensities and according to different mechanisms. A certain correlation was seen between the severity of the trauma, correspondingly of the cerebral damage, and the occurrence of the gastric changes, which, when the acute effects of the trauma were survived, showed a tendency towards prompt and complete healing.

⁶ Moritz, A. R., *The Pathology of Trauma*, Lea & Febiger, Phila., 1942.

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Experiments on the Sensitizing Properties of Penicillin.

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In the clinical application of penicillin toxic reactions are not very common. Nevertheless, reactions have been observed which are at least suggestive of an allergic manifestation. Keefer and associates¹ stated that in the treatment of 500 cases with penicillin toxic effects were rare, though occasional chills with fever, headache, and flushing of the face, muscle pain and constriction of the chest, and

urticaria have been noted. Cohn² reported no toxic effects in a series of 48 cases, while Dawson and Hobby³ observed occasional instances of various reactions in a series of 100 cases. Usually the toxic reactions were of a mild nature. Urticaria was recorded in 3 cases. In discussing toxic reactions from penicillin, Lyons⁴ noted urticaria with fever

¹ Keefer, C. S., Blake, F. G., Marshall, E. K., Jr., Lockwood, J. S., and Wood, W. B., *J. A. M. A.*, 1943, **122**, 1217.

² Cohn, A., Studdiford, W. E., and Greenstein, I., *J. A. M. A.*, 1944, **124**, 1124.

³ Dawson, M. H., and Hobby, G. L., *J. A. M. A.*, 1944, **124**, 611.