NEUROSURGICAL PATHOLOGY

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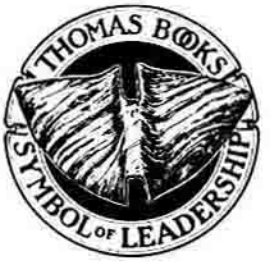

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NEUROSURGICAL PATHOLOGY

DEDICATED TO

MARY MATTHEWS SCHEINKER

MY WIFE

WITH GRATITUDE AND AFFECTION

PREFACE

NEUROSURGERY, a field of medicine which was little specialized only a few decades ago, is today a field of major specialization. Much of the rapid development of neurological surgery is due to Harvey Cushing's perfecting of neurosurgical techniques and to the genius and industry of his pupils. The discovery and development of ventriculography by Dandy and the establishment by Bailey of a newly oriented classification of intracranial tumors are but two of the milestones in the rapid evolution of neurosurgery.

Treatment of mental disorders with "psychosurgery" (prefrontal lobotomy), though still in its infancy, heralds a promising era of future achievements. Its foundation is laid; its promise awaits fulfillment.

With respect to the problem of intracranial tumors, three successive stages mark the development of neurosurgery. When *recognition* of the presence of a tumor was the major problem, physicians were content to differentiate a tumor from other pathologic conditions of the brain. The subsequent rapid development of cerebral physiology enabled neurosurgeons to concern themselves with tumor *localization*. It followed that localized brain tumors were removed with increasing frequency and with steadily improved results. In a number of cases, however, (according to Bailey, in 15 to 20 per cent), exact localization of the cerebral neoplasm continued to be hazardous. But both recognition and localization of cerebral neoplasms were considerably furthered with Dandy's discovery of ventriculography.

Cushing and Bailey were the first to stress the primary importance of preoperative knowledge of the biologic pecularities of each type of tumor. The introduction of the histogenic principle in tumor classification by Cushing and Bailey, and subsequent contributions made by Globus, Kernohan, Marburg, Penfield, Roussy and Oberling, not to mention others, added much to the understanding of the pathology of brain tumors.

Even so, postoperative prognosis was uncertain. There are, on the one hand, many instances of a benign tumor (a meningioma)

CONTENTS

CHAPTER III TUMORS OF THE NERVOUS SYSTEM: INTRACRANIAL TUMORS

"It goes without saying that the more intimate knowledge the neurosurgeon has of the pathology of the lesion with which he is called upon to deal, the more intelligently he will approach this problem."

—Bailey and Cushing: *Tumors of the Glioma Group,* 1926, p. 167

"As is our pathology, so is our practice."

—Osler

CHAPTER I

CEREBRAL SWELLING

Introduction

THE appalling frequency of cerebral swelling in neurosurgical practice dealing with brain injuries, cerebral neoplasms or brain abscess gives special significance to the study of this condition. Neurosurgeons have long realized that swelling often is the greatest obstacle to the exact localization of brain tumors. The operability of a cerebral neoplasm cannot always be determined with certainty from its histopathologic structure alone. The presence of swelling may at times be of greater significance for postoperative prognosis than is the structural character of the tumor itself.

Clear understanding of the histopathology and physiology of brain swelling is of paramount importance, for postoperative prognosis frequently depends upon it more than upon any other single factor.

The paucity of histopathologic studies concerning the problem of cerebral swelling is surprising. Moreover, the terms cerebral swelling and cerebral edema are used by both clinicians and pathologists with quite different connotations. There is great diversity of opinion as to what histologic changes characterize cerebral swelling, and any attempt to group such descriptions as are

available results in apparent confusion. Until relatively stable histopathologic definitions are established, this confusion will persist.

History

The term cerebral edema is one of long usage. Local edema of the brain has long been recognized as occurring in the vicinity of cerebral neoplasms and abscesses. Diffuse cerebral edema, on the other hand, has been reported in such diverse conditions as cerebral vascular accidents, uremia, severe intoxications and in status epilepticus.

Anton (1904) defined cerebral edema as an increase in volume of the brain secondary to an increase of fluid in the perivascular and pericellular spaces. Reichardt (1905) was the first to introduce the concept of cerebral swelling ("Hirnschwellung") as a specific reaction of nerve tissue. He defined it as an increase in brain volume, not due to hyperemia or to excess of free fluid. According to Reichardt, the brain is considered swollen when the difference between brain volume and skull capacity is less than 8 per cent. (The normal correlation between brain volume and skull capacity was first established by Rieger in 1885.)

The relation between brain tumor and cerebral swelling and edema has been the subject of many papers, most of which are in German (Stengel, 1927; Spatz, 1929; Fünfgeld, 1930; Jaburek, 1936; and Scheinker, 1938). Spatz came to the conclusion that true swelling of the brain is of common occurrence in cases of cerebral neoplasm, and is the direct cause of increased intracranial pressure. He also expressed the opinion that a distinction should be drawn between cerebral swelling and cerebral edema. It must be noted that in English and American literature the concept of cerebral swelling, as distinct from cerebral edema, does not exist; in fact, cerebral edema is the only term in common use. In French articles the two terms appear to have been employed indiscriminately, and Le Beau (1938) was of the opinion that it was not possible to make a distinction between them. His conclusions, however, were based entirely upon a gross study of the brain.

Until recently, cerebral swelling was considered as a pathologic reaction of the brain without any evident histologic changes.

In a series of cases of cerebral swelling the only abnormal findings noted by Wohlwill (1914) was the presence of Alzheimer's ameboid glial cells. Spatz (1929), too, was unable to find any definite histologic alterations characteristic of brain swelling. Only in some of his cases did he observe swelling of the processes of the astrocytes in the white matter and signs of clasmatodendrosis. In a clinical review of the subject, Pette (1938) stated that, to date, investigations into the problem of the histopathology of cerebral swelling had proved unsuccessful.

The first attempt to outline the characteristic histopathologic fea-

tures of brain swelling was made in 1938 (Scheinker). In subsequent papers (1941 and 1945) the author repeatedly emphasized that, despite the histologic difference between cerebral swelling and cerebral edema, the two conditions are actually two stages of the same biologic process. Both pathologic conditions include morphologic signs of vascular alterations with increase in permeability of the vessel walls. It was concluded that circulatory disturbances are essential to the pathogenesis of both cerebral swelling and edema.

In cases of cerebral edema associated with brain tumors, Greenfield (1939) described degeneration of myelin sheaths and varicosities of axis-cylinders, swelling of astrocytes and slight proliferation of microglia. Kernohan (1943) came to the conclusion that increased intracranial pressure is the direct result of edema which, in cases of brain tumor, may either remain local or be generalized throughout the whole brain. He accepted the view that edema is caused by circulatory disturbances resulting in hypoxia and acidosis of the brain tissue.

Histologic study has been supplemented by relatively few physicochemical and experimental investigations.

The relationship between the wet and dry weight of the brain tissue was studied by Alexander and Looney (1938). They concluded that edema is confined almost entirely to the white matter of the brain. The gray matter of edematous brain disclosed the normal ratio between wet and dry weight.

Very significant contributions to improved understanding of both the histopathology and the physiology of cerebral edema are the experimental studies by White, Brooks, Goldtwart and Adams (1943) and the recently reported study made by Prados, Strowger and Feindel (1945).

Definition and Terminology

A thorough study of a large number of cases seems necessary to bring order out of the chaotic diversity of opinions and findings relating to the pathology and pathogenesis of cerebral swelling and edema. After many years of systematic investigation of the problem, the author reached the following conclusions:

"Cerebral swelling" is the term with which the author proposes to denote the *gross* appearance of a brain characterized by a local or diffuse increase in bulk of one or both hemispheres, *regardless of the underlying histopathologic findings.*

The *gross* findings of "cerebral swelling" are characterized by: (1) increase in brain volume; (2) flattening of the gyri and narrowing or obliteration of the sulci; (3) considerable enlargement of

the central and subcortical white matter with consequent narrowing and compression of the cortical gray; (4) loss of demarcation between white and gray matter; (5) decrease in size or complete obliteration of one or both lateral ventricles; and (6) shift of the

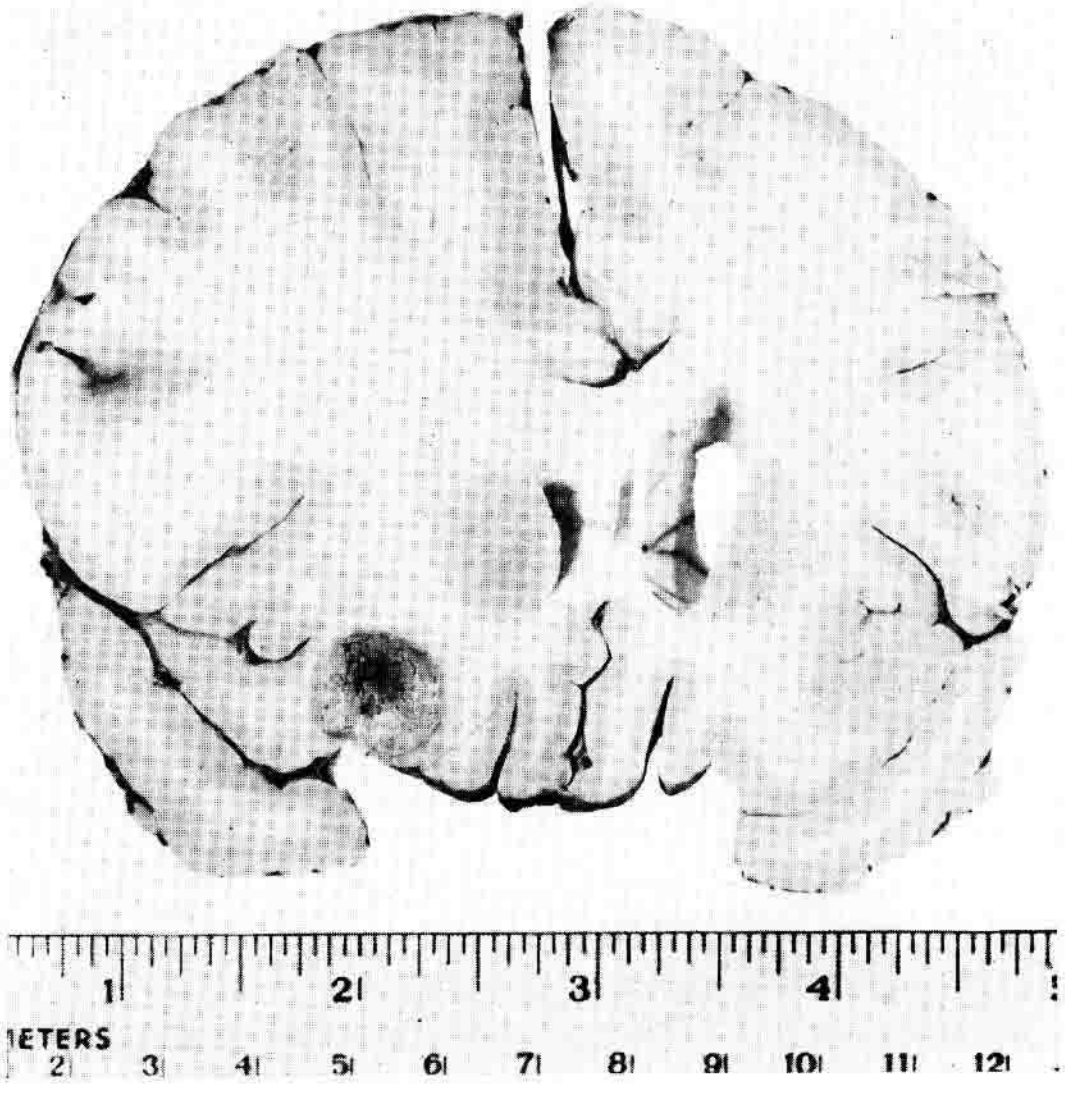

FIGURE 1. Swelling of the right hemisphere produced by a small carcinoma metastasis at the base of the right frontal lobe. Note the considerable increase in bulk of the entire right hemisphere, the enlargement of the white matter and compression of the right lateral ventricle.

midline structures and of the third ventricle from the side of the cerebral swelling toward the opposite hemisphere when the swelling is unilateral (Fig. 1).

It is the author's belief that the condition referred to grossly as "cerebral swelling" is represented microscopically by *three* under-

lying histopathologic syndromes which the author proposes to designate as (1) tumefaction, (2) edema, and (3) liquefaction.

Despite discrepancies in the histopathologic features of the syndromes of cerebral tumefaction, edema and liquefaction, it is quite evident that fundamentally they represent three different stages of the same biologic process; occasionally these stages may merge insensibly with one another.

The three conditions can be differentiated histologically. Criteria for their recognition will be given in detail together with illustrations from representative cases.

I. Cerebral Tumefaction

Microscopic findings characteristic of cerebral tumefaction may easily be overlooked in routine sections stained with hematoxylin and eosin. They are best noted with careful study of silver impregnations, such as Bodian or Bielschowsky stains.

Pertinent histologic findings characteristic of cerebral tumefaction may be summarized thus: (1) *parenchymatous changes* with evidence of swelling of the nerve fibers, myelin sheaths, glia and particularly of the oligodendroglia; (2) *vascular alterations* confined to the small veins and capillaries, characterized by (a) congestion and stasis, and by (b) swelling and degeneration of the endothelial cells. These changes are predominant in the white matter; seldom do they extend into the gray substance.

Preparations stained with hematoxylin and eosin fail, as a rule, to reveal any abnormalities other than a slight degree of tissue rarefaction and congestion, and stasis of the small veins and capillaries with occasional perivascular hemorrhages. Careful analysis of sections impregnated with silver (Bodian stain), however, discloses a tremendous swelling of most of the nerve fibers of the white matter (Figs. 2, 3). More advanced changes are indicated by irregular, ragged outlines of some of the larger axis-cylinders and by the formation of numerous varicosities and end-bulbs. The most obvious swelling of the nerve fibers is noted in sections taken from the central white matter. In most sections taken from the subcortical white matter the degree of nerve fiber swelling gradually recedes in the vicinity of the cortex; the "u" fibers are spared, for the most part, and are of normal appearance.

Changes in the myelin sheaths were studied in sections stained by the Loyez and Spielmeyer methods. Less obvious than those

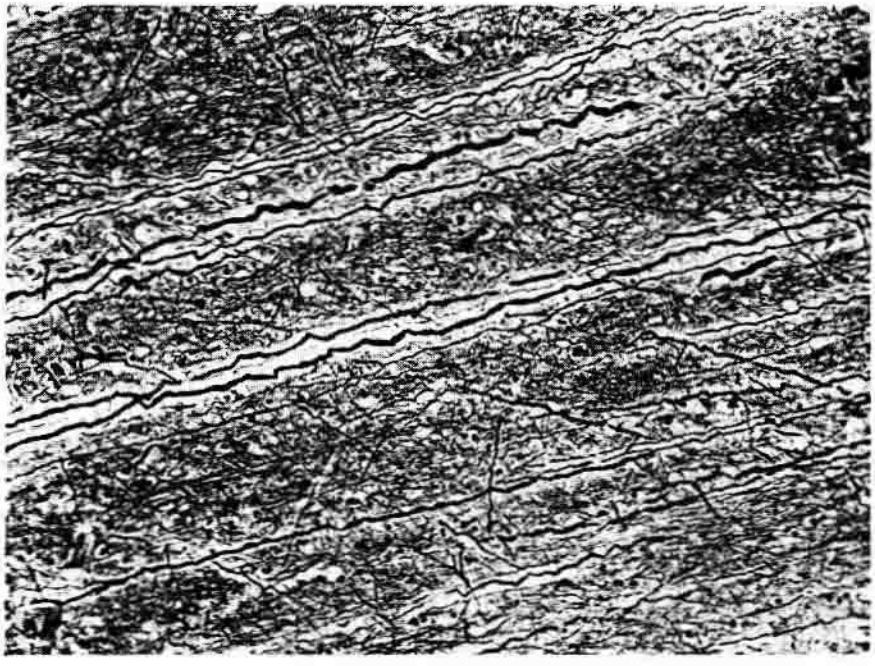

FIGURE 2. Tremendous swelling of the nerve fibers of the white matter. Bodian silver impregnation; × 260.

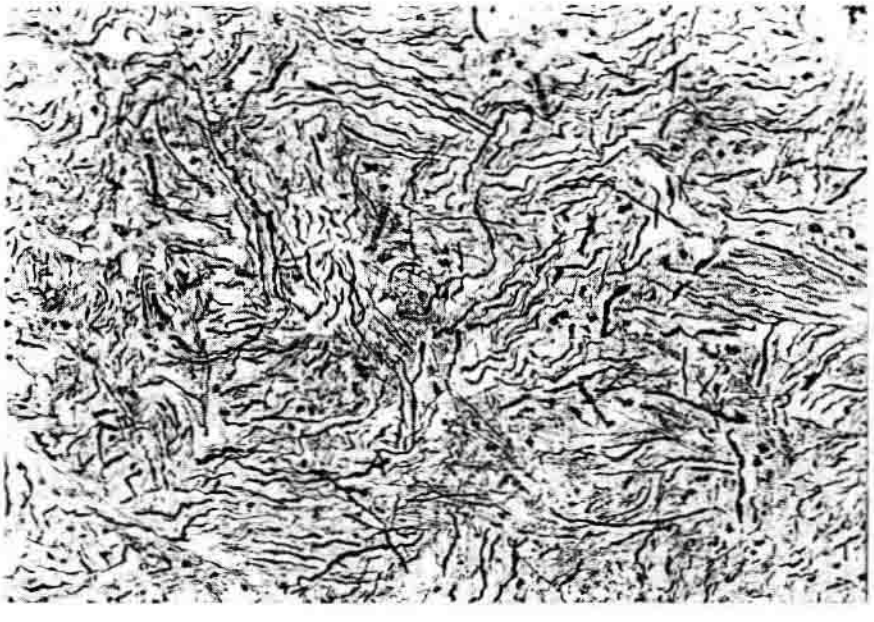

FIGURE 3. Swelling and tortuosity of the nerve fibers. Bodian silver impregnation; × 220.

in the axis-cylinders, they consist of diffuse, irregular swelling and beading of the large majority of myelin sheaths. Occasionally, within some of the myelin sheaths, there are fusiform enlarge-

ments and end-globules, together with black-staining, granular masses. In sections taken from the centrum semiovale there is diffuse pallor of the tissue, with many sheaths unstained and widely separated from each other.

In preparations stained with cresyl violet there is occasional swelling or loss of stainability of some of the nerve cells. All stages of ischemic degeneration, beginning with swelling and chromatolysis and ending with shrinkage, homogenization or complete loss of stainability and formation of "ghost cells," are occasionally present.

Changes of the glia are less conspicuous. There is, however, a moderate degree of swelling of most of the oligodendroglia cells. Some of the cells have a large oval, swollen nucleus and rounded cytoplasm harboring numerous fine granules. The astrocytes appear to be little affected. There are no signs of microglial proliferation.

The distended capillaries and small veins show signs of congestion and stasis. Many of the small vessels are surrounded by small accumulations of extravasated red blood cells.

Striking are the hypertrophic and hyperplastic changes of the capillary endothelium (Fig. 4). The nuclei of the endothelial cells are markedly swollen and the surrounding cell protoplasm occasionally contains a few vacuoles. Many of the capillaries are conspicuous for the increased cellularity of their walls. Actual infiltration with hematogenous cells, however, is not present. Definite signs of degenerative alterations of the capillary endothelium are seldom seen.

II. Cerebral Edema

Whereas parenchymal changes in the early stage of cerebral tumefaction may be easily overlooked unless analysed with special staining methods for nerve fibers and myelin sheaths, the more advanced changes of cerebral edema are quite conspicuous in preparations stained with the routine hematoxylin eosin stain.

Histologic differentiation between the two conditions is relatively simple. Essential criteria for the histopathology of cerebral edema are specified as follows (Scheinker, 1941): (a) alveolar or sieve-like appearance of the nervous tissue; (b) maximal distention

of the perivascular and pericellular spaces; (c) signs of venous congestion and stasis; and (d) evidence of degeneration and necrosis of the endothelium of the capillaries.

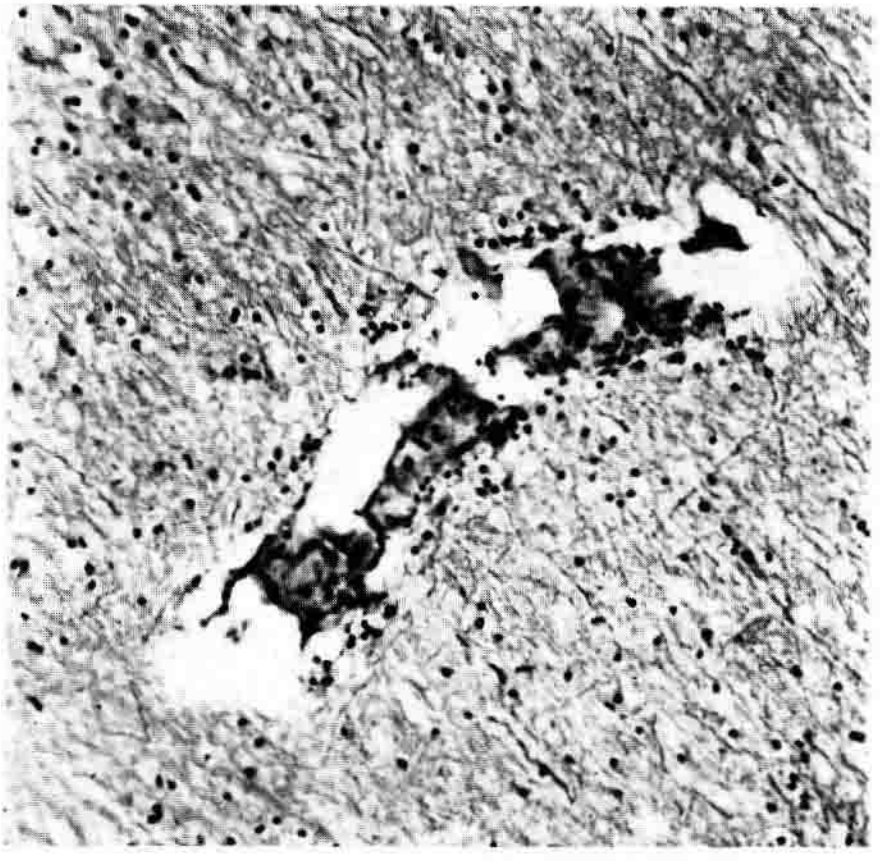

FIGURE 1. Pronounced swelling of the nuclei of the capillary endothelium. Cresyl violet stain; × 220.

There is little doubt that cerebral edema is to be considered as an advanced stage of cerebral tumefaction. The histopathologic process characterizing cerebral tumefaction apparently is the result of an *intra*cellular hydration with consequent swelling of the individual cells and fibers. This process of physicochemical hydration is histologically apparent only when it has attained a certain degree of intensity (which may explain the absence of structural findings, as reported by many workers). The initial stage of intracellular hydration, however, is soon followed by extracellular fluid accumulation together with a tremendous increase of tissue fluid within the interstitial, pericellular and perivascular spaces, resulting in the histopathologic changes characteristic of cerebral edema.

Sections taken from different portions of the centrum semiovale