THE EFFECT OF CORTISONE ON EXPERIMENTAL CEREBRAL EDEMA*

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The medical management of cerebral edema consists mainly of variations of osmotherapy. This is based on the principle that the edema may be relieved by causing a shift of fluid out of the central nervous system. Substances used in this manner have included glucose, sucrose, sorbitol, sodium chloride, urea and concentrated human serum albumin. They have met with varying degrees of success, but none really proved entirely satisfactory.

Early in our experience at the Mayo Clinic with the use of cortisone before and after operations for pituitary tumors and parasellar lesions, we were impressed with the marked improvement in the postoperative course and the relative infrequency of signs and symptoms suggestive of cerebral edema after operation.

In 1952, Ingraham et al.11 reported on the use of adrenocorticotropic hormone and of cortisone in the preoperative and postoperative management of 4 patients with craniopharyngioma. The postoperative course in these cases as in 2 later cases was notably stable and uneventful. Of special interest is their statement that “a particularly desirable effect of cortisone and adrenocorticotropic hormone is the beneficial action on the development of cerebral edema.”

In 1954, Raaf and associates18 reported 18 successive cases of parasellar tumors in which adrenocorticotropic hormone was given before and after operation; they also remarked about the stable postoperative course. They stated, “It seems likely that control of cerebral edema is one of the chief reasons for the smooth postoperative convalescence.” Tytus et al.25 using cortisone in 7 of 21 cases of craniopharyngioma coming to surgery observed similar benefit. The potential risk of cerebral edema because of the salt-retaining properties of cortisone did not occur; on the contrary cerebral edema seemed to be less severe than in other cases both at operation and afterwards. Tytus and associates favored, as a possible explanation, a pre-

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ventive action of cortisone against intracellular water retention. Gurdjian and co-workers\textsuperscript{10} cited an improved mortality rate among patients treated with adrenocorticotropic hormone or cortisone or both.

In 1956, Troen and Rynearson\textsuperscript{24} studied the endocrine status of 153 patients undergoing parasellar operations during the period 1949 through 1953. Sixty patients received cortisone, and 93 did not. The over-all mortality rate was 12 per cent, but it was only 6 per cent among the cortisone-treated patients in contrast to 17 per cent among the others. They concluded that “the improved mortality when cortisone was given preoperatively is not completely explained on the basis of specific replacement therapy.”

Dramatic regression in neurologic symptoms associated with cerebral metastasis from cancer of the breast has been observed after the use of prednisone or prednisolone. Kofman and associates\textsuperscript{44} in reporting such improvement observed reduction in swelling and tension at the site of a temporal decompression during corticoid therapy which recurred on withdrawing therapy. Reduction of cerebral edema and the anti-inflammatory effects of prednisolone are suggested as the beneficial mechanisms.

Reduction of cerebral edema is postulated to explain the improvement when cortisone is administered within 24 to 48 hours to patients suffering from “acute apoplectic strokes.”\textsuperscript{29} Cortisone may play a similar role in the improved neurologic status of patients with tuberculous meningitis\textsuperscript{1,2,8} and Sydenham’s chorea.\textsuperscript{21} Williams\textsuperscript{26} in discussing coma in Addison’s disease stated, “high hydrocortisone or cortisone levels protect against cerebral edema.” Jefferson\textsuperscript{12} and Boudin and associates\textsuperscript{3} cited cases of cerebral edema apparently incident to states of adrenal hypofunction.

Prados et al.\textsuperscript{16} produced cerebral edema by exposing a cat’s brain through a small cranietomary. Noting severe vascular congestion in the tuber cinereum and hypothalamic regions, they postulated that this may result in a disturbed response to stress that contributes directly to cerebral edema. Pursued further, they found that adrenal cortical extract and anterior pituitary extract applied locally reduced cerebral edema as indicated by diminution of visible swelling and trypan blue staining.\textsuperscript{17} Grenell and McCawley\textsuperscript{8} and Grenell and Mendelson\textsuperscript{9} repeated this work and obtained similar results.

Elliott and Jasper\textsuperscript{6} and Elliott and Yrrarazaval\textsuperscript{6} examined the changes in volume in slices of liver and brain suspended in isotonic solution of glucose. Specimens from previously adrenalectomized rats showed a 30 per cent increase in volume compared to 17 per cent for normal rats. Addition of cortisone to the solution prevented this excessive swelling. Robinson and McCance,\textsuperscript{19} using a balanced electrolyte solution, obtained similar results. The erythrocytes also were noted to swell in hypoadrenaline states.\textsuperscript{26}

Adrenalectomy produced a 24 per cent increase in potassium in the brains of rats.\textsuperscript{7} Leiderman and Katzman,\textsuperscript{13,18} using radioactive potassium (K\textsuperscript{42}), found two intracellular fractions of cerebral potassium, one in constant equilibrium with extracellular potassium, the other, a “nonexchange-