DIODRAST STUDIES OF THE VERTEBRAL AND CRANIAL VENOUS SYSTEMS
TO SHOW THEIR PROBABLE ROLE IN CEREBRAL METASTASES*

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The incidence of cerebral metastases is increasing. In Cushing's series of verified intracranial tumors 3.2 per cent were of metastatic origin 9 but more recent reports variously state the incidence as being from 5 per cent to 20.5 per cent, depending in large part upon the source of material and the number of complete autopsies performed. 8 In a series of 1076 verified intracranial tumors reviewed by the writer the incidence of metastatic tumors was found to be 8.4 per cent. Often the various surgical and physical measures directed at the primary lesion are of necessity incomplete and although the subject gains in comfort and his years of life are extended, the possibility of the development of cerebral metastases before his death is increased.

Cerebral metastatic lesions are blood-borne since no lymphatics are present in the brain. 11,15 Moreover, their frequent multiplicity and widespread distribution throughout the brain attest to their vascular spread. 22 Frequently, the cerebral involvement is the only point of implantation secondary to a distant primary lesion. This is difficult to explain on a vascular basis and, although other factors are involved, it would seem that the simple mechanics of hematogenic spread of metastases should be considered first.

The commonly accepted route of the vascular spread of tumor cells to the brain is along the arterial tree. The fact that tumors of the lungs are among the largest contributors to cerebral metastases would support such a consideration since their position allows direct passage of tumor cells to the heart and thence to the brain via the arterial system. 7 The manner in which the pulmonary filter is bridged in cases of blood-borne material from the portal system, caval system and general circulation has not been easily explained. Hence the common expression "paradoxical embolism." Of course, instances of congenital heart lesions would answer this question, and cases of patent foramen ovale and ventricular septal defects associated with metastatic lesions have been described. 21

However, cases of cerebral metastases secondary to pathology in the

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pelvis, or of the genito-urinary tract, in the absence of evidence of metastases to the lung and without patent foramen ovale or other congenital cardiac defects, would indicate that other modes of hematogenic spread must exist. Also, the spread of carcinoma of the breast to the brain in the absence of intrathoracic extension would indicate that other vascular routes are present.

Although Willis in 1664 and Bock in 1823 accurately described the vertebral and cranial venous plexuses\(^\text{12}\) and although von Recklinghausen\(^\text{17}\) in 1885 pointed out the phenomenon of retrograde venous metastases, it remained for Batson\(^\text{5}\) in 1940 to postulate the role of the vertebral venous system in the spread of metastases. By the use of various radiopaque substances injected into the venous systems of human cadavers, he demonstrated roentgenologically the ease with which media could pass along the vertebral venous system, its close association with the veins of the body wall, pelvic and shoulder girdles and finally, its continuity with the venous sinuses within the cranium. Similar cadaver studies were repeated by Collis\(^\text{1}\) in 1944 and he presented clinical evidence which implicated the vertebral venous system as a mode of spread of cerebral metastases complicating various forms of intrathoracic suppuration.

In 1941, Harris\(^\text{15}\) reviewed previously known anatomical facts regarding the spinal and cranial venous systems and emphasized that the anatomical conditions were well documented but that the clinical pathological implications had not been recognized. Recent dissection studies by Anson et al.\(^\text{2,3}\) with attention directed to the pararenal venous system have indicated the close relationship of this venous complex with the vertebral venous system. They pointed out the avenues of possible hematogenic migration through the renal, lumbar, intervertebral veins and vertebral plexuses to the spongyous bone of the vertebrae; or, upward along the vertebral venous system to the dural or diploic veins of the cranium.

The pathological evidence that tumor cells in general tend to invade adjacent veins and that their venous spread is a common occurrence has been emphasized by Willis\(^\text{20}\) and others. Further, it is known that venous emboli frequently move in a direction opposite to that of their usual flow. This is particularly true in the vertebral veins where there is an absence of valves.\(^\text{6}\) There is a tendency toward stasis in the multiple sinuses of this system where there are frequent reversals of blood flow as a result of postural changes and variations in intrathoracic and intra-abdominal pressures.

By the employment of diodrast (3,5-diido-pyridone-N-acetic acid and diethanolamine) and newer injection techniques it was believed that (1) the cadaver experiments could be repeated and (2) that similar studies could safely be performed on living subjects to determine whether venous patterns obtained in cadaver studies would be found in the presence of normal circulating mechanisms. To this end, employing a 52\(\frac{1}{2}\) per cent diodrast solution, a series of 12 cadaver studies were made and 22 injections in living humans were performed.