The dysraphic states

from syringomyelia to anencephaly

W. James Gardner

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Foreword

W. James Gardner, M.D., a neurosurgeon, is a scientist whose training, practice, and interests encompass a wide range of disciplines. His talents, joined with a constantly inquiring mind, seemingly boundless energy, and a fair amount of serendipity, have enabled him to bring to fruition his investigations of several neurosurgical problems. The goal of one of his career-long pursuits has been the unraveling of the mystery of the dysraphic states.

The theory of hydrocephalomyelia as the pathogenesis of dysraphism is undoubtedly his most significant contribution. This work began from observations of surgical findings in adult patients with syringomyelia. The author's ability to translate observations at the operating table and bedside into fruitful avenues of investigation has amazed and has won the admiration of a long succession of neurosurgical residents. Doctor Gardner has repeated-

ly pointed out to his students that the surgeon has the unique opportunity to observe the pathophysiology of disease processes in the living state. Unlike the surgeon, the internist must be content with observations during physical examinations and results of laboratory reports, the radiologist with review of roentgenograms, the pathologist with study of necropsy material and biopsies, the physiologist with observations of human or animal behavior, and the embryologist with study of normal and deviant development. The surgeon may enhance his knowledge from observations made at the operating table by utilizing studies from these disciplines; the nonsurgical specialist seldom has the opportunity to observe pathology in vivo.

Firmly ensconced in the medical literature, the older theories of the pathogenesis of dysraphism challenged the author to prove his concept correct. Doctor Gardner, utilizing clinical studies as well as expertise in physics, physiology, embryology, anatomy, and ultrastructure, has gradually built a sound and plausible explanation of the mechanism of dysraphism. Most investigators now accept his hypothesis that the cause of syringomyelia is a malformed hindbrain, and that 'syringomyelia is symptomatic hydromyelia'. It is most gratifying to his former students and, of course, to Doctor Gardner himself, to realize that more and more his theories are becoming widely accepted.

However satisfying acceptance of theories might be, it is doubly rewarding to know that this endeavor has opened new therapeutic approaches for patients with syringomyelia, diastematomyelia, Arnold-Chiari malformation, and other related forms of dysraphism. Diagnostic procedures and surgical treatment founded on a more rational basis can now be offered to these unfortunate individuals.

Whatever the reader's convictions, I know that he will admire this monograph as the culmination of a career's effort. He will be impressed by the logic of the argument and the clarity of the exposition. What he will not know is the toll of hard work, dogged determination, and the unfailing search by the author for new and more convincing evidence. Each reader will benefit by a profound understanding of dysraphism.

DONALD F. DOHN, M.D.

'...*in every... art, fundamental matters are perennially being discovered, discredited, forgotten, rediscovered and reaffirmed.*'

JOHN HOMANS (1936)

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Introduction

In medicine it is an accepted principle that a theory which attributes a single cause to a disease process is more likely to prove correct than one which implicates several causes; and further, that there is no more effective way to stifle thinking concerning a disease process than to apply to it some vague, possibly misleading title, such as 'dysraphia'. Whereas 'araphia', meaning non-closure of the neural tube, constitutes an anatomic entity, 'dysraphia', implying faulty closure, is purely hypothetical.

The purpose of this monograph is to point out that all dysraphic states, with their accompanying distortions and adhesions to surrounding non-neural structures, may be explained on the basis of a single factor — inadequate escape of cerebrospinal fluid at various stages of embryonal and fetal development.

During internship I was assigned my first case of hydrocephalus

with meningocele in an infant. This combination suggested that there must be a causal relationship between these two abnormal collections of fluid. A study of the subject disclosed that 200 years ago, Morgagni (1769), unencumbered with the knowledge that the sac of the myelocele consists of an open neural tube, naively concluded that these watery tumors of the vertebrae resulted from the pressure of fluid descending from the hydrocephalic head through the tube of the spine and pressing the bones asunder. More than a century later, this hydromyelic theory of Morgagni (1769) was discredited by Von Recklinghausen (1886). Because his microscope revealed an open portion of the neural tube within the sac, he stated that it was the result of failure of the neural tube to close. Since then, Von Recklinghausen's belief has been confirmed repeatedly, albeit by investigators who based their studies upon this idea. This concept undoubtedly is correct in some instances. However, it does not explain how a neural tube that fails to close can become overdistended, as is so frequently the case in most of these states. Therefore, in these instances, Morgagni's disruption hypothesis surely merits reconsideration. Furthermore, his theory will explain every feature of the distorted anatomy, not only of myelocele and its associated hindbrain hernia, but also of related malformations ranging from syringomyelia of adulthood to diastematomyelia of adolescence, to congenital hydrocephalus, to meningocele, to encephalocele, to iniencephalus, and finally to anencephalus of the stillborn. In each of these dysraphic states, except the last, not only is the central canal often overdistended, but the same may be said of the bony canal. Such distention may be expected, since the central nervous system originates as an ectodermal invagination surrounding a cavity which has no outlets, but into which fluid is secreted. The fluid must establish its own means of returning to the circulation. This it accomplishes by dissecting a phylogenetically false passageway (i.e., unlined by epithelium) through the surrounding mesenchyme. It is not surprising that this means of escape is sometimes inadequate.

Still another axiom in medicine is that to obtain a proper perspective of a disease process, one should begin with the study of its early or mild stages, and then progress to the later and more severe. In congenital malformations, compared with acquired diseases, this sequence is reversed. Here, the severe forms such as myelocele are obvious at birth, whereas the milder forms become symptomatic either in adolescence as, for example, in diastematomyelia, or in adult life as in syringomyelia. By serendipity, it was my privilege to establish that the cause of syringomyelia is not in

the spinal cord but in the malformed hindbrain; that syringomyelia is merely symptomatic hydromyelia. Further investigations disclosed that the adult with syringomyelia may have all of the anatomic abnormalities present in the infant with myelocele, except an open neural tube; and that the same is true of the adolescent with diastematomyelia. Naturally, these abnormalities are less severe, less frequent, and less readily demonstrable in these milder forms of the dysraphic states.

History has shown that those who have excessive faith in their own theories are not only poorly prepared for making discoveries, but they also make poor observations (Bernard, 1865). They observe with a preconceived idea, and often neglect important facts which do not further their aims. It also happens quite naturally that those who believe too firmly in their own theories do not believe enough in the theories of others. Their dominant objective is to find the theories of others in error and to try to contradict them. At the same time, they choose only those observations that suit their objective, neglecting whatever is not related to it, and carefully setting aside everything which might tend to refute it.

I am quite aware that I may believe too firmly in my own ideas; of that each reader must judge for himself. However, I am encouraged by the fact that nothing is more practical than a good theory that proves to be correct.

CHAPTER I

Embryology

The neural tube is derived from the ectodermal layer, the primordial function of which is to form an impervious covering of skin, in order to conserve water and solutes, particularly plasma protein. Closure of neuroectoderm to form this tube begins in the cervical region and progresses in both directions like the closing of a zipper (Fig. 1). The anterior neuropore closes at the 25th day, by which time the heart has begun to beat; the posterior neuropore closes at the 29th day forming a closed, continuous cavity that constitutes the primitive ventricles and central canal of the cord. Approximation of cutaneous ectoderm occurs only when and if the converging edges of the neural groove come together to form this tube. The original continuity between cutaneous and neural ectoderm is then interrupted by invading mesoderm.

Weed (1917) studied the development of the neural tube in living

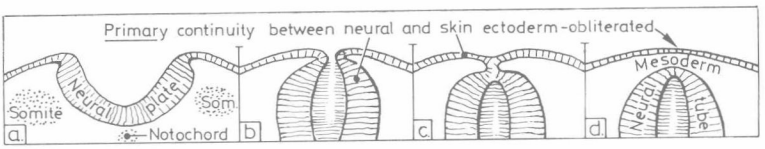

Fig. 1. Normal: closure of the embryonic neural tube. (Reproduced from D. H. Padget, *Johns Hopkins Medical Journal*, 1968, *123*, 233. By courtesy of the editors).

pig embryos by irrigating it with a solution of potassium ferrocyanide and iron ammonium citrate and, following a period of incubation, precipitated crystals of prussian blue by fixation in an acid medium. His studies showed that immediately after closure the neural tube is filled with a protein-rich fluid. Since this early cerebrospinal fluid is present before the choroid plexus appears, it may represent primitive blood plasma not yet enclosed by the immature capillaries. Kappers (1960) believes it collects in the neural tube by a process of transudation through ependyma. Coincident with the first tufting of the choroid plexus of the fourth ventricle, the neural tube begins to distend and the protein content of the fluid diminishes, constituting the earliest evidence of the blood-brain barrier to plasma protein. This protein-diluted fluid first begins to filter through a permeable area in the rostral portion of the rhombic roof anterior to its choroid plexus, Weed's area membranacea superior (AMS) (Fig. 2A, B, C). The anterior choroid plexus then appears, accompanied by further distention of the neural tube, with which a second permeable area appears caudal to the choroid plexus of the fourth ventricle, Weed's area membranacea inferior (AMI). Simultaneously, the AMS begins to thicken and forms the anlage of the cerebellum, including its anterior and posterior medullary vela. Meanwhile the AMI becomes increasingly permeable, and the fluid escaping from it dissects open the subarachnoid space and its arachnoid villi (Fig. 2D, E).

Weed's illustrations indicate that the lumen of the primitive central canal, originally oval or circular in cross-section, becomes slit-like as the subarachnoid space develops and the lateral plates thicken (Fig. 2F). At this stage, the head of the embryo resembles a translucent bubble about to burst. Since the distention involves also the central canal of the primitive cord, it follows that both hydrocephalus and hydromyelia are physiological in embryonal life. Because of increasing permeability of the rhombic roof, this obstructive (internal) stage of hydrocephalomyelia becomes com-

municating, i.e., external. Then as the 'escape valves' of the arachnoid villi are dissected open, this communicating stage, in turn, becomes compensated. This physiological compensation happens well before the permeable AMI perforates to form the foramen of Magendie. This is a critical time for the developing embryo. As Weed pointed out, if for any reason the rhombic roof does not become adequately permeable at this stage, fluid will not escape in quantity sufficient to effectively dissect open the subarachnoid space. In this case, even though the roof subsequently does perforate (rupture) to form the foramina, the communicating stage of hydrocephalus may persist. Thus more than half a century ago, Weed explained not only the mechanism of congenital hydrocephalus, both obstructive and communicating, and why both forms often coexist, but his demonstrations also showed why hydrocephalus developing at this stage usually is accompanied by hydromyelia. By the same token, if hydrocephalus with hydromyelia is found postnatally, and particularly if the outlets of the fourth ventricle are unperforated, this represents not some new condition, but the persistence of a state that is normal in fetal life. Dohrmann (1970), in a comprehensive review, described the embryonic development of the choroid plexus. He found that it appeared first in the fourth ventricle, then in the lateral ventricles, and lastly in the third. He described the macroscopic, microscopic, and ultramicroscopic appearance of the choroid plexus, the tufted and ciliated surface of which makes up about 63% of the ventricular surface. He pointed out that ventricular fluid constitutes a secretion, since its chemical content shows that these cells do work to produce it. The total osmotic pressure of the CSF he found to be identical with plasma as estimated by the freezing point method.

Pathologic embryology

In supporting the failure of closure concept as opposed to rupture, Boulter (1967) pointed out that myeloschisis has been found in some embryos before there is a choroid plexus to secrete the fluid necessary for rupture. He overlooked the fact that primitive CSF collects within the neural tube before the choroid plexus appears (Weed, 1917). Should this fluid accumulate too rapidly or escape too slowly, overdistention will be inevitable. As in an overinflated inner tube, a localized bulging, i.e., an embryonic syringomyelocele, probably precedes external rupture. Because of the delicacy of the tissue, the bulging stage must be very transient and mild in degree. Although failure of closure unquestionably is an embryonic entity,