THE CEREBELLUM IN CHILDREN

WITH MENINGOMYELOCELE

by

Sadick Variend

A thesis submitted to the Faculty of Medicine of the University of Cape Town for the degree of Doctor of Medicine, the result of work carried out in the Department of Pathology of the Children's Hospital, Sheffield, England.

November, 1977

PREFACE

We are now approaching a century since the first recognition of the hindbrain deformity associated with neural tube malformations. The considerable speculation and confusion which still exists regarding the nature and pathogenesis of this hindbrain deformity is evidence of the amount of progress made in this field.

Widespread population screening using maternal serum α-feto-protein will almost certainly reduce the number of children born with these malformations. However, this should not be allowed to detract from continued effort to unravel the important problem of pathogenesis of the hindbrain deformity. Examples of the deformity will continue to be found albeit in lesser degrees of neural tube malformations, and occasionally in adults with apparently normal spines. It is also a sound medical concept that the best form of cure is prevention and certain ethical considerations will continue to pervade the issue of therapeutic abortion consequent upon screening results.

Also, there are probably many like myself who believe that locked in the puzzle of this hindbrain deformity are important biological insights that far outweigh the significance of the condition itself. This study strives to solve the riddle of pathogenesis and, by clearing our understanding of its nature, it is hoped that more effective therapeutic measures will evolve for those children who will continue to be born with the malformation.

ACKNOWLEDGEMENTS

I am indebted to Professor J. L. Emery for his encouragement and valuable advice during the preparation of this thesis.

I am also indebted to Jean Baddeley for her patience and expertise in preparing the many histological sections required, and to Mr. Tunstill and his staff of the Photography Department for producing such good quality prints.

Finally, my thanks are also due to Mrs. B. P. Wilson for her patient typing of the manuscript.

SUMMARY

The surface anatomy of the cerebellum was studied and analysed in 100 cases of children with meningomyelocele. The study dealt with the superior surface, ventricular surface and the segment displaced into the cervical canal. A histological survey of a mid-sagittal section from each cerebellum was also performed.

It was found that the degree of infraforaminal cerebellar dislocation was extremely variable ranging from no displacement to one which was considerable. Milder degrees of displacement found in these children seem to correspond to the malformation as described in adults; other features common to both these age groups suggest a similar pathogenesis.

Histology of the mid-line sections showed the most significant changes in the caudal lobules and suggest that these are secondary to ischaemia from tissue compression in the foramen magnum and bony compartment of the upper cervical canal. It is argued that these changes are probably of relatively late occurrence, as are the cystic dilatations described in the fourth ventricle.

The key to the pathogenesis is most likely to be found in earlier alterations which include fissural changes on the superior surface and elongation of the ventral lobules. It is concluded that the cerebellum is primarily deformed as a result of a "pulsion-traction sequence". The cerebellum is probably mildly displaced at an early stage, possibly due to collapse of the

embryonic neural tube secondary to tubal rupture. The resultant obliteration of the cisterna magna interferes with normal formation of the basal foramina.

Cerebrospinal pubatile forces cause a caudal cystic prolongation of the intact rhombic roof which exerts a simultaneous traction of the early caudal lobules; the ventral lobules are the first to develop and therefore, the most severely deformed.

Abnormal fissuration of the superior surface is described and explained as secondary to growth within a confined space as well as differential growth within the organ itself. The fact that this occurs despite probable patency of the tentorial notch raises the possibility of concomitant prenatal forebrain hydrocephalus obstructing the tentorial "outlet".

INDEX

INTRODUCTION

That the problem of failure of fusion of the spine as a congenital human anomaly has afflicted man since the Palaeolithic age is emphasised in a recent report by Ferembach (1963). Hippocrates recognised water in the head but had no notion of the ventricular system (cited by Boulter, 1967). Morgagni (1769) was the first to associate hydrocephalus with the sac of meningomyelocele in infants.

It is now well known that the Arnold-Chiari malformation of the hindbrain is a common accompaniment of meningomyelocele and related spinal defects. Its association with hydrocephalus is now well established. Less certain, however, is the precise role it plays in the pathogenesis of hydrocephalus. For instance, whether it results from the hydrocephalus or is the cause of it, is still not entirely settled.

The majority (about 60%) of congenital abnormalities have no clear cut aetiology (Claireaux, 1970). Well over half of all major malformations involve the central nervous system; these are mainly anencephalus and meningomyelocele.

Congenital abnormalities account for 15-20% of infant mortality in the Western world. In spite of modern advances in other branches of medicine, no significant decrease in the incidence of congenital abnormalities has occurred in the last decade.

The incidence of "neural tube defects" in England and Wales

..../2

is estimated at 1 in every 2,000 live births. Thus, approximately 1,500 affected babies are born each year. Although the precise aetiology is unknown it is thought to be multifactorial, having both genetic and environmental components (Carter, 1971). There has been an increased survival of children with meningomyelocele over the past few decades and this may be attributed to recent advances in fields such as paediatric surgical management, neonatal anaesthesia, early surgical closure of the spinal defect, antibiotics, and the introduction of various shunting devices to relieve the frequently associated hydrocephalus.

However, within recent years has come the realisation that the quality of survivors was far from reaching initial expectations (Department of Health and Social Security, England, 1973). Apart from defects of locomotion, there were the physical handicaps of hydrocephalus, defects of sensation, scoliosis, pathological fractures, disorders of the urinary tract and faecal incontinence. As expected, the social and emotional problems for the family with an affected child are considerable. The cost of maintaining the special units to care for these children, to educate the survivors and to house them separately are inordinately high (Lightowler, 1971). It has been estimated that, of those who survive to school age, about 60% require special education, 30% in schools for the physically handicapped.

Surgical closure of the spinal defect is sometimes accompanied, or more usually followed, by the problem of hydrocephalus, the treatment of which is usually based on the

principal of by-passing the obstruction. Despite great advances in development of such by-passing devices, mortality in shunt-treated children still approaches 3% a year (Lorber, 1971). This continuing mortality necessitates frequent reappraisal of current therapeutic measures. It is conceivable that, in the forseeable future, there will be a return to a more direct surgical approach on the hindbrain malformation; Russel and Donald (1935) recommended occipital decompression and pointed out that the only previous report of a surgical attack on the condition was that of van Houweninge Graftdinjk (1932); the operation had a fatal outcome. However, before such ideas are put into practice it would be advisable to delineate more precisely the pathology of the hindbrain deformity as well as the exact relationship between it and the hydrocephalus.

A new advance in this field has come with the discovery of raised levels of α-fetoprotein in the amniotic fluid of mothers bearing a foetus with an open neural tube defect (Brock and Scrimgeour, 1972). Apart from amniotic fluid, it is possible to use maternal blood; a raised serum level of α-fetoprotein permits one to select mothers at risk for amniocentesis. This measurement is possible in the fifth month of pregnancy and would permit affected foetuses to be selected for abortion.

Until recently, such estimations were usually only performed on women at risk, i.e. those with a history of an affected pregnancy. However, screening of all pregnancies has become possible in certain districts and a more substantial decrease in the number of deformed children might be expected. A large-scale

screening service of this type carries, inevitably, the disadvantage of enormous cost and there are certain very significant ethical considerations which cannot be entirely disregarded. In the meantime, babies with meningomyelocele and related defects will continue to be born, and the problem of their management and care will continue, albeit on a smaller scale.

The literature on the Arnold-Chiari malformation is extensive. Past studies have usually considered the malformation as a whole and the cerebellum has not previously been studied as an isolated unit; it could be that such a study might add information which has eluded a more general approach to the subject.

This study involves 100 cerebellums in children with meningomyelocele. An attempt has been made to delineate more precisely the role played by the cerebellum in the malformation, and to see if the controversial issue of the pathogenesis of the Arnold-Chiari malformation could be more satisfactorily resolved.

PATHOGENESIS OF THE MALFORMATION:

A Review of Current Theories

Introduction

Because of the profusion of literature in this field dating back to the middle of the last century, any complete account of pathogenetic theories relating to the Arnold-Chiari malformation must inevitably include a historical review. The frequent association between this malformation and some forms of spinal defect, mainly meningomyelocele, makes it useful also to incorporate some aspects of pathogenesis relating to this part of the deformity.

In 1883 Cleland described the autopsy findings in an infant with a hindbrain malformation in which the brain stem was elongated and the fourth ventricle extended well down into the cervical canal. He concluded that primary dysgenesis of the brain stem was responsible for this human malformation. Hydrocephalus was discounted as a causative factor and was thought to be of later origin.

Nine years later Chiari (1891) described three types of hindbrain anomaly associated with hydrocephalus. His Type 1 anomaly showed dislocation of the cerebellar tonsils into the cervical canal; the abnormality was restricted to the cerebellum. "The first type consists of elongation of the tonsils and the medial portions of the lobi inferiores ... of the cerebellum into conical extensions that accompany the medulla oblongata and extend into the vertebral canal...". In the Type 2 there was caudal dislocation of the cerebellum together with elongation of the fourth ventricle. "A second type consists of the displacement of portions of the cerebellum into the enlarged vertebral canal, the cerebellum lying within the fourth ventricle, which is elongated

..../6

and also extends down into the vertebral canal". In his Type 3 deformity he described dislocation of the entire cerebellum into a cervical meningocele. "Of the third type of consecutive changes in the cerebellum caused by chronic congenital hydrocephalus... I have seen only one case. It demonstrated the greatest degree of displacement of the cerebellum, out of the cranial cavity through the foramen magnum into the vertebral canal ..., involving the deposition of nearly the entire cerebellum which was itself hydrocephalic, into the cervical spina bifida.....".

In his second paper (1895) Chiari enlarged his original description of the Type 2 anomaly to read 'displacement of part of the lower vermis, displacement of the pons and displacement of the medulla oblongata into the cervical canal and elongation of fourth ventricle into the cervical canal'. In his drawing to illustrate the Type 2 anomaly the cerebellar indentation caused by the foramen magnum is just discernible; below this level there is a striking prolongation of the tonsil, uvula, pyramid and tonsils. In general, the Type 2 anomaly occurs in infants with meningomyelocele. Chiari thought that the cerebellum and brain stem were pushed down by the hydrocephalic cerebrum.

Arnold (1894) described multiple abnormalities in a newborn infant. Much of his paper is devoted to details of the viscera and little attention is given to the brain stem; parts of the cerebellum and fourth ventricle were herniated through the foramen magnum, but the medulla appeared normal. Schwalbe and Gredig (1907), working in Arnold's laboratory, added Arnold's name to the Type 2 deformity and coined the term "Arnold-Chiari malformation".

..../7

They further distinguished the cerebellar malformation as Arnold's deformity and the medullary malformation as Chiari's deformity.

Russel first introduced the malformation into the English literature (1935). She added little to the morphogenesis but noted the common association between Arnold-Chiari malformation and meningomyelocele; she suggested that the hindbrain malformation was probably the cause of the hydrocephalus.

Aring (1938) was probably the first to report on an Arnold-Chiari malformation in an adult with a normal spine. His description involved certain histological features which are not relevant to this discussion and it did not contribute to pathogenesis in any positive sense.

Mechanical Theories

The almost constant association between the hindbrain malformation and meningomyelocele led to the proposal that the cerebellum and brain stem are pulled down into the cervical spinal canal. Fixation of the spinal cord at the site of the spinal defect is held to be responsible. Subsequent differential growth between the bony spine and spinal cord causes traction on the cerebellum and brain stem. This theory was first advanced by Houweninge Grafdink (1932) and was subsequently supported by a number of writers. Most notable among these were Penfield and Coburn (1938) and Lichtenstein (1942). Lichtenstein argued that, in many instances, the first cervical cord segment may be displaced as low as the fourth or fifth cervical vertebra. He also emphasised a sudden ascent of the cord when the fixation to the

site of the spinal defect was transected; from this he deduced that the cord must have been under tension.

Ingraham and Scott (1943), in support of this theory, were impressed by the association of the hindbrain abnormality with meningomyelocele in contrast to simple meningocele; they believed that fixation of the spinal cord was not as effective in meningocele; they also felt that until the condition is produced experimentally, it would be unwise to accept traction as the complete answer.

In a later report Bucy and Lichtenstein (1945) described an Arnold-Chiari malformation in an adult without a spinal abnormality; they suggested that even under perfectly normal conditions, "the hindbrain is subjected to a force that tries to draw it into the spinal canal".

Gumberg (1956) produced a spectrum of spinal defects in rats using trypan blue; he noted the presence of a condition resembling the Arnold-Chiari malformation in many of the rats with a myelocele. He found that the frequency of the hindbrain malformation increased with the linear extent of the spinal lesion which led him to speculate that the traction was probably responsible. Recently, several investigators have criticised this theory and there is now much evidence which seriously questions its validity as a genuine cause of the malformation.

Russel (1949) contested this pathogenesis on autopsy evidence of two cases of spina bifida occulta. In one case (her case 23), even though the caudal end of the spinal cord was tethered at the sacral level, there was no evidence of a hindbrain malformation.

Stretching of the cord was evident but seemed to be confined to segments immediately above the site of tethering. Similar findings were present in the second case which also showed hydrocephalus with stenosis of the aqueduct. In another of Russel's cases, i.e. a 27 year old female with a simple meningocele, there was fixation of the cord at the sacral level but an Arnold-Chiari formation was not observed. Malis, Cohen and Gross (1951) stated that this concept of pathogenesis failed to explain the existence in some cases of cerebellar displacement without medullary displacement; it also failed to explain the over-riding of medulla and cervical cord to produce the characteristic medullary kink.

Barry, Patten and Stewart (1957), after careful dissection of two early fetuses with meningomyelocele and an Arnold-Chiari malformation, found that stretching of the spinal cord was dissipated within the segments immediately above the exposed neural plaque; this was based on volumetric measurements of the spinal cord segments at various levels compared with age-matched controls. The course taken by the spinal nerve roots from their origin to the exit foramina was also assessed. Stretching of the spinal cord in this region could not be substantiated by Naik and Emery (1968) who studied the spinal cords of children with meningomyelocele; however, they did find compression of the cervical segments in this study as well as in an earlier one (Emery and Naik, 1968).

Goldstein and Kapes (1966) put the traction theory to test by tying the caudal end of the spinal cord to the level of the first sacral segment in newborn rats. Those who reached adulthood were then sacrificed. As differential growth between the spinal

..../10

canal and the spinal cord also occurs postnatally in rats, the absence of an Arnold-Chiari malformation in the mature animals led them to conclude that traction was an unlikely cause.

Peach (1965) also stressed that in many cases the cerebellar component lies at a lower level than the medulla which would be difficult to explain on the basis of traction alone. Moreover, the occurrence of the malformation with a normal spine would clearly not be compatible with this hypothesis and the explanation given by Bugy and Lichtenstein (1945) (see above) cannot be accepted.

Hydrocephalus as a Primary Cause of the Malformation

That the hydrocephalus might be directly responsible for the hindbrain malformation also needs to be considered. As previously mentioned, this theory was first proposed by Chiari (1895) who believed that the expanding forebrain encroached on the hindbrain structures causing them to be displaced caudally. Margolis and Kilham (1969) were able to produce a cerebellar malformation closely resembling that found in the Arnold-Chiari malformation in suckling hamsters; they injected Reovirus type 1 into 90 two-day old hamsters and the animals were sacrificed at various intervals. Hydrocephalus resulted from ependymitis and narrowing of the aqueduct. In their description of the malformation they state "most of the cerebellum is displaced downward as an elongated conical sleeve-like structure investing the posterior and lateral aspects of the pons, medulla and cervical cord, and extending far through the foramen magnum". This description is well illustrated in their Fig.7 and closely resembles the more

marked degrees of the cerebellar deformity found in the human situation. They attributed the experimentally produced malformation to the concomitant, rapidly evolving hydrocephalus and the postnatal cerebellar growth spurt in the hamster.

If this were the full explanation one would expect to find more severe cerebellar deformities in those children with congenital hydrocephalus but without meningomyelocele. Shillabear and Emery (1975) reported a number of children with hydrocephalus, not associated with meningomyelocele; in many cases the cause of the hydrocephalus was considered to be congenital. In nine cases there was a minor degree of hindbrain anomaly; four of these had a congenital cause. There was no instance of any significant cerebellar displacement (Shillabear, 1975).

It is generally accepted that the main objection to theories implicating "a pushing down from above" is that it does not explain the cause of the foregoing hydrocephalus. In a study of rat embryos with trypan blue induced myeloschisis, a hindbrain malformation resembling an Arnold-Chiari malformation was present in those at twenty-one days gestation; those less than eighteen days with myeloschisis showed no hindbrain deformity. There was no demonstrable evidence of hydrocephalus at any stage (Warkany, Wilson and Geiger, 1958), suggesting that hydrocephalus probably occurs later.

Primary Dysgenesis of the Hindbrain

It has also been suggested that the hindbrain malformation represents a primary developmental arrest. This theory was initially conceived by Cleland (1883). It has recently been

revived by Daniel and Strich (1958); they were impressed by failure of the pontine flexure to develop as well as the intraventricular position of the choroid plexus, features normally found in the embryonic stage. Peach (1965) reviewed the associated anomalies of the nervous system in this condition and also decided that the Arnold-Chiari represented a primary developmental arrest; he concluded that the malformation was failure of the pontine flexure to develop due to a preceding developmental arrest. This led to the medulla and fourth ventricle being herniated into the upper cervical canal.

The Hydrodynamic Concept

As long ago as 1761 Morgagni described several cases of 'spina bifida' and anencephaly which he explained as being secondary to the associated hydrocephalus. This was probably the start of the hydrodynamic concept.

Hydrodynamic theories have recently gained ground and commenced with the idea of Cameron (1957) who believed that the myelocele resulted from failure of closure of the neural groove; this resulted in a fistulous communication between the amniotic cavity and the central canal. When ventricular fluid leaks through the fistula at the site of the spinal defect, there is a disturbance in the balance of pressures between the intracranial and amniotic cavities; the intracranial contents tend to be driven out of the skull secondary to the relative increase in amniotic pressure. VanHoytema and van den Berg (1966) who studied a 140 mm. foetus with 'spina bifida' found undue persistence of the caudal velum which they described as being fairly thick. Their

views on the pathogenesis of the malformation essentially agreed with those of Cameron. They suggested that because the ventricular fluid escapes into the amniotic cavity, pressure in the ventricular system does not increase and results in failure of the caudal velum to perforate.

These theories may be criticised on a number of issues, and one commonly quoted is that Pascal's law states that pressure is transmitted equally in all directions in a fluid-filled chamber. Thus, any increase in intra-amniotic tension would be transmitted equally to the region of the spinal defect as to the region of the skull and, theoretically, no fluid should leak out of the ventricular cavities. Moreover, these theories do not explain the malformation in the absence of a spinal defect.

Williams (1969, 1971, 1975) approached the hydrodynamic concept from an entirely different viewpoint. Basically, he believed the malformation to exist in a relatively minor degree at birth. After birth, crying and feeding movements by way of increased intra-abdominal pressure causes filling of the spinal epidural veins; there is thus a periodic increase in intraspinous pressure. This displaces spinal fluid into the ventricles through the hindbrain malformation which acts as a one-way valve. The resulting hydrocephalus then pushes the hindbrain structures further through the foramen magnum; eventually, obstruction at the foramen magnum is complete and the valve effect ceases. He supported his idea with manometric studies in which he demonstrated a rise in intraventricular pressure by compressing the abdomen and meningomyelocele sac. Compression of the skull did not produce the reversed effect.

Hydromyelia and syringomyelia are cord abnormalities commonly encountered in children with meningomyelocele (Lichtenstein, 1942; Cameron, 1957); they are also described in adults with the hindbrain malformation in the absence of a spinal defect (Gardner, 1959). Imperforation of the fourth ventricular foramina are found in both children and adults with the hindbrain malformation (Gardner, 1964, 1968) and is thought to result in a diversion of spinal fluid from the ventricles into the central canal of the cord giving rise to a generalised dilatation (hydromyelia) or more localised cysts in the grey matter of the cord communicating with the central canal (syringomyelia).

Gardner's idea consolidates all these features into a single pathogenetic concept; he based this on the principle of rupture of the neural tube after closure. A transient period of physiological hydrocephalus is present in the first few weeks of embryonic life following neural tube closure. The rhombic roof, which is still intact at this stage, then undergoes progressive permeability and the "hydrocephalus becomes compensated". If permeability fails to take place, the hydrocephalus progresses and the neural tube ruptures at its weakest point, i.e. in the region of most recent closure, usually the posterior neuropore.

One of the characteristic features of the hindbrain malformation is a small posterior fossa associated with a low insertion of the tentorium cerebelli (Cameron, 1957). The migration of the tentorium cerebelli is dependent on the enlarging forebrain (Padget, 1957); with neural tube rupture, according to Gardner, there must be some collapse of the forebrain so that

over-distension of the ventricles, as such, cannot be responsible for the excessive caudal migration of the tentorium.

Gardner felt that the exaggerated migration could be explained on the basis of ventricular fluid pubatile pressure acting in the presence of an open neural tube, which offers no opposition.

The result is a small posterior fossa which cannot accommodate the enlarging cerebellum; the cerebellum, therefore, grows out caudally through the foramen magnum. Gardner believes that excessive caudal migration of the cerebellum can occur in the absence of a spinal defect; this he feels would explain the milder degrees of herniation (Chiari type I), but he does not elaborate.

The expanding mass of hindbrain results in obstruction to the fourth ventricular outlet; forebrain hydrocephalus now becomes established which further displaces the hindbrain caudally.

Visceral abnormalities including diaphragmatic herniae have been described in infants with neural tube malformations (Dodds, 1941); enterogenous cysts have also been reported (McLetchie, Purves and Saunders, 1954), although in the latter case the spinal defect was merely a small cleft in the bodies of the cervical vertebrae ("anterior meningomyelocele"). In some cases filamentous cords (neurenteric connections) extend from the spinal cord to the site of the gut abnormality. Gardner (1968) claims that abnormal distension of the primitive neural tube prior to rupture predisposes to these neuro-ectodermal-endodermal adhesions

..../16

and is directly responsible for the visceral abnormalities. He felt that, as a result of the neural distension, the neural ectoderm made contact and adhered to the endoderm across the mesodermal barrier. Marin Padilla (1966) also described widening of the spinal canal as a feature in a series of human foetuses with craniorhachischisis, thus further supporting the idea of a preceding dilated central canal. This concept has also been supported by Padget (1968) who described "blebs" in the dorsal midline region of early embryos which she described as representing "neural tube blow outs" secondary to neural tube over-distension. Hall, Kalsbeck, Campbell and Miller (1975), using radioisotope and ventriculography found hydromyelia in "myelodysplastic" patients who were not shunt-treated, but not among those who were.

The much quoted argument against the Gardner hypothesis is the report of a meningomyelocele in a 5mm. embryo (Lemire, Shepard and Aavord, 1965). At this stage (approximately 28 days), the choroid plexus, and consequently cerebrospinal fluid, has not formed, so that the spinal defect could not have resulted from neural tube distension and rupture. It must be stated here that the neural tube is usually considered complete at about three weeks (Smith, 1974) so that there is little question of the spinal defect in Lemire's embryo being an unclosed neural groove; moreover, they used a normal 5mm. human embryo for comparison. Gardner (1968), however, met this argument by citing Weed's work (1917) on the development of the cerebrospinal fluid spaces; according to the latter author, the development of the choroid plexus is antedated by the elaboration of a protein-rich fluid which fills the embryonic ventricular spaces after closure of the neural tube. The source of this fluid

was thought to be the neuroepithelium.

The Neural Overgrowth Theory

Boerema (1929) advanced the theory that the hindbrain malformation resulted from an overgrowth of neural tissue. Patten (1953) who described his findings in two human embryos, one early human foetus and a rabbit foetus, all with meningomyelocele, also supported the overgrowth hypothesis. He measured sections through the malformed area in the spine and showed that the bulk of the neural plate tissue was much greater in the region of the spinal defect than in the adjacent normal areas of the cord.

In a later report Barry, Patten and Stewart (1957), using the same human embryo and foetal specimens reported by Patten (1953) as well as another foetus, described their findings after carefully dissecting the entire length of the cord and the brain. Two early foetuses (17 weeks and 18 weeks) showed an unmistakable Arnold-Chiari deformity while the youngest (embryo - 10 weeks) showed a condition suggesting an incipient hindbrain malformation. Their 8mm. (5 week) embryo was not dissected as they doubted the existence of the malformation at this early stage. In the two older foetuses, linear and configurational measurements of the medulla and cerebellum indicated that the hindbrain was of a greater mass compared with age-matched controls, although volumetric measurements were not performed. They were also impressed by overgrowth of the cerebral hemispheres and met the objection of the cerebellum being hypoplastic at birth by its differential growth during the second half of gestation.

Boulter (1967), in an overview of the literature, argued strongly in favour of this hypothesis. Often quoted in this connection is the work of Potter (1961) who found an increase in cerebral hemisphere weight in her series of children with meningomyelocele. Similar results were reported by Emery (1964) and Jacobs, Landing and Thomas (1961); for the same reasons the latter authors also favoured the overgrowth hypothesis.

Padget (1970) believed that the increase in neural volume in the region of the "neural cleft" to be abnormal folding and fusion of the neural tube walls and separation and "jumbling" of the neural cells.

Gardner (1968) argued that at about twelve weeks when the excursion of the primitive transverse sinuses is complete, the forebrain is little more than a thin-walled bag of water and not capable of the overgrowth of solid tissue, as suggested by Barry and colleagues.

Fowler (1953), in experimental studies in chick embryos, found that an overgrowth of neural tissue occurred in the region of an artificial opening of the neural tube. The possibility, therefore, that overgrowth is a secondary response cannot be ruled out.

Summary

There is now a great body of evidence against caudal traction as a valid pathogenetic concept and any attempt at its further perpetuation without good scientific grounds should be seriously discouraged.

In the present state of our knowledge it is perhaps unwise

to be too dogmatic about the temporal relationship between the occurrence of the hindbrain malformation and the onset of hydrocephalus, although there is some evidence (in rats) that the malformation precedes the hydrocephalus. In the latter situation the malformation may be explained on the basis of neural overgrow, primary dysgenesis or one of the hydrodynamic theories.

Certainly the neural overgrowth theory may also be criticised on a number of points, including the experimental production of overgrowth in neural tissue by mechanical interference in animals, suggesting that it might be a secondary phenomenon. More important, however, is that at the crucial time when the malformation is supposed to occur, the forebrain is a thin bag of water and therefore not capable of overgrowth of solid tissue.

Hydrodynamic theories, as proposed by Cameron and Gardner, are attractive and have the advantage of crystallising all the associated anomalies of this condition into a unified concept. It also explains the possible development of the malformation in the absence of hydrocephalus which could be a later event. However, the difficulties still encountered with this idea include failure to explain the malformation in the absence of a spinal defect.

It would, therefore, appear that no satisfactory pathogenetic concept presently exists which would fully explain the hindbrain malformation in all its possible combinations.

MATERIAL AND METHODS

The material comprised 100 cerebellums from children with meningomyelocele, being a random series coming to necropsy at the Childrens's Hospital, Sheffield (England). The ages of the children varied from birth to six years. Nineteen of the children had received decompression treatment for the hydrocephalus by means of a Holter valve for periods longer than two weeks. The causes of death varied from renal and pulmonary complications to ventriculitis and shunt blockage (for details see Appendix 1).

The brain was fixed within the skull prior to dissection. Fixation was achieved by needling one of the lateral ventricles through the anterior fontanelle or a burr hole. A quantity of cerebrospinal fluid was removed and replaced with an equal volume of concentrated formalin. The viscera were removed as in a routine post mortem. This was followed by carefully dissecting the skin away from the meningomyelocele; the entire skull and attached spinal column was then dissected out and the whole specimen placed in 10% formol saline for at least four weeks. The method is similar to that described by Laurence and Martin, (1959).

The upper cervical canal was then opened and, with the neck in midposition between full extension and full flexion, the distance between the posterior lip of the foramen magnum and the most caudal part of the cerebellum was measured with calipers. The fissural and lobular arrangement of the dislocated segment of the cerebellum was mapped out and photographed. The skull was then opened from above and the cerebral hemispheres were

..../21

removed by cutting through the cerebral peduncles.

An assessment was made of the tentorium cerebelli with special reference to the level of attachment of the lateral leaves and extent of patency of the tentorial hiatus. The level of the rostral surface of the cerebellum in relation to the free edge of the tentorial leaves was noted and classified. The hindbrain structures were removed and the cerebellum was dissected free by cutting through the cerebellar peduncles and along the superior medullary velum.

A detailed study was carried out with regard to the fissural and lobular pattern of the posterior surface above the level of the foramen magnum. This area was mapped out and photographed; the lobules within the herniated part of the cerebellum were then identified in relation to the rest of the lobules constituting the posterior surface of the organ. In such a way it is possible to confirm or change the initial assessment of the lobular composition of the infraforaminal portion of the cerebellum.

The rostral (superior) surface was also mapped out and photographed. On the ventral (ventricular) surface the presence and position of the flocculus was noted; observations were also carried out with regard to the nodule and inferior medullary velum.

Each cerebellum was bisected in the mid-sagittal plane. The midline lobules were photographed and identified and a gross assessment was made of compression, necrosis and loss of tissue in the different lobules. A midline sagittal block was taken from the right half of each specimen for histology and

microscopy. The midline photographs and histology of the midline sections were collated and a survey was made of the state of each of the six main lobules of the cerebellum, i.e. the central lobule, the culmen, the declive, the pyramid, the uvula, and the nodule. The lesions were classified in the following way. The presence of haemorrhagic necrosis and recent liquefaction of brain tissue with phagocytosis was termed acute necrosis (both recent and old haemorrhage were included under this heading). Cases in which the brain tissue was not markedly disorganised, but where there was loss of cellular elements and apparent atrophy of tissues, was termed 'longstanding necrosis'.

Calcification and old haemorrhage were usually confirmed by special staining techniques. An assessment was made of the proportion of Purkinje cells that had been lost; this was based on a scan of the Purkinje cell layer, on knowledge of the normal variability in these parts, and on the values of the most normal part of the cerebellum under study. In most of the specimens there were small areas of relatively normal cerebellar cortex, if not in the central lobules, then in sections from other parts of the cerebellum.

The whole cerebellum was weighed in each case. For comparison, the weights of cerebellums from apparently normal brains were used; these came from sixty children, almost all of whom died from 'cot deaths' and were handled in the same way as described for the abnormal series. Those of the 'normal' children had been well-nourished. Their mean gestational age was 37 weeks; for the children with meningomyelocele it was 40 weeks.

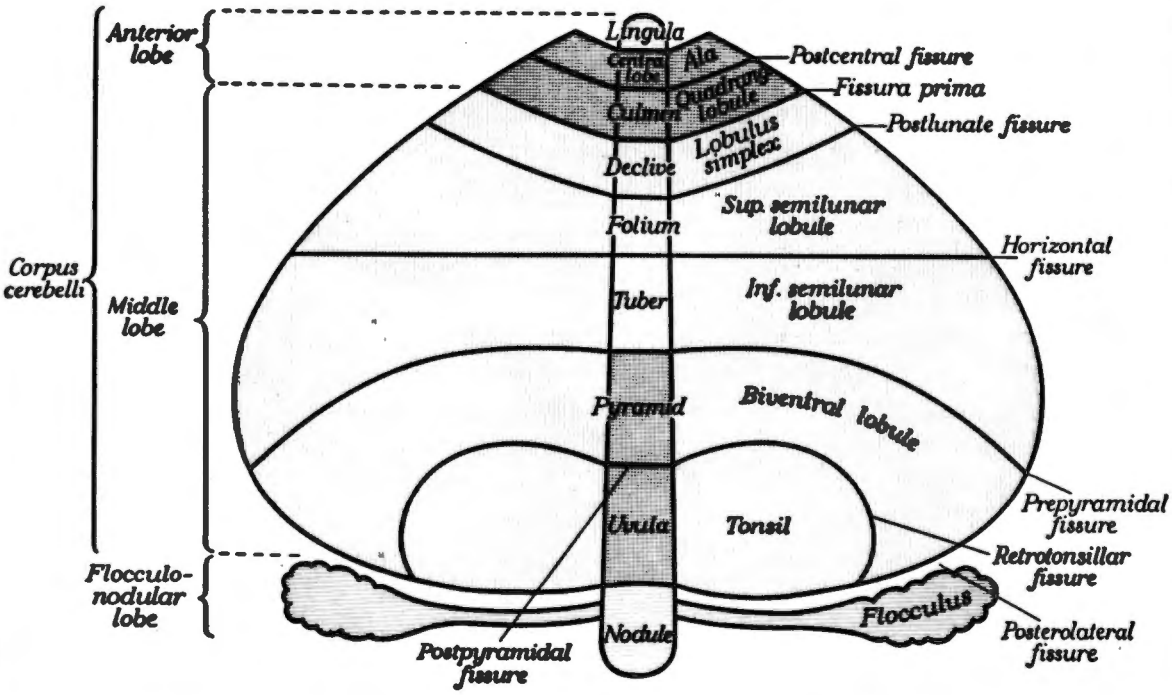
Detailed descriptions of other deformities of the spinal cord of these cases have already been reported (Emery and Levick, 1966; McKenzie and Emery, 1971; Emery and McKenzie, 1973; Emery and Lendon, 1973).

The terminology used in this account are those in current use in the popular texts on the subject; those specifically relating to cerebellar lobules and fissures are taken from Gray's Anatomy (1967). (See Fig.1)

...../24

Figure 1

Diagram to show the morphological and functional subdivisions of the cerebellum.



From Gray's Anatomy (1967)

PART 1

THE WEIGHT OF THE CEREBELLUM

The cerebellum in children with meningomyelocele has often been noted to be small or hypoplastic. However, such references have usually been anecdotal; in no study, as far as I know, has the cerebellum been weighed in this hindbrain malformation.

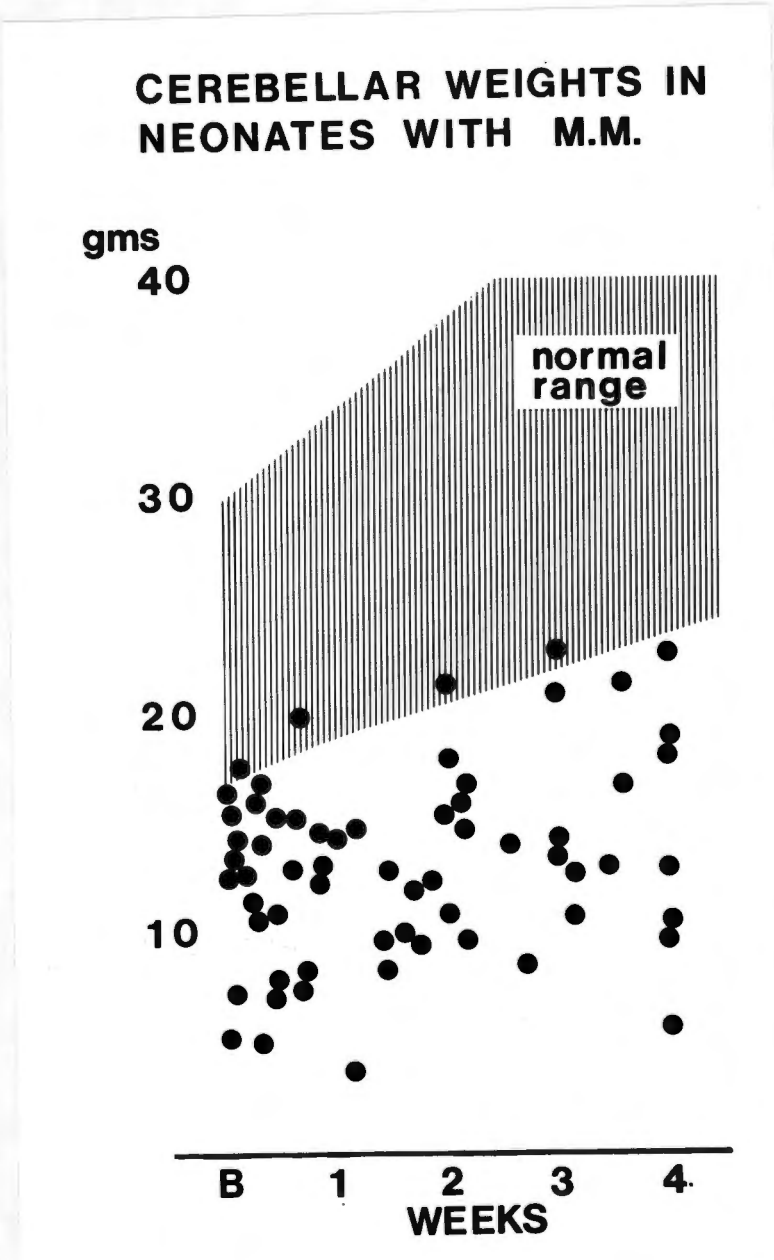
In this section the weights of 100 cerebellums from children with meningomyelocele are presented and compared with the weights of cerebellums from a "normal" series.

The weights of the cerebellar hemispheres of sixty-three children with meningomyelocele who died before the age of one month are shown in Figure 2, superimposed upon the total range of cerebellar weights of fifteen apparently normal children of the same age. There is an obvious reduction in weight of the cerebellar hemispheres in the children with meningomyelocele as compared with the apparently normal controls.

The equivalent data for the children over one month of age (with an age range up to six years) are shown in Figure 3. This shows the mean line for the weights of the normal cerebellar hemispheres and also distinguishes between the children treated with a Holter valve and those who were not. It would appear that the diminution in the weight of the cerebellar hemispheres seen in the newborn period persists throughout the age groups surveyed.

Figure 4 shows the relationship between the weights of the cerebral hemispheres and the cerebellar hemispheres over the whole age range. It is obvious that the ratio of cerebral: cerebellar hemisphere weights in the cases with meningomyelocele

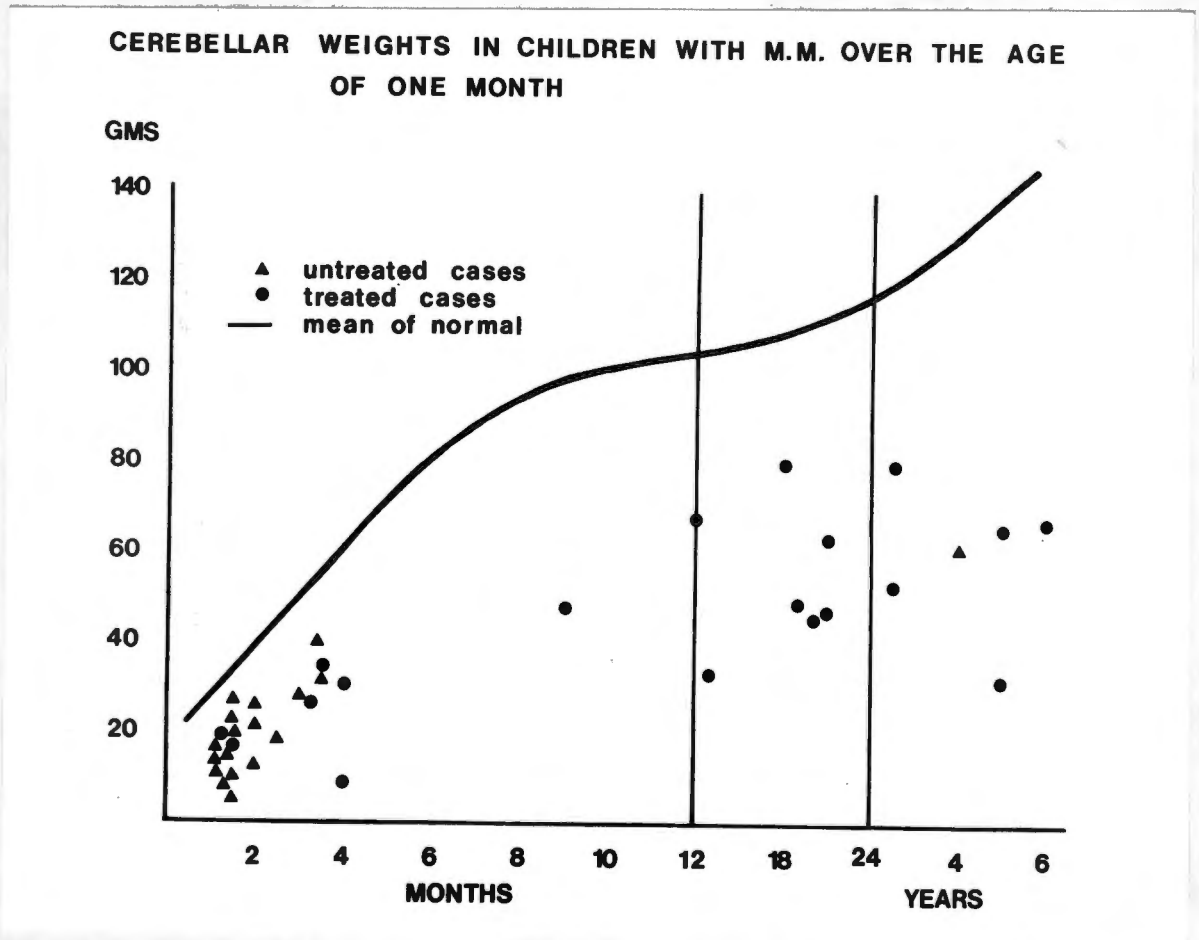
Figure 2



The weights of the cerebellum in children with meningomyelocele dying within four weeks of birth, compared with the weights from overtly normal children.

...../27

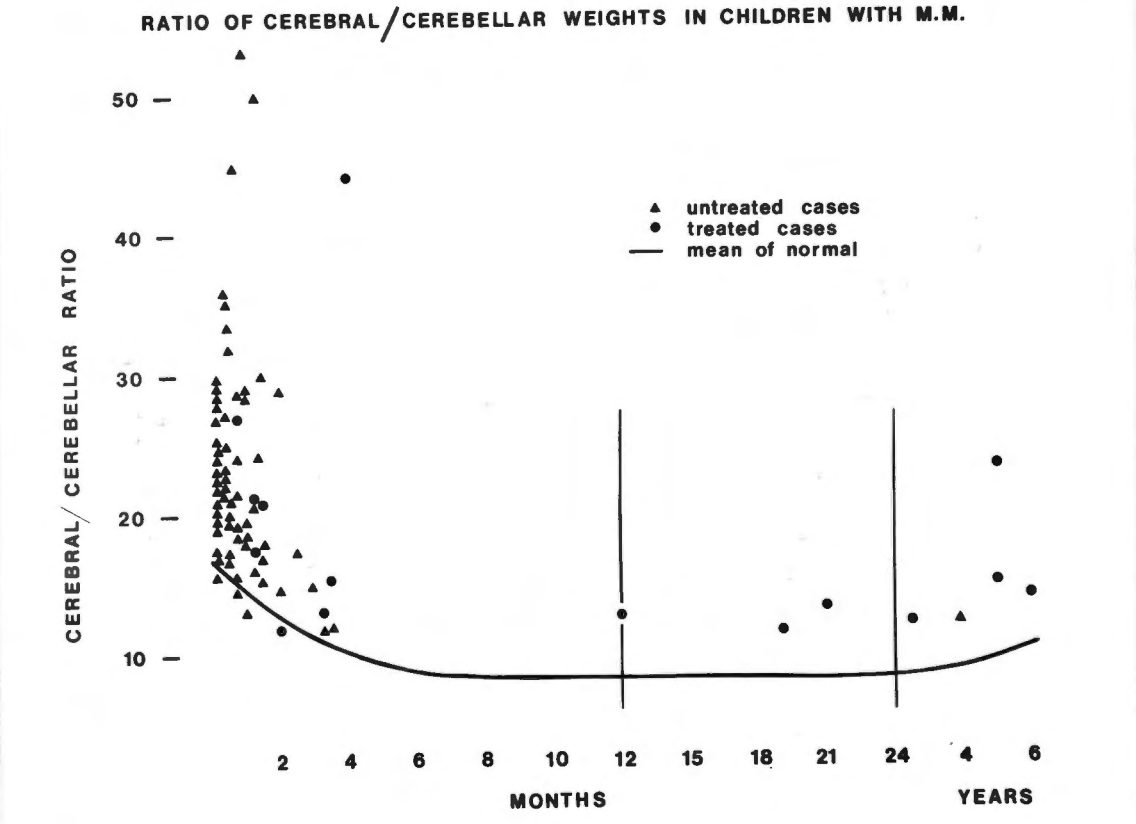
Figure 3



The cerebellar weights of children with meningomyelocele dying after the age of one month compared with the mean of normal.

..../28

Figure 4



The ratio of weights of the cerebral hemispheres to cerebellum in children with meningomyelocele compared with the mean of normal.

..../29

remains above the mean of the normal series. This appears to be a constant finding throughout the whole age range studied and to be unaffected by treatment in the older children. The older age group shown in Fig.3 includes a single cerebellum which has come from a child (aged 4 years) in whom there was no evidence of hydrocephalus and no shunt treatment was necessary. Special reference is made later to this specimen which will be described as a "split cerebellum".

The disparity between the rates of growth of the cerebrum and the cerebellum is well known. The cerebellum grows more rapidly during the first two years after birth; the greater proportion of growth occurs during the first twelve months, at the end of which time it has reached almost two-thirds of its adult weight. After the end of the first year the growth is less rapid, and by the second year the weight of the cerebellum is about four-fifths the adult weight (Ellis, 1920).

In contrast, the cerebrum increases in weight more slowly; by the second year the wet weight has increased about three-fold compared with a seven-fold increase in the wet weight of the cerebellum (Winick, Rosso and Waterlow, 1970). This differentially more rapid growth of the cerebellum has also been emphasised by others (Dobbing and Sands, 1973).

It is not so well appreciated that there is marked variation in the absolute cerebellar weights in infants of the same age, 30g. or more during the first three months after birth (Pfister, cited by Ellis, 1920). The weight of the cerebellum in children has been established by some other workers. The results of the

...../30

study by Blinkov and Glezer (1968) are not very satisfactory, as they were derived mainly from hospital material at the end of the last century. Ellis (1920) calculated values for the weights of the cerebrum and cerebellum from a smooth curve based on the results of three different authors and involving a large number of children.

The average cerebellar weights for males and females have been calculated from the table presented by Ellis (1920). For this reason I have also calculated my values for cerebral and cerebellar weights from a smooth curve. The results of my normal series are compared with those of Ellis in Table 1. The range of cerebellar weights in this series is somewhat higher than that of Ellis, which could reasonably be explained by the different populations studied. As an essentially identical procedure was used with the normal and abnormal brains, I have used my own material for local comparison rather than incorporating outside data.

The weights of the cerebellum of the deformed children in this series are uniformly diminished, not a single child having a cerebellar hemisphere weight reaching the mean of normal in the immediate postnatal period. This finding is markedly in contrast with that in the same children when the weights of the cerebral hemispheres are compared with the normal range. It has been pointed out by Potter (1961), and confirmed by Emery (1964), that the hydrocephalic cerebral hemisphere weight at birth is higher than the mean weight in normal children of the same age. In untreated cases of hydrocephalus dying before the age of six

Table 1

Cerebellar Weights in Present Series Compared with Ellis (1920)

Age	Ellis (1920)			Present Series		
	Cerebral weight (g)	Cerebellar weight (g)	Cerebral/ cerebellar weight ratio	Cerebral weight (g)	Cerebellar weight (g)	Cerebral/ cerebellar weight ratio
Newborn	367	21	17.5	340	20	17.0
2 months	471	34	13.9	520	40	13.0
4 "	565	48	11.8	620	62	10.0
6 "	662	60	11.0	738	82	9.0
9 "	765	76	10.0	833	98	8.5
12 "	827	86	9.6	852	104	8.2
18 "	922	98	9.4	935	110	8.5
24 "	1000	106	9.4	1018	117	8.7
8-14 years	1231	129	9.6	1543 (6 yrs)	147	10.5

months, there appears to be a suppression of growth of the cerebral hemispheres, as determined by weight. In the untreated cases who survive for more than eighteen months, the hemisphere weight approaches the normal range.

The weight of the cerebellum in the older children in this study is uniformly diminished in comparison with the normal range; even in children over the age of three years, the weight does not approach the normal range. It would appear, therefore, that in children with meningomyelocele there is a consistently different weight pattern of the cerebellum compared with that of the cerebral hemispheres in the postnatal period. When the ratio of the weights of the cerebral hemispheres to the cerebellum is considered (see Fig.4), it is seen that the greatest disparity lies in the immediate postnatal period, and that after about six months of age the ratio stabilises at a level just above the mean of normal. No difference was observed between the ratios of children who had been treated by Holter valve decompression and those who had not.

Dobbing and Sands (1973) identified two phases of human brain development and related these to 'periods of vulnerability'. The first represents the period of neuronal multiplication (approximately between 10-18 weeks gestation). The second is a period of rapid brain growth (approximately 30 weeks gestation) which continues well into the second postnatal year and probably longer. The latter phase is associated with glial cell proliferation and myelination; this corresponds with rapid increase in brain weight. Cerebellar growth starts later compared with other regions of the

brain, and also finishes earlier (Dobbing and Sands, 1973); these authors argue that if vulnerability is related to rate of growth, the part of the brain which is growing fastest will show the greatest effects of growth restriction. The effect of nutritional restriction and x-irradiation on the developing rat cerebellum during the second vulnerable period has been described (Dobbing, 1970). Therefore, these deleterious influences can be expected to result in permanent reduction in brain size and cell number.

The reason for the diminution in weight of the cerebellum in children with meningomyelocele has not yet been elucidated. Schwalbe and Gredig (1907) and Russel and Donald (1935) have referred to the cerebellum as being hypoplastic, but whether this is due to necrosis of particular lobules that have herniated out of the posterior fossa of the skull, to a general growth arrest, or to vascular and ischaemic changes within the substance of the cerebellum is not known.

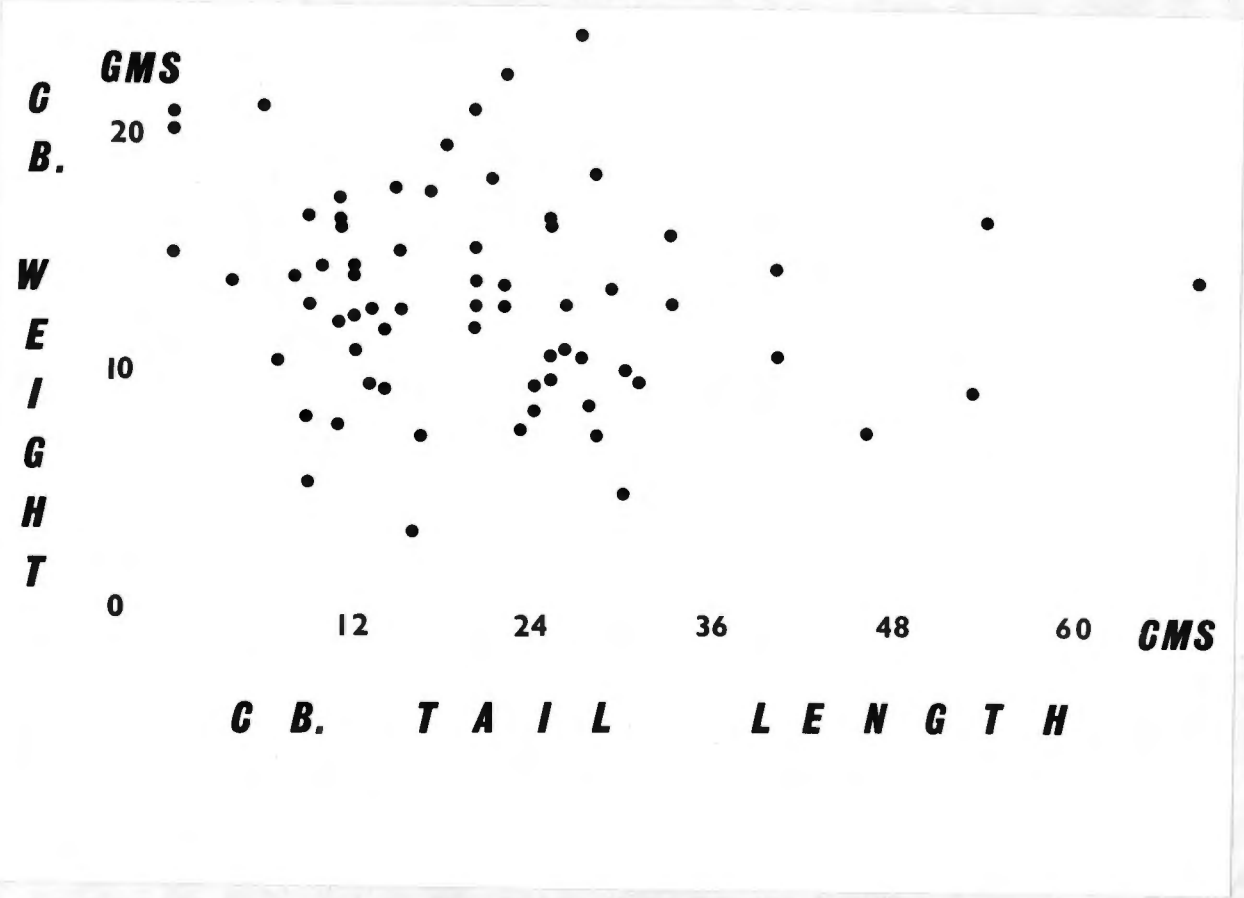
From the foregoing it may be deduced that the cerebellum is subjected to certain influences during the latter part of intrauterine life; this will coincide with the beginning of the rapid phase of glial proliferation. The evidence shows that the reduction in cerebellar weight is already manifest at birth. This reduction in weight persists into the postnatal life and occurs despite shunt treatment of the hydrocephalus. It may also be argued that the influence on the cerebellum appears to be a localised one; a generalised influence, such as a metabolic disease, would also have involved the cerebrum.

...../34

In a recent report Wallace (1973) described a significant neurological defect in the upper limbs in a large series of children with meningomyelocele. The upper limb disability was associated with signs of cerebellar dysfunction in a large number of the children studied and this occurred irrespective of whether the hydrocephalus was treated. In those cases in which the lower limbs escaped paralysis, evidence of cerebellar dysfunction was still discernible. It would seem that the small cerebelluma described here probably represent the pathological basis for this clinically manifest neurological deficit.

Figure 5

(Addendum to Part 1)



Comparison between cerebellar weight and length

of the cerebellar "tail" in 67 neonates with meningomyelocele.

..../36

PART 2

CERVICAL DISLOCATION OF THE CEREBELLUM

In many reports the Chiari type 2 deformity is often completely associated with meningomyelocele and this relationship is now well established. Russel and Donald (1935) stated that they doubted the existence of a type 2 deformity in the absence of meningomyelocele. On the other hand, the Chiari type 1 deformity may be found in a wide range of conditions including cerebral tumours, platybasia (Peach, 1964) and cerebral oedema (Emery and Reid, 1962).

In an effort to further characterise type 2 deformity, a number of new associated neuro-anatomical features have been described, and some of these have been re-emphasised with time. These include over-riding of the medulla onto the cervical cord causing a characteristic kink (Schwalbe and Gredig, 1907); a cephalad course of the upper cervical nerve roots from their points of origin (Russel and Donald, 1935); the low insertion of the tentorium cerebelli resulting in a small posterior fossa (Penfield and Coburn, 1938; Cameron, 1957); a "hypoplastic" appearance of the cerebellum (Schwalbe and Gredig, 1907; Russel and Donald, 1935); a beak-like deformity of the midbrain (Feigin, 1956). Certain radiological features of the skull have also been reported: an enlarged foramen magnum and shallow posterior fossa (Kruyff and Jeffs, 1966) and significant concavity of the basiocciput (Yu and Deck, 1971). However, it is now evident that of these features, many may also be found associated with the Chiari type 1 deformity. For instance, caudal displacement of the pons and medulla has been reported with acute cerebral oedema in children, even producing a kink

...../37

in the region of the medullo-cervical junction (Emery, 1967) and the peculiar course of the upper cervical roots have also been described with intracranial space-occupying lesions (Gardner and Goodall, 1950) implying caudal displacement of the pons and medulla in the Chiari type 1 deformity.

However, despite this rather significant overlap in features between these two hindbrain anomalies, attempts to categorise them into two distinct groups have continued. Peach (1964) drew attention to the considerable confusion in the use of the terms "Chiari type 1 deformity" and the "Arnold-Chiari malformation" and quoted a number of reports in which the deformity had apparently been wrongly designated the "Arnold-Chiari malformation" and were, in fact, examples of Chiari's first type. Most of the cases to which he referred were adults with apparently normal spines and who presented clinically with symptoms referrable to cerebellar and brain-stem disease.

In an effort to clarify the situation he stressed the difference in morphology of the cerebellum in the two deformities, i.e. herniation of the cerebellar tonsils in the type 1 deformity and herniation of the cerebellar vermis in the type 2 deformity. In the same report he described the autopsy findings in a three-day old male infant with gross hydrocephalus and a normal spine and spinal cord; there was a typical Arnold-Chiari malformation. This was described as follows: "a thick tongue of cerebellar tissue derived from the inferior vermis and tipped by a tuft of choroid plexus extends down through the foramen magnum for a distance of 2cm. It forms the roof of an elongated fourth

ventricle, the floor of which consists of the elongated and deformed medulla. At the junction of the medulla and spinal cord is a Z-shaped kinking so that the medulla overlaps the cord in its posterior aspect. The caudal extremity of the cerebellar "tail" is firmly bound to the medulla by dense fibrous adhesions".

Cerebellar tonsillar herniation in association with a normal spine have been described in a five year old female (Swanson and Fincher, 1949) and in a twenty-three year old female (Hurteau, 1950); in the former case there was also displacement of the fourth ventricle into the cervical canal and in the latter case the caudal six cranial nerves followed an oblique rostral course from their points of origin. These features suggest a slightly more complex morphology than the usual Chiari type 1 deformity. (It is interesting that neither case showed evidence of hydrocephalus). Several other cases showing varying degrees of hindbrain herniation in the presence of a normal spine have also been recorded; Buey and Lichtenstein (1945) - forty year old female: displacement of cerebellar tonsils and medulla; Teng and Papatheodorou (1965) - thirty-six year old female: displacement of the inferior vermis, fourth ventricle and humped medulla; Carmel and Markesbery (1970) - sixty-five year old female: displacement of cerebellar tonsils and vermis and fourth ventricle.

Similar cases, but without detailed descriptions of the herniated portion, were reported by Gardner and Goodall (1950) (seventeen cases) and by Appleby, Foster, Hankinson and Hudgson

..../39

(1968) (seventeen cases); the latter authors also reported radiologically abnormal cervical spines in nine of their cases. These included a wide cervical canal, occipito-vertebral fusion, fusion of C2 and C3 and unfused posterior arch of C1. According to Logue (1971), one third of these cases show a bony abnormality.

McConnell and Parker (1938) also reported five patients with ages ranging from ten to thirty-two years. All had internal hydrocephalus and all showed some degree of tonsillar displacement at operation. In most cases the tonsils were bound together as well as to the dorsum of the medulla by adhesions and separation at operation produced a sudden efflux of cerebrospinal fluid into the spinal subarachnoid space. These authors also report six infants with meningomyelocele who died at or soon after birth; in four of these there was a "fully-fledged" Arnold-Chiari malformation but in two the deformity, when exposed at operation, resembled closely those described in their adult cases.

Caetano de Barros, Farias, Ataide and Lins (1968) reported sixty-six adult cases of basilar impression alone, Arnold-Chiari malformation alone, and Arnold-Chiari malformation associated with basilar impression. Among those cases verified at operation or autopsy, the combination of the Arnold-Chiari malformation and basilar impression formed the numerically most important group (twenty-two cases); there were also three cases of pure Arnold-Chiari malformation. The authors believed that the basilar impression was of the congenital type. Ogryzlo (1942) also noted an association between the hindbrain malformation and basilar impression and supported a congenital origin of the platybasia.

Rydell and Pulec (1971) studied twenty-nine cases of Arnold-Chiari malformation in adults and presented four illustrative case reports in which they emphasised the oto-neurological symptoms. There were three cases of type 1 deformity; two were confirmed at operation and one suspected clinically and radiologically. The latter case showed moderate platybasia and a bifid C1 was fused with the occiput. The fourth case,(a forty-one year old woman), was found at operation to have a type 2 deformity with displacement of the tip of the fourth ventricle below the foramen magnum.

Ogryzlo (1942) presented a detailed description of seven cases: four in infants and three in adults. Two of the infants had meningoceles and two had meningomyeloceles. All the adults apparently had normal spines, although there was a suggestion of platybasia in one; in two cases both the cerebellar tonsils and fourth ventricle were displaced into the cervical canal. One adult case showed the ventricular cavity to extend to a lower level than normal, but the ventricle was not displaced into the cervical canal, although the cerebellar tonsils were. Two infants (one with a meningocele) showed cerebellar displacement only; there was no displacement of the fourth ventricle, features consistent with a Chiari type 1 deformity. The other two infants showed a classical Arnold-Chiari type deformity.

Malis, Cohen and Gross (1951) described similar cases of type 1 deformities in three adults.

In Chiari's second report (1895) in which he described

twenty-four cases of congenital hydrocephalus there were seven instances of the type 2 deformity and these were all associated with meningomyelocele. Fourteen cases were of the type 1 deformity and it is interesting that among these there was one case of meningomyelocele. Also, Cameron (1957), who described twenty-six cases of meningomyelocele, found two cases in which only the tonsils formed the cerebellar defect.

In the original report by Cleland, and more recently by Chiari (1891), Lichtenstein (1942), Cameron (1957), Daniel and Strich (1958) and Peach (1965), the displaced segment of the cerebellum in the type 2 deformity has been consistently referred to as "the inferior vermis" or "an elongation of the inferior vermis". Other authors have referred to it as a "tongue-like process from the inferior poles of the cerebellar hemispheres" (Ingraham and Scott, 1943) or a "tongue of variable length consisting of cerebellar tissue" (Russel and Donald, 1935).

According to Ogryzio (1942) the displaced segment consisted of a tongue-like fold of cerebellar tissue of variable length always present to some degree; this consisted of a median dorsal fold, or occasionally two lateral folds embracing the postero-lateral surfaces of the medulla.

It is noteworthy that "Chiari malformations" are also found in children in various types of cranium bifidum (Barrow and Simpson, 1966), but no detail is given concerning precise morphology.

It is thus evident that there is no uniform agreement as to what precise part of the cerebellum is displaced. Furthermore,

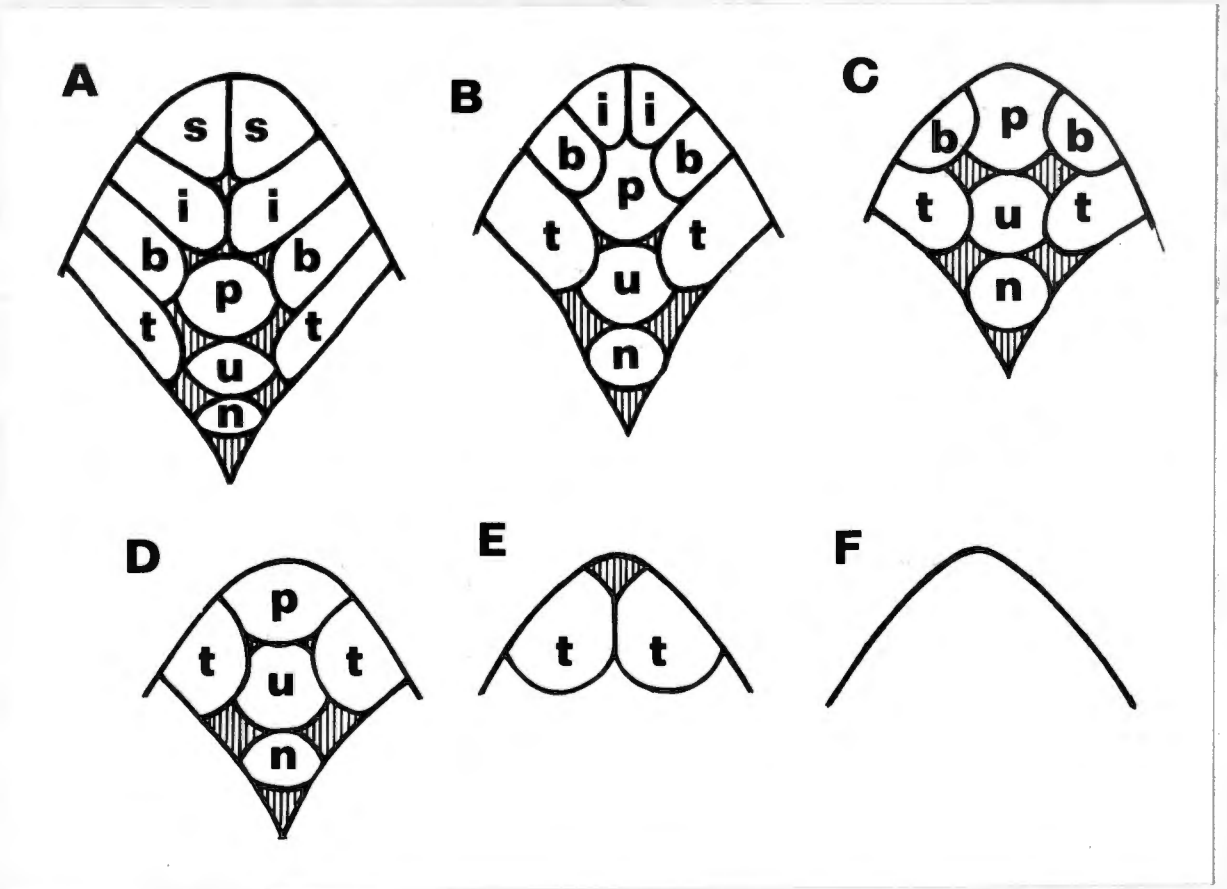
it can be seen that the hindbrain deformity occurs in children with meningomyelocele and is usually of the severe type. A similar deformity, but of lesser degree, is encountered in adults; here there is no open spinal defect but "minor" abnormalities such as platybasia or "minor" structural abnormalities of the cervical spine may be present. The congenital nature of these associated abnormalities strongly suggests that the adult type of hindbrain deformity is also of a congenital nature, and is probably related to the infantile type. This is further borne out by features in some adult cases not strictly conforming to the type 1 deformity but also showing characteristics reminiscent of the type 2 deformity. Also, some infants with meningomyelocele may have a hindbrain deformity which may be of such a mild degree as to qualify for a type 1 deformity.

In this section it was decided to record the actual cerebellar tissue which had herniated through the foramen magnum in 100 cases of children with meningomyelocele. Apart from delineating the precise lobular anatomy of the herniated portion of the cerebellum, an attempt was also made to see if the cerebellar deformity was in any way specific.

The cases were divided according to the extent of the cerebellar dislocation through the foramen magnum (see Figure 6):-

Group A (18 cases) - showed displacement of the horizontal fissure into the upper cervical canal so that the dislocated segment of the cerebellum included the superior semilunar lobules, the inferior semilunar lobules, the biventral lobules,

Figure 6



Diagrammatic representation of the various groups to show the pattern of the lobules in the dislocated segment.

Key: n = nodule u = uvula b = biventral lobule
p = pyramid t = tonsil i = inferior semilunar lobule
s = superior semilunar lobule

the tonsils, the pyramid, the uvula and the nodule (see Figure 7).

Group B (32 cases) - showed all the lobules below the level of the horizontal fissure to be displaced into the cervical canal. The horizontal fissure itself was still above the level of the foramen magnum. The dislocated segment of the cerebellum, therefore, included inferior semilunar lobules, biventral lobules, tonsils, pyramid, uvula and nodule. This was the most common group encountered (see Figure 8).

Group C (20 cases) - showed the biventral lobules together with the tonsils, the pyramid, the uvula and the nodule to be displaced into the upper cervical canal (see Figure 9).

Group D (14 cases) - showed the tonsils together with the uvula and nodule displaced below the level of the foramen magnum (see Figure 10).

Group E (2 cases) - the tonsils alone were displaced (see Figure 11).

Group F (10 cases) - showed no cerebellar tissue below the level of the foramen magnum (see Figure 12). In some of these cases a close inspection often revealed cerebellar tissue approximating the foramen magnum from above but there was no displacement of tissue beyond this point. Of these ten cases, five were in the untreated population and five in the shunt-treated group.

Minor degrees of asymmetry in the cerebellar hemispheres were common so that one side of the dislocation often involved more lobules than the other. Occasionally, the asymmetry was more marked; in one case the right side showed tonsillar tissue only while the opposite side showed displacement up to the level

Figure 7

Cerebellum from Group A showing the level of indentation of the posterior margin of the foramen magnum (straight arrow); the horizontal fissure (curved arrow) has been displaced below this level so that the superior semilunar lobules form part of the dislocated cerebellar segment, together with the more caudal lobules.

Figure 8

A cerebellum from Group B showing the inferior semilunar lobules (arrows) immediately below the posterior margin of the foramen magnum. The more caudal lobules are relatively compressed and lack differentiation.

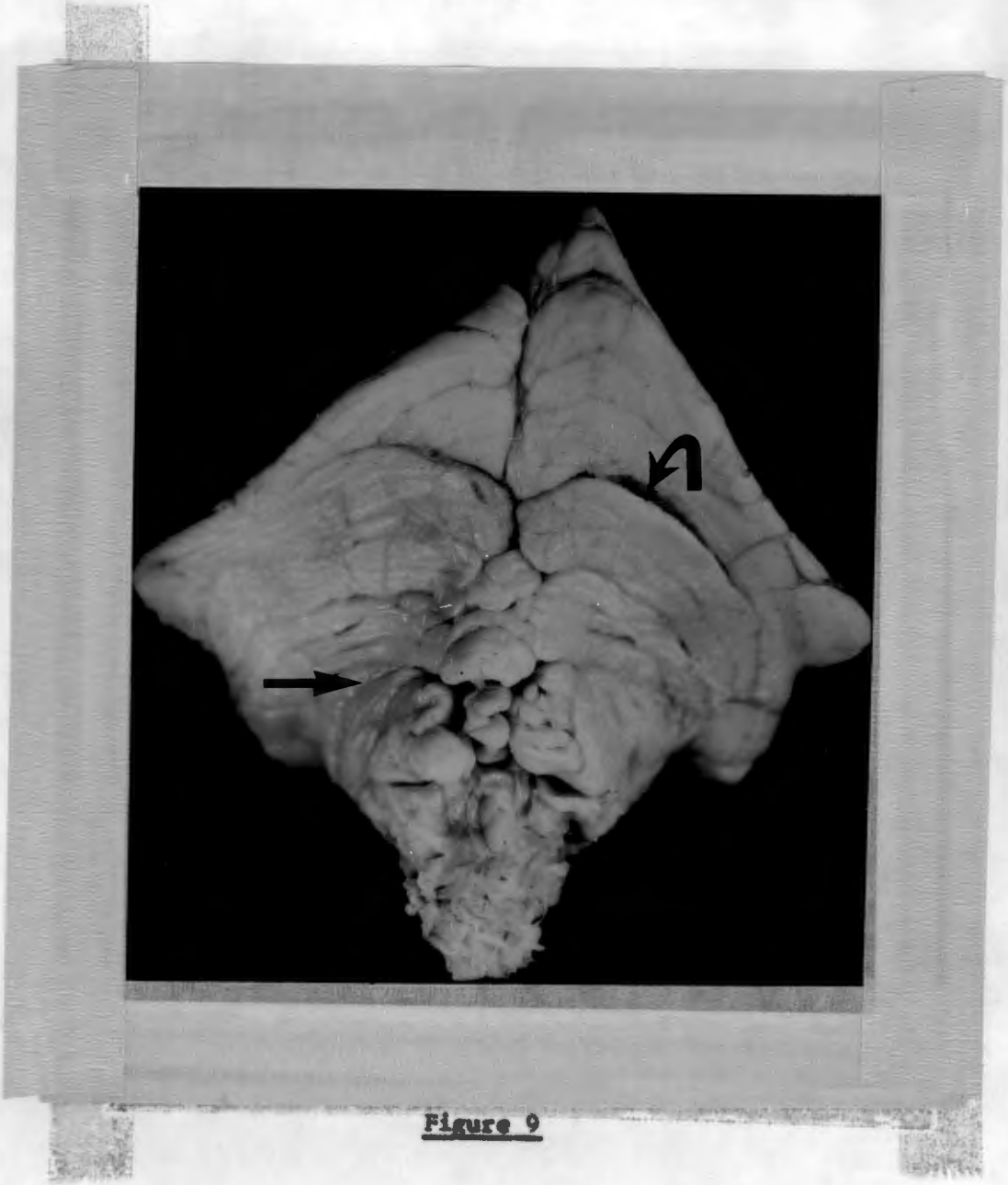


Figure 9

The posterior aspect of the cerebellum is indented at the level of the biventral lobules (straight arrow) which, together with the tonsils, pyramid, uvula and nodule, form the dislocated cerebellar segment. The horizontal fissure (curved arrow) is displaced about half-way down the posterior surface.

...../47

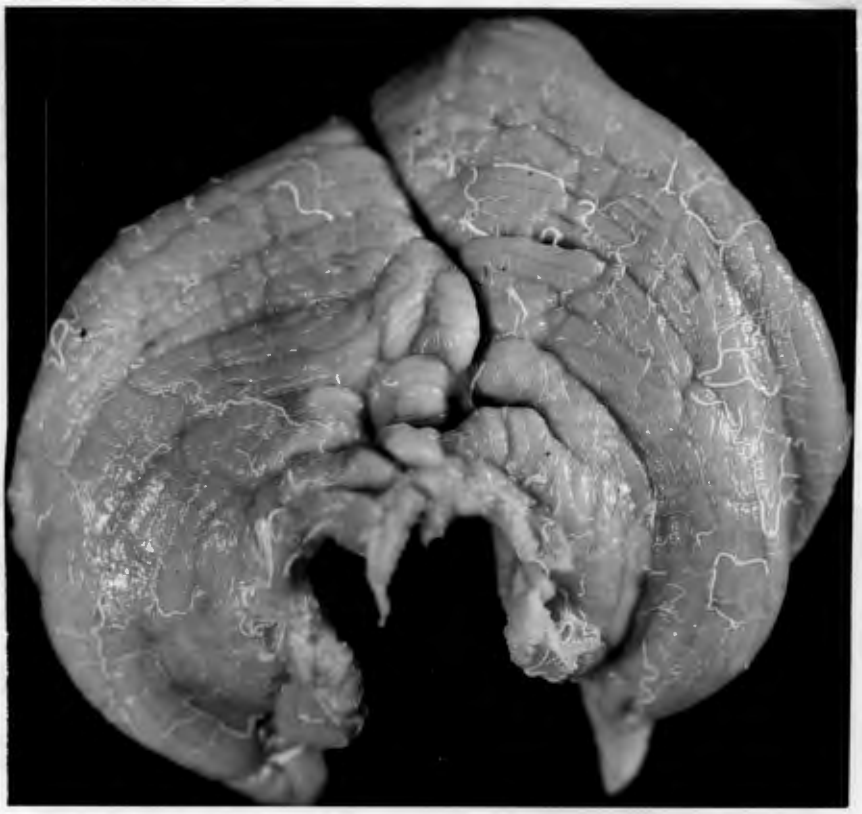


Figure 10

The tonsils, pyramid, uvula and nodule are inferior to the foraminal indentation. This is an example of the cerebellar deformity of Group D.

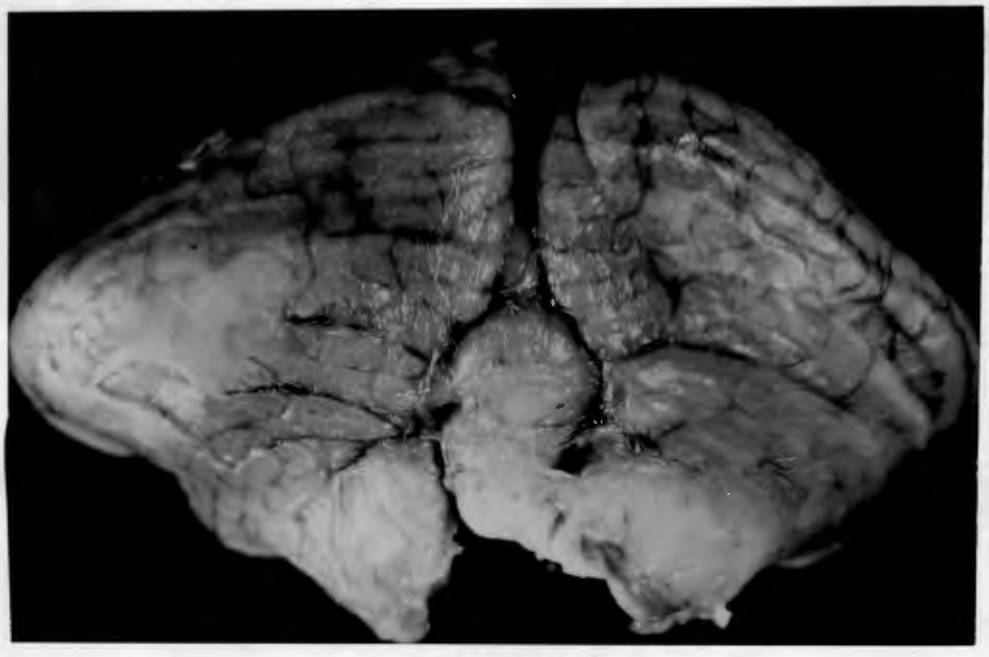


Figure 11

Cerebellum from a child with meningomyelocele in which only tonsillar tissue was displaced into the upper cervical canal. The organ is poorly differentiated into hemispheres and the inferior vermis is obliterated. The pyramid is more superficial than normal.

..../48

of the inferior semilunar lobules. In this classification the highest level was taken into account so that the latter case was classified as Group B. In some cases the infraforaminal lobules were clearly smaller than one would have expected for the age of the child and, in comparison with the rest of the cerebellum, gave the impression of having undergone atrophy. This was especially so in the older shunt-treated group. In other cases, atrophy appeared to result in complete loss of lobular differentiation so that any attempt to identify individual lobules in this region had to be abandoned. However, it was still possible to determine the level of cerebellar displacement as the lobular tissue above this level was relatively well preserved. In four cases the entire cerebellum had undergone such degeneration as to render them totally unsuitable for inclusion in our classification.

In some cases the degree of displacement was so extreme as to include lobules of the superior surface anterior to the superior semilunar lobules. Among the cases in Group A there were nine in which the lobuli simplex were found in the upper cervical canal and two cases also showed the quadrangular lobules. Such severe cerebellar deformities can only really be appreciated by referring to Figure 13, which classically shows the fissures of the superior surface passing almost directly to the foramen magnum so that the most anterior lobules of the superior surface are displaced through the foramen magnum.

In those cases showing significant atrophy of the caudal lobules the choroid plexus was frequently absent. As a rule,

...../49

Figure 12

There is no cerebellar tissue below the level of the foramen magnum in this child with meningomyelocele. However, the caudal lobules are situated nearer to the foramen magnum than normal.

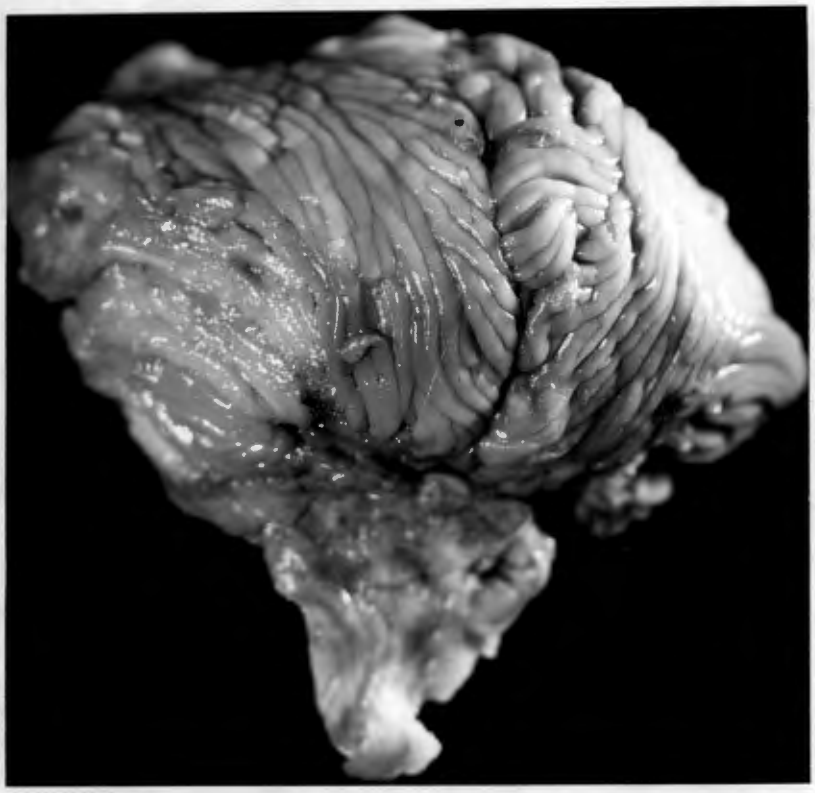


Figure 13

A severe deformity with part of the superior surface dislocated into the foramen magnum. The tissue in the caudal part of the cerebellum is atrophied and cannot be differentiated into lobules.

..../50

the choroid plexus was seen at the apex of the most caudal point of the cerebellar displacement and usually within the ventricle; it was a useful indicator of the lowest point of the fourth ventricle.

Discussion

A wide range of deformity was found in the cerebellar component of the hindbrain anomaly, and the common statement that the displaced segment of the cerebellum is simply an elongated inferior vermis is both vague and inaccurate. In 10% of this series no cerebellar tissue appeared in the upper cervical canal. The least severe cerebellar deformity showed displacement of the tonsils only, while the most complex deformity was associated with displacement of the horizontal fissure below the foramen magnum so that the superior surface of the cerebellum presented in the upper cervical canal.

There were two cases in which only tonsils were displaced and this is compatible with the cerebellar defect in the Chiari type 1 deformity. These cases were aged three days and thirty-one months. In each case the nodule, as well as the other lobules, were easily identified and there was no question of loss of tissue.

It is impossible to explain the more complex deformities of the cerebellum simply on the basis of caudal displacement of a normal organ through the foramen magnum. It would appear that the cerebellar lobules of the upper and posterior surfaces are displaced dorsally and caudally respectively, which results in lobules being more concentrated in the caudal end of the organ,

and this is well illustrated in Fig.8. The lack of depth of the posterior fossa associated with low insertion of the tentorium cerebelli is almost invariably present in the type 2 deformity and necessitates the cerebellum occupying a more caudal position relative to the foramen magnum. The two factors most likely to explain the infra-foraminal component of the cerebellar deformity include first, the displacement of the lobules within the organ itself and second, the displacement of the cerebellum relative to the posterior fossa. The complex nature of the cerebellar deformity has not been alluded to before in any detail, except perhaps by Margolis and Kilham (1969) who described a similar malformation in hamsters with viral induced hydrocephalus. Although the cerebellar lobules were not specifically mentioned, they noted that "most of the cerebellum was displaced downwards as an elongated conical sleeve-like structure investing the posterior and lateral aspects of the pons, medulla and cervical cord, and extending far through the foramen magnum".

In the ten cases without cerebellar tissue in the upper cervical canal, the cerebellum was invariably found to be abnormal. Such cases could be divided into two groups. The first belonged to the younger age group without shunt treatment. They showed compression of cerebellum resulting in a squeezing together of the hemispheres over the posterior surface so that the normal depression of the inferior vermis was obliterated and, at the same time, the tonsils seemed to approximate to the foramen magnum from above (see Fig.12). There were five cases in this

group. The other five cases were in older children where decompression treatment of the hydrocephalus had been established for a long time and where an additional finding was a loss of tissue in the caudal aspect of the cerebellum, i.e. lobules had apparently been present and had undergone necrosis (see Fig.38).

It was often impossible to identify the individual lobules below the foramen magnum without stripping off the pia-arachnoid and relating the displaced lobules to the lobular pattern of the posterior surface above the foramen magnum. It is likely that the identification of individual lobules of the displaced segment of the cerebellum in some cases would not be possible during limited surgical exploration.

The results of this study, as well as the results of others, show that the cerebellar defect of both the Chiari types 1 and 2 deformities occur in children with meningomyelocele although type 2 deformities are far more frequent. In half of the cases with no herniation, the cerebellum closely resembles that found in the type 1 deformity, but with the tonsils approximating but still above the foramen magnum. In cases showing the classical cerebellar defect of the type 2 deformity, there was marked variation in the number of displaced lobules. This was interpreted to mean that they are degrees of severity of the same basic defect of the cerebellum.

It is well known that the lobular arrangement of the caudal aspect of the foetal cerebellum changes with gestational age; the nodule forms the most caudal part at an early stage of

development. According to Langelaan (1919), the flocculo-nodular lobe from which the nodule eventually develops is a well developed structure at the beginning of the fourth month of intrauterine life, but it soon lags behind in development. This "regression" of the nodule seems to be augmented by the caudal movement of the posterior lobules secondary to increased growth in the inferior similunar lobules so that the tonsils now assume the most caudal aspect of the foetal cerebellum. This transition seems to occur over a relatively short space of time and it is easy to imagine that a common insult acting at either end of this time period could produce two different cerebellar deformities, compatible with the two types already described.

It therefore seems likely that the cerebellar deformities described have a common pathogenetic mechanism whichis variable in terms of time of onset relative to cerebellar development and in the rapidity of action of the pathogenetic mechanisms themselves, or possibly both. Since Chiari's original description, these hindbrain deformities have been traditionally classified as Chiari type 1 and "Arnold-Chiari malformation" (Chiari type 2 deformity), but it would seem from the foregoing evidence that these terms have perhaps outlived their usefulness from a viewpoint of developmental pathology of the central nervous system. It would be more accurate and certainly more useful in future descriptions to record the precise lobular composition of the displaced segment of the cerebellum. In addition, such graded alterations in the form of the cerebellum

..../54

indicate a secondary rather than a primary developmental anomaly. It also supports Chiari's original impression that his type 2 deformity is but a severe form of his type 1 deformity. 87% of the cases described here could, traditionally, be regarded as type 2 deformities.

Many reports indicate that those cases with a closed spinal column show a hindbrain deformity which is generally of mild degree; however, lesser degrees of the type 2 are also described. So-called type 1 deformities must be differentiated from "coning" of the hindbrain; in the latter group a primary lesion such as oedema or tumour will usually be recognised. The congenital nature of the type 1 deformity in adults is supported by the association with other congenital abnormalities; these are usually of minor degree and include platybasia or a bony abnormality of the cervical spine.

Hydrocephalus is not always present in the adult type of deformity. According to Gardner and Goodall (1949) one possible explanation for the late occurrence of symptoms in cases of type 1 deformity in adults is as follows: "mild and unrecognised hydrocephalus with Arnold-Chiari malformation or with Type 1 deformity is present in infancy but becomes compensated so that growth of the brain catches up with that of the skull. Thus, when adulthood is attained, the circumference of the skull may be normal, although some degree of platybasia may be present. Then, due to the increasing density of aging connective tissues, aggravated perhaps by infection or trauma, the outlets of the fourth ventricle become less pervious to fluid so that an

increased head of pressure is required to filter the fluid through to the subarachnoid cisterna. The resulting progression in the foraminal herniation is responsible for the gradually developing symptoms".

Deformities of the cervical spine are well documented in adults in the absence of open defects of the spine: these include wide cervical canal, occipito-vertebral fusion, fusion of C2 and C3, unfused posterior arch of C1 (Appleby, Foster, Hankinson and Hudgson, 1968). Other associated anomalies include hydrocephalus, hydromyelia and syringomyelia (Gardner and Goodall, 1950). These cases are invariably associated with minor degrees of cerebellar herniation such as tonsillar displacement with or without the inferior vermis and correspond to Chiari type 1 and "minor degrees" of the Arnold-Chiari malformation (type 2).

The complex deformities of the cerebellum described in children with meningomyelocele do not seem to occur in adults. On the other hand, the malformation seen in the adult may be found in children with meningomyelocele. The latter may occur solely as displacement of cerebellar tonsils. Although this type was only found in 2% of cases studied, similar degrees of deformity in infants have been described by others (Chiari, 1896), one case; (Cameron, 1957), two cases; (Ogryzlo, 1942), two cases, one of the latter with meningocele; (McConnell and Parker, 1938), two cases. It is possible that these examples are more common than reported cases would suggest; in this study I have been dealing with an autopsy series which could easily have been

biased by a high incidence of the severe type of deformity. It is conceivable that minor degrees of the deformity might be more frequent in those who survive or who, because of their lesser associated disability, are more readily selected for operation.

Clinical diagnosis of the hindbrain malformation is possible in adults and children using special radiological techniques (Verbiest, 1953); this method, apart from being used for diagnosis, can also be used to assess the extent of the lesion. More frequent use of these diagnostic techniques in larger numbers of children with meningomyelocele might reveal more of these minor deformities.

An adult or adolescent with the hindbrain malformation can be offered a relatively good prognosis using proper surgical techniques (Malis, Cohen and Gross, 1951). This may take the form of decompression by occipital craniectomy and upper cervical laminectomy. Tonsillar resection has also proved successful (Hurteau, 1950). With the present high incidence of complications of currently used shunting devices in the treatment of hydrocephalus, similar surgical techniques might be applied to the infant type of deformity, especially where this is found to be of mild degree.

Summary

In a study of 100 specimens of the cerebellum from children dying with meningomyelocele, the lobular pattern of the dislocated segment was identified and classified. There was a graded variation in the degree of cerebellar deformity ranging from the complete absence of cerebellar tissue in the upper cervical canal

to one in which the upper cerebellar lobules were displaced through the foramen magnum. Within this range there were two instances in which the cerebellar defect conformed to that found in the Chiari type 1 deformity, consisting of prolapse of tonsillar tissue only.

During foetal life the lobular relationship in the caudal aspect of the cerebellum undergoes considerable change and it is likely that the type of deformity presenting in the cervical canal is closely related to the stage of cerebellar development at which the pathogenetic insult occurs. The evidence presented argues against the defect being of a primary developmental nature.

The terms Chiari type 1 deformity and "Arnold-Chiari malformation" have outlived their usefulness and future descriptions of the cerebellum in children with hindbrain deformities should indicate the shape and precise lobules involved in the herniation.

The lesion in the infant has been compared with the lesion described in the adult, which is almost always of comparatively mild degree, usually showing tonsillar herniation only or tonsillar herniation associated with mild displacement of the fourth ventricle. It has been pointed out that a similar mild hindbrain anomaly may occur in children with meningomyelocele, and it is conceivable that such minor degrees are more common in those infants who survive. Because the lesion in the adult is amenable to surgical relief with improvement in brainstem symptoms and associated hydrocephalus, similar surgical procedures might conceivably be applied to the infant; in this way the

frequent complications associated with present day shunt procedures could be avoided. This aspect will, of course, require further thought and study.

PART 3

THE SUPERIOR SURFACE OF THE CEREBELLUM

This surface of the deformed cerebellum has been investigated from two aspects: 1) the fissural and lobular pattern; and 2) the level of the superior surface relative to the level of the tentorial hiatus.

Although the fissural and lobular pattern have not received much attention in previous reports, upward herniation of the cerebellum has been briefly described by Peach (1965) and Emery (1965). Daniel and Strich (1958) have also briefly referred to this aspect of the cerebellum. In their description of twenty-six cases of the hind-brain malformation in children ranging in age from birth to twenty-two months, there was flattening of the superior surface in all cases.

In Peach's series of twenty cases (1965), 35% showed herniation of the apex of the cone-shaped superior surface. The tentorial 'notch' was enlarged and the free edge of the tentorium caused deep indentation of the cerebellum at the site of the herniation. The ages of the children showing this feature varied from two weeks to seven months. A ventricular drainage operation was performed in three cases; one had repeated ventricular aspirations; in three there had been no operative interference.

Emery (1965), in a purely descriptive report, implied that supratentorial herniation of the cerebellum was a direct result of therapeutic relief of the hydrocephalus and lowering of the intracranial pressure; associated changes included some relief of impaction at the foramen magnum, distortion of the third to sixth cranial nerves, stretching of the pituitary stalk, and distortion of the occipital poles of the cerebral hemispheres.

1) The Fissural and Lobular Pattern

In this study the fissural and lobular patterns of the

...../60

superior surface of the cerebellum were found to be complex and heterogeneous; for clarity they were classified into seven groups. For comparison the superior surface of a normal cerebellum is shown in Figure 14.

Group A (33 cases) - there is a moderate degree of dorsal displacement of the two major fissures, i.e. the fissure prima and the postlunate fissure (see Figure 15).

Group B (30 cases) - dorsal displacement of these major fissures is more advanced. The postlunate fissure passes onto the posterior surface of the cerebellum; it is accompanied by dorsal displacement of the fissure prima so that the 'posterior lip' of the culmen is nearer the posterior margin of the superior surface than normal (see Figures 16 and 17).

Group C (16 cases) - the fissure prima with the culmen is displaced even further dorsally and may reach the posterior margin of the superior surface. The postlunate fissure forms a loop on the posterior surface (see Figure 18).

Group D (6 cases) - there is a small longitudinal fissure in the area of the declive. The postlunate fissure and the fissure prima pass dorsally; they converge towards the midline posteriorly and frequently enter the aberrant fissure in the area of the declive (see Figure 19).

Group E (6 cases) - a longitudinal midline fissure involves the whole superior vermis reaching anteriorly up to the precentral fissure and merges with the posterior vermis posteriorly. Continuity of this fissure is, however,

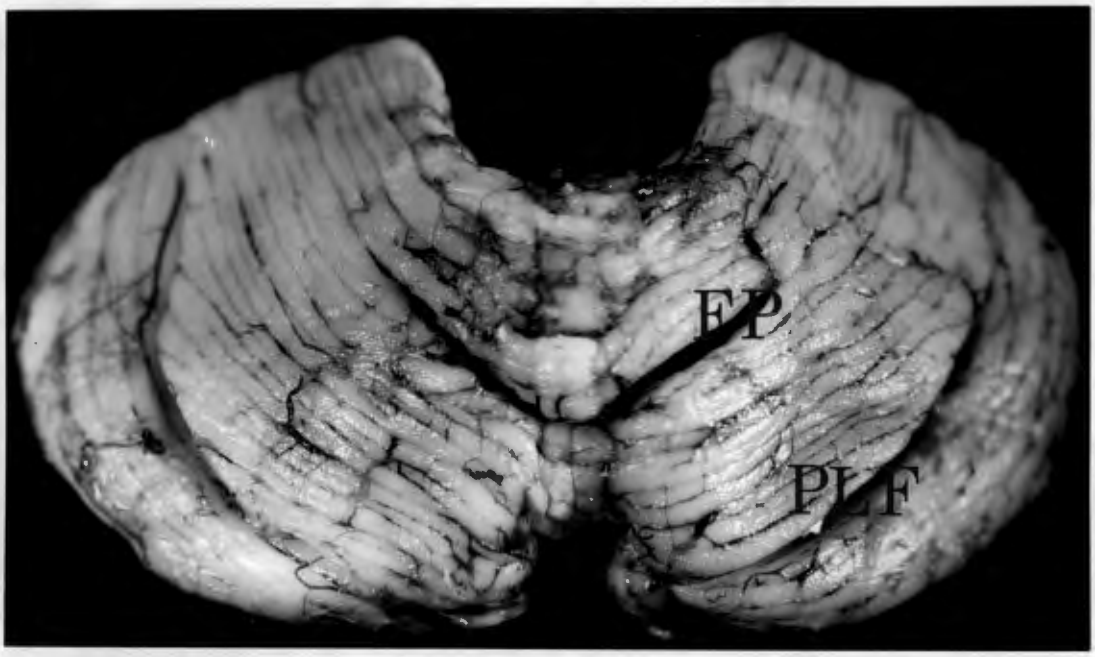


Figure 14

The superior surface of a normal cerebellum from a child aged three months showing the fissure prima (FP) and the postlunate fissure (PLF).

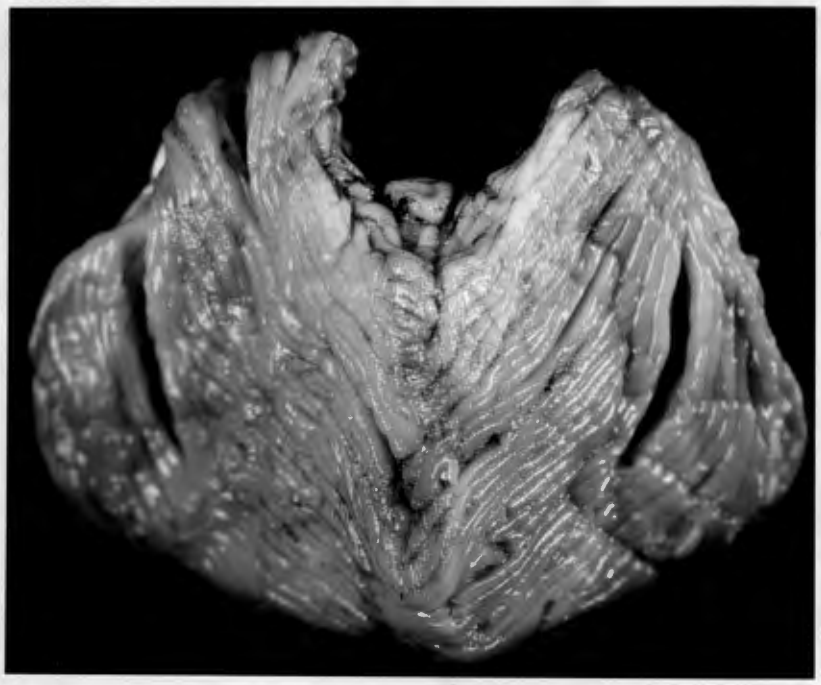


Figure 15

Showing mild dorsal displacement of the fissures.

...../62

Figure 16

Fissural displacement is more advanced; the fissure prima (arrowed) extends closer to the posterior margin of the superior surface.

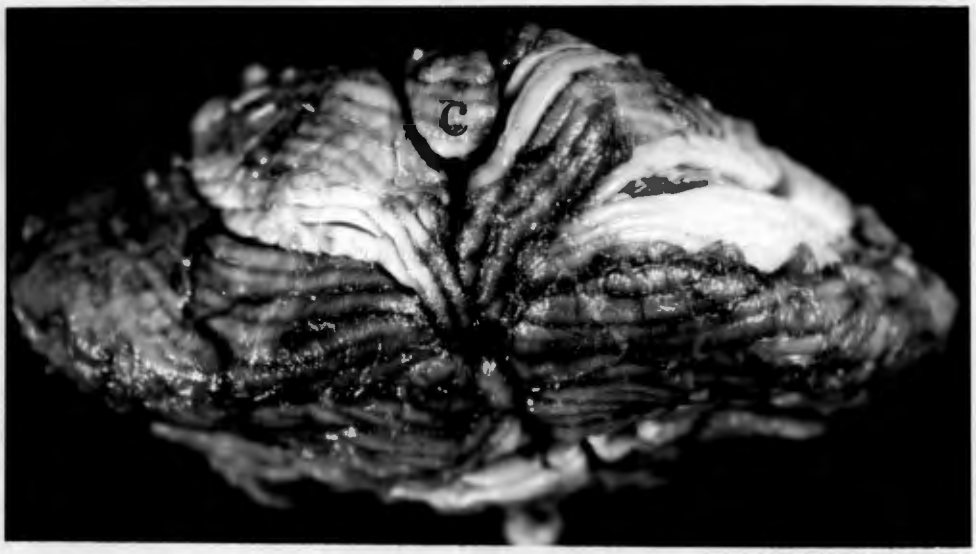


Figure 17

The posterior view of a cerebellum described in Group B showing the dorsally displaced culmen (C).

...../63

Figure 18

The posterior part of the culmen (C), and the fissure prima extend up to the posterior margin of the superior surface.

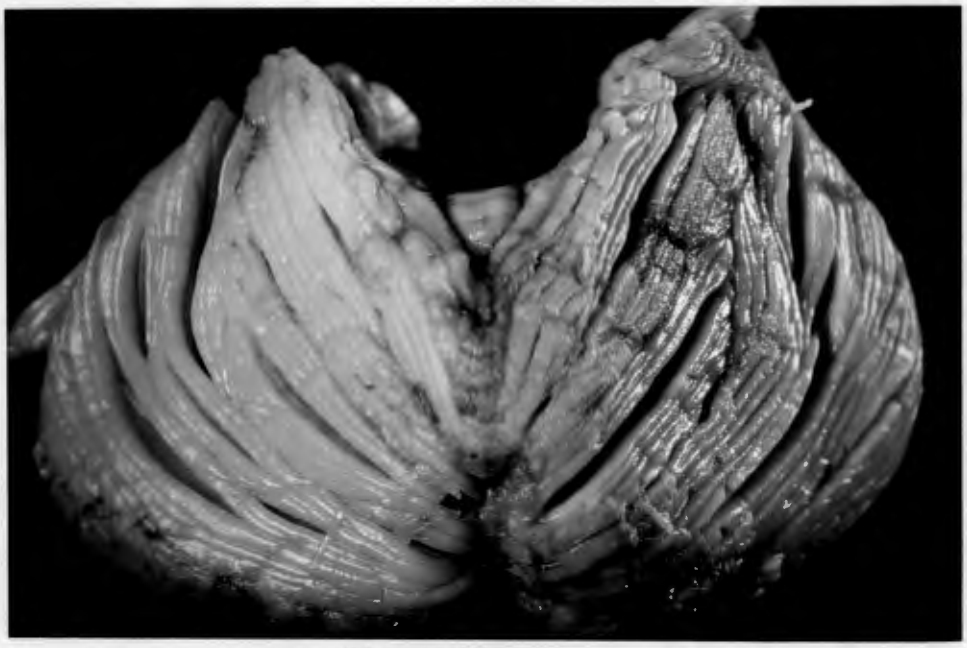


Figure 19

A longitudinal fissure has formed in the region of the declive (arrowed).

interrupted by an 'island' of vermis within the line of the fissure (see Figures 20 and 21).

Group F (5 cases) - the longitudinal midline fissure is now 'complete' in that there are no islands of tissue in its length as in Group E. The fissure prima and postlunate fissure pass dorsally and onto the posterior surface, or into the new midline fissure (see Figure 22).

Group G (4 cases) - the longitudinal midline fissure is wider than in Group F with relatively wide separation of the cerebellar hemispheres (see Figure 23). The major fissures on the superior surface are inclined dorsally.

It is apparent from the above description that the lobular pattern on the superior surface ranges from a mild degree of displacement to one that is considerable. The latter is accompanied by the appearance of entirely new fissures involving a part or the whole superior vermis; these are longitudinal and midline. This contrasts with the smooth even contours seen on the superior surface of the normal cerebellum. At one end of this spectrum of changes a peculiar deformity is seen; this is characterised by wide separation of the cerebellar hemispheres with a depression in the region of the superior vermis giving a superficial impression of an absent superior vermis. This will be referred to as a "split cerebellum" and will be described in greater detail in a later section.

Figure 24 is a diagrammatic representation of these changes. It would appear that such alterations are a sequential event which ultimately result in the formation of a Group G deformity;

...../65

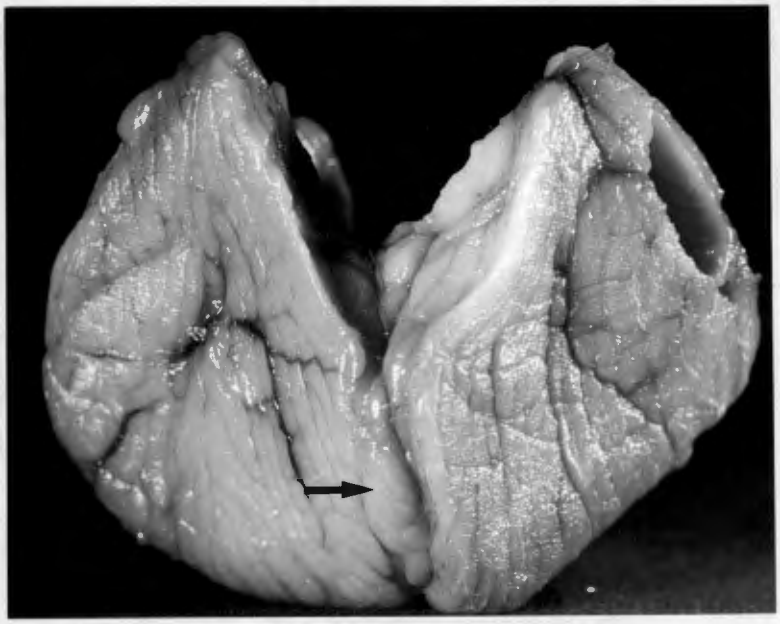


Figure 20

Showing an 'island' of vermis (arrowed) within the midline longitudinal fissure. Also note the deep indentation anteriorly caused by the midbrain.

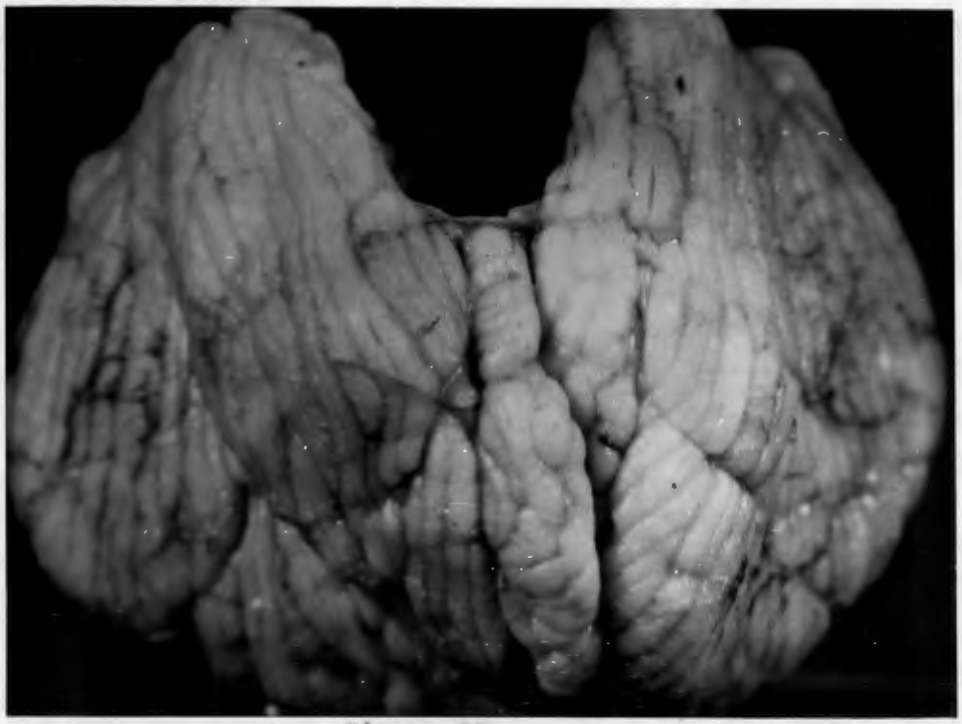


Figure 21

A fissure runs on either side of the superior vermis; this is probably a variant of Group B.

...../66

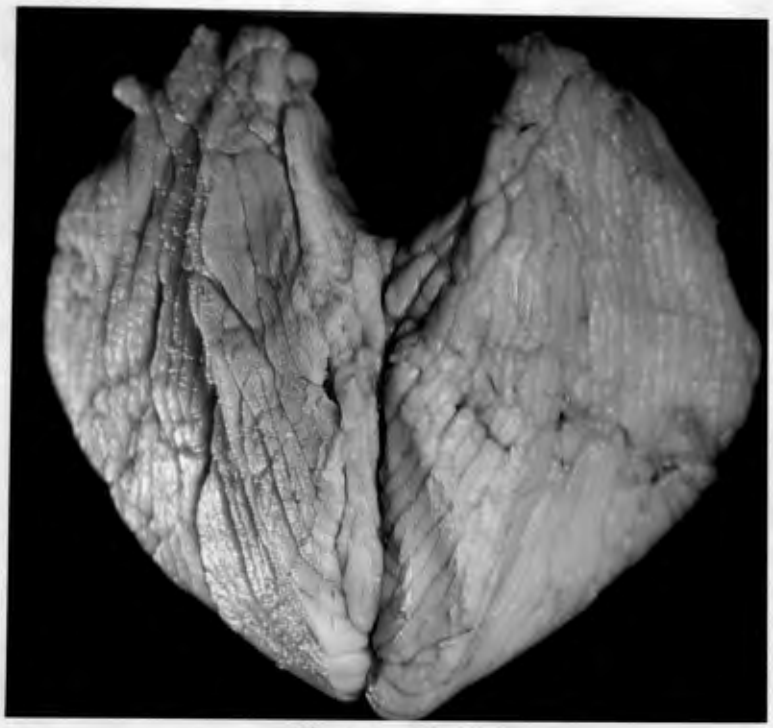


Figure 22

A midline longitudinal fissure extends from the central lobule along the superior vermis onto the posterior surface where it merged with the posterior vermis.

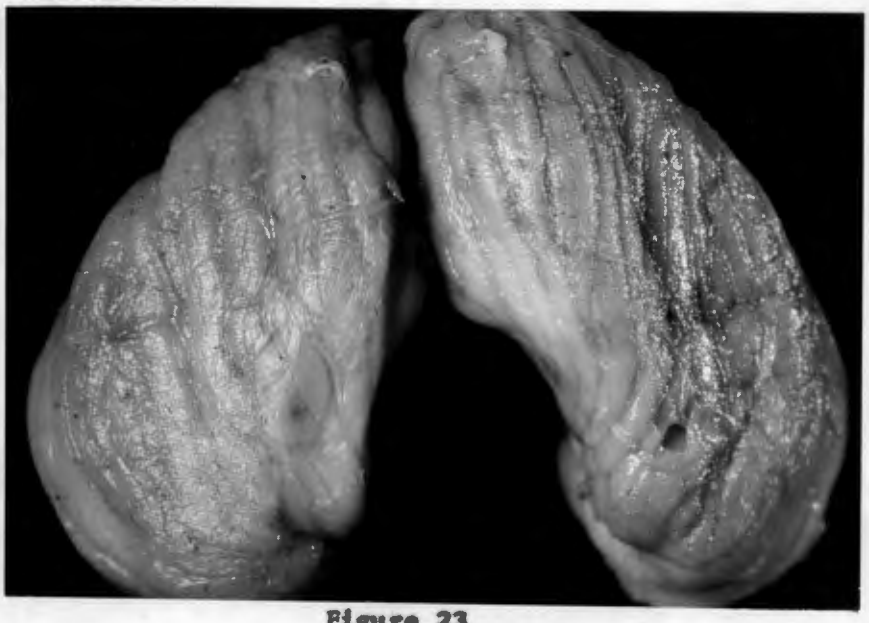


Figure 23

There is wide separation of the hemispheres on the superior surface and the superior vermis is absent. The hemispheres are joined caudally. Also note that the fissures on the superior surface run in a sagittal plane.

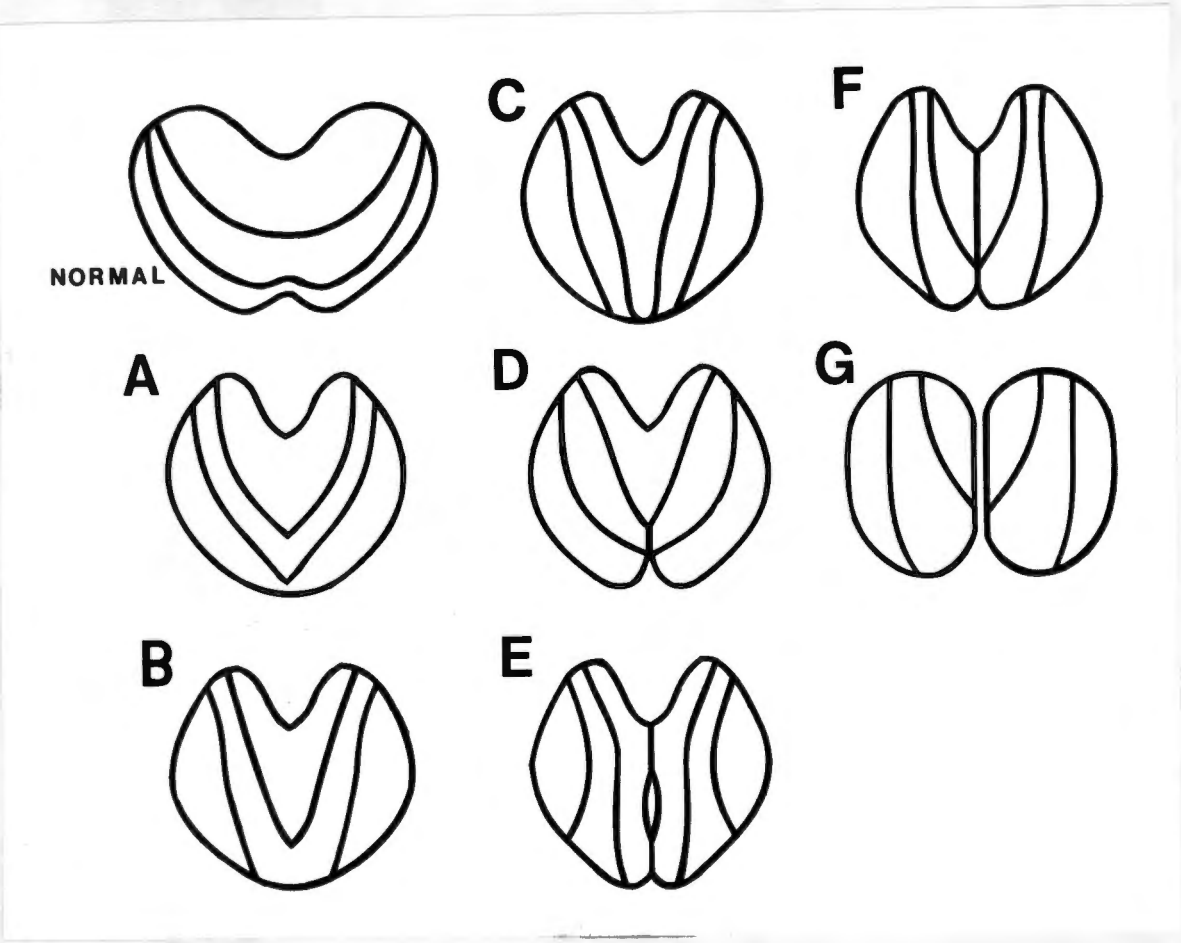


Figure 24

A diagrammatic representation of the changes seen in the fissural and lobular pattern on the superior surface.

...../68

an important feature of this group is an "absence" of a normal superior vermis. It is tempting to speculate on the pathogenesis of this severe malformation, particularly in relation to the normal development of the cerebellum. Any conclusion could reasonably be extrapolated to explain the less severely deformed specimens, as the latter would appear to be part of the overall spectrum.

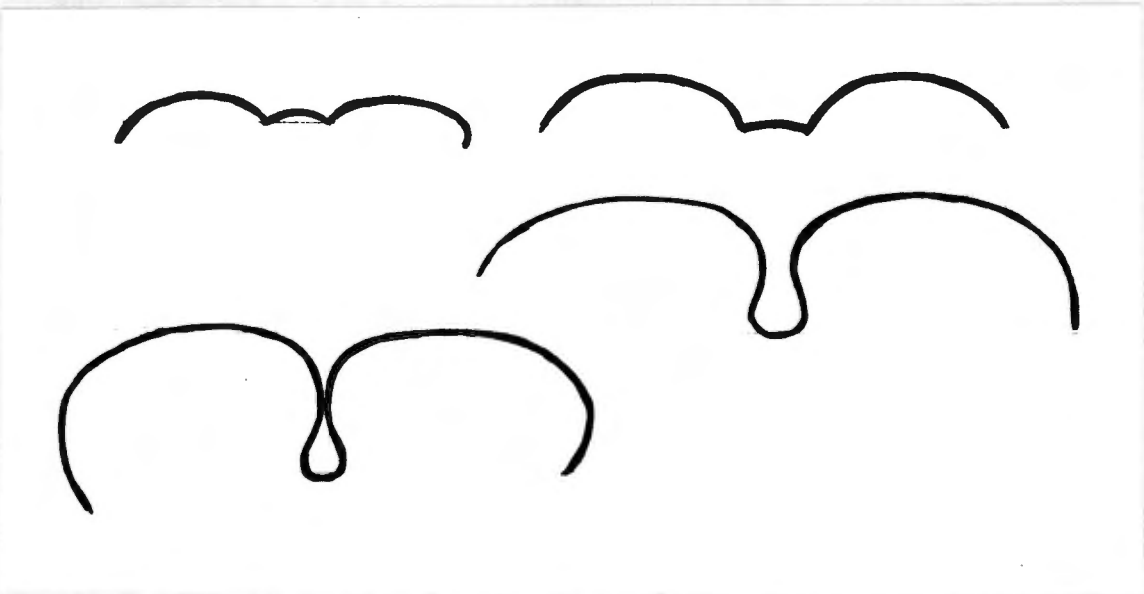
According to Langelaan (1919), normal early fissure formation is both an active and passive process; the latter is due to regional difference in growth and the former a local proliferation of cells in an anterior-posterior direction, which is followed by the appearance of a transverse fissure, perpendicular to the direction of cell proliferation. The sulcus paramedianus are two transient longitudinal furrows on the superior surface on either side of the primitive superior vermis present from the second half of the third month. Langelaan suggested that the sulcus paramedianus resulted from the passive process.

This suggests one possibility in the pathogenesis of the superior aberrant longitudinal fissures. After the fourth month the growth of cerebellar hemispheres overtakes that of the vermis; within the limited space of the small posterior fossa the competition for space could well result in the hemispheres overgrowing the superior vermis (see Figure 25). The hemispheres thus meet in the midline above the superior vermis; The result is an apparent inward displacement of the latter.

In midline sagittal drawings of the early human cerebellum Larsell (1947) clearly shows that the foetal arrangement of the

...../69

Figure 25



A diagrammatic representation of the proposed stages of "overgrowing" of the superior vermis which results in longitudinal midline fissuring on the superior surface.

...../70

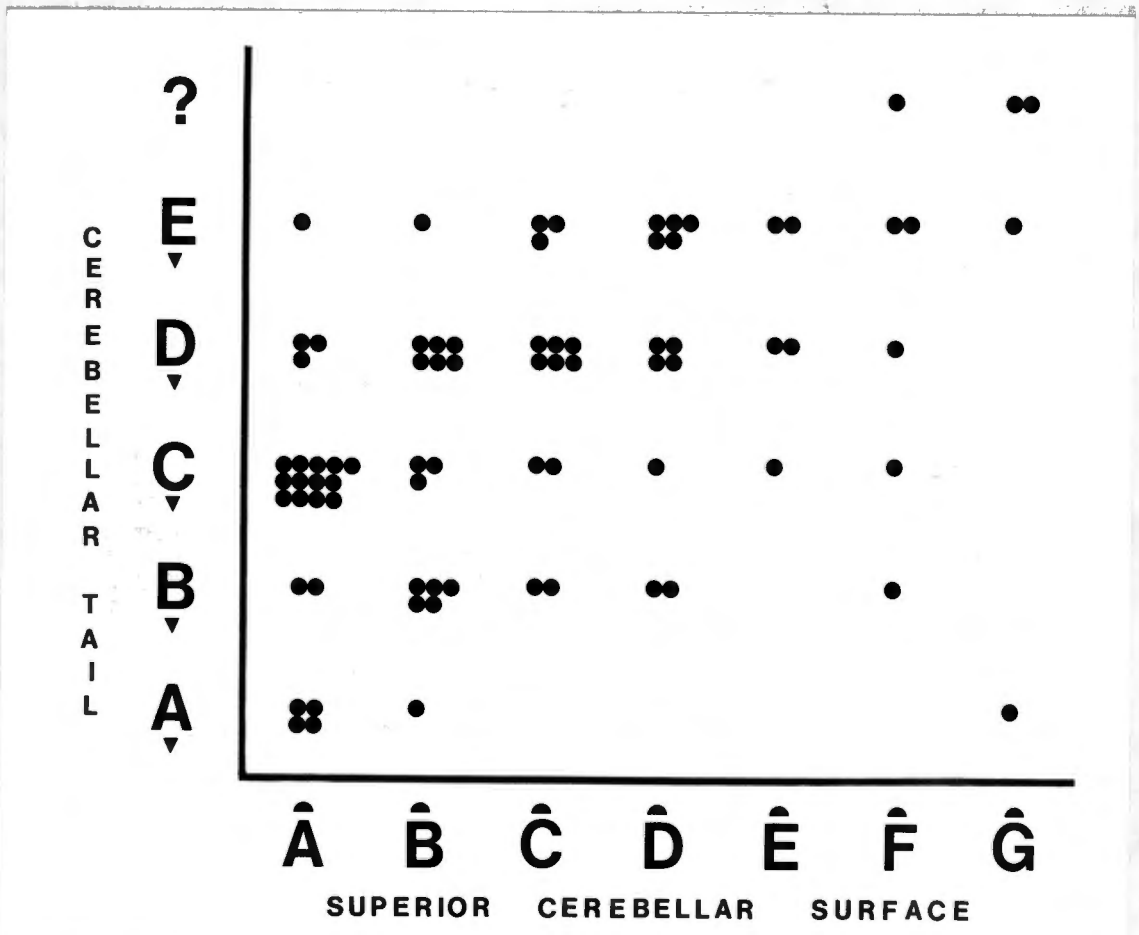
major fissures on the superior and posterior surfaces are placed more dorsally and caudally respectively. This foetal configuration of the fissures is similar to the pattern seen in some of the cases studied here; this applies to Groups A, B and C in which the deviation of the major fissures ranges from mild to moderate.

The difference in growth rate also occurs between the "stalk" of cerebellum and its external surface; while the "stalk" lags behind in development, the surface undergoes enormous expansion. This leads to the anterior and inferior borders of the cerebellum being rolled inwards.

An impaction between the superior cerebellar surface and the roof of the posterior fossa could reasonably prevent migration of the major fissures superiorly and anteriorly. In this way, especially due to impaction of the midbrain anteriorly, normal inward rolling fails to take place. Thus, the foetal fissural pattern is maintained.

The changes on the superior surface have been compared with the complexity of the infraforaminal segment of the cerebellum, described in the previous sections (see Figure 26); it would appear that the more severe the change on the superior surface, the more complex the composition of the cerebellar 'tail', i.e. the greater the number of lobules displaced through the foramen magnum. The impression is that the two groups of changes do not occur independently but result from a common factor. This could be growth within a confined space, the cerebellum grows and virtually squeezes itself out through the foramen. In this

Figure 26



A comparison between changes described on the superior surface and the complexity of the cerebellar 'tail'.
("?" refers to the group in which the caudal lobules were not individually identified.)

...../72

way the degree of "alteration" seen on the superior surface would equate with the amount of cerebellar tissue presenting through the foramen magnum. The process might be enhanced by hydrocephalic occipital and temporal lobes pushing through the tentorial hiatus to occupy a part of the already reduced posterior fossa.

Conclusions

Alteration in the lobular/fissural pattern of the superior surface of the cerebellum in this hindbrain malformation has not been previously described. The changes reported in this series range from mild to severe; at the severe end of what appears to be a spectrum, additional midline longitudinal fissures make an appearance; these can be complete by involving the entire length of the superior vermis. On the other hand, only a part of the length of the superior vermis may be affected.

The "split cerebellum" probably represents an extreme change. It is suggested that the deformities are mainly due to cerebellar growth within the limited space of the small posterior fossa; the cerebellar growth spurt commences from the beginning of the third trimester and is probably of much importance in this connection.

The size of the posterior fossa is fixed by the lateral leaves of the tentorium cerebelli. A greater part of the overlying cerebral cortex is in direct contact with the superior surface of the cerebellum as a result of the deficient tentorial leaves. Further reduction in the size of the posterior fossa could be brought about by the hydrocephalic occipital and temporal lobes herniating through the tentorial hiatus. This

"blockage" of the tentorial outlet, together with midbrain impaction (more anteriorly), probably accounts for the major fissures failing to migrate forward. Normally, the anterior superior part of the cerebellum undergoes inward rolling in response to the massive expansion of the cerebellar hemispheres relative to the lesser growth of the cerebellar stalk; similar inward rolling also occurs in the anterior/inferior part of the cerebellum. For reasons to be discussed later, this movement is also obstructed.

The degree of cerebellar deformity is probably dependent on both cerebellar growth and the size of the posterior fossa. The latter appears to be variable whereas cerebellar growth is probably constant. The more severe deformities might result from cerebellar growth within the smaller posterior fossae.

It is possible that those specimens showing superior longitudinal midline fissuring represent cases of greater obstruction to cerebellar growth. Expansion of the cerebellar hemispheres during the foetal period, being greater than the superior vermis, soon overgrow the vermis which is then displaced inferiorly to form longitudinal fissuring.

A comparison between the degree of deformity and the size of the posterior fossa would be informative. In view of the foregoing, the weight of the cerebellum might be regarded as a reasonable indicator of the size of the fossa in which it developed. For this reason it was decided to compare cerebellar weight with the degree of fissural deformity on the

...../74

superior surface (see Table 2). From this it can be seen that the mean of the weights of the various groups showed a steady decrease with increase in the severity of the fissural pattern. Although the results may be criticised on the grounds of marked variation in the numbers of the different groupings, these findings are, nevertheless, suggestive of the more complex deformities being the direct result of increased cerebellar moulding secondary to greater degrees of obstructed growth.

2) The Level of the Superior Surface Relative to the Level of the Tentorial Hiatus

In this section the phenomenon of supratentorial herniation of the cerebellum is analysed. This part of the deformity has been classified according to severity and the various groups compared with such parameters as head circumference, shunt treatment and cerebellar weight.

The most common situation was a mild degree of herniation of the cerebellum through the tentorial hiatus, occurring in 50% of the series. At one extreme the upper surface was scalloped and at the other, a "mountainous" supratentorial hernia was present.

The degrees of supratentorial herniation were classified as follows (see Figure 27):

Group A - a scalloped superior surface of the cerebellum occurred below the level of the free edge of the T. cerebelli. Thus, the contiguous overlying cerebral cortex was found to a variable degree within the upper part of the posterior fossa, that is, between the superior cerebellar surface and the tentorial notch (see Figures 30 and 31).

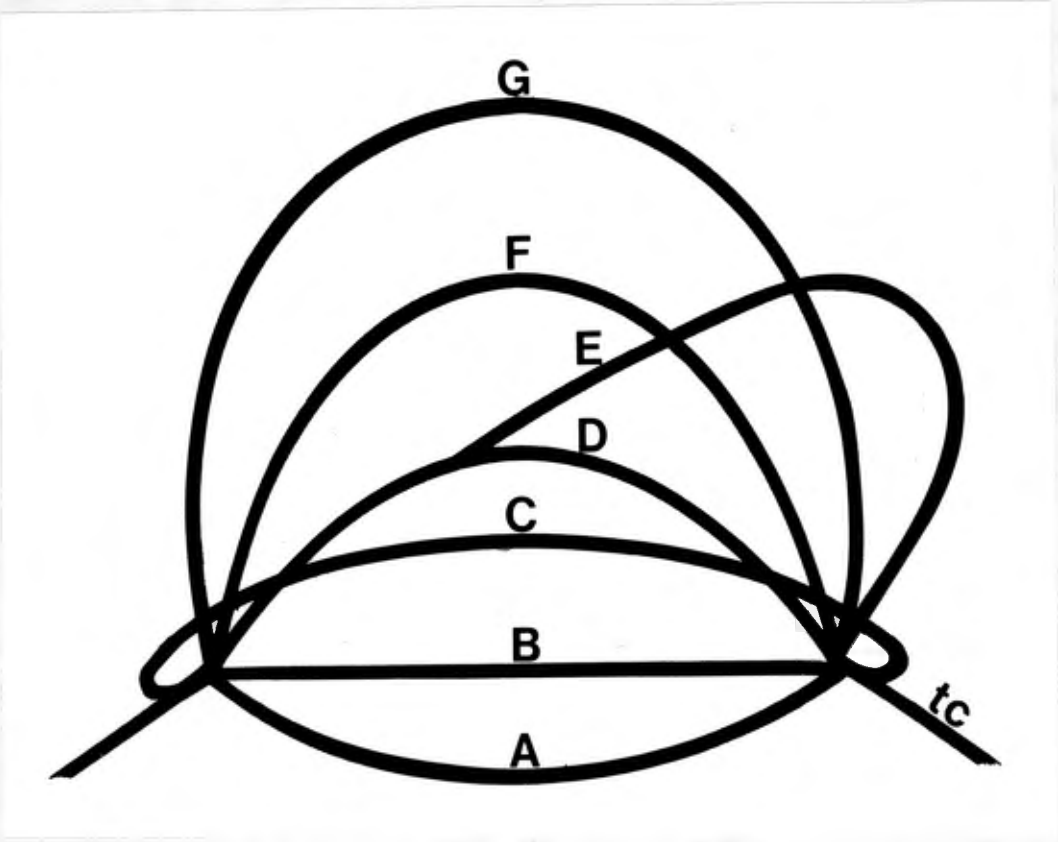
...../75

Table 2

Type of Superior Surface (fissural pattern)	A	B	C	D	E	F	G
Number of Cases	18	10	13	12	4	5	1
Cerebellar weight-range (gms.)	9.8-22.9	9.5-24.7	8.4-18.6	7.9-20.0	7.9-16.9	3.7-16.9	
Mean Weight	15.7	14.8	13.5	13.3	11.1	9.4	5.7

Showing the number of cases, cerebellar weight range and mean weight in the different groups of superior surface fissural pattern in the 63 neonates.

Figure 27



A diagrammatic representation showing variation in the projection of the superior surface of the cerebellum relative to the level of the tentorium cerebelli (tc = Tentorial level)

...../77

Group B - shows a relatively flattened upper surface, usually at the level of the free edge of the T. cerebelli.

Group C - shows mild upward herniation with cerebellar tissue over-riding onto the upper surface of the tentorial leaves ("mushrooming") (see Figure 34).

Group D - mild herniation.

Group E - shows upward herniation with the supratentorial part of the cerebellum deflected laterally. This is perhaps best described as a "buckling" deformity (see Figure 33).

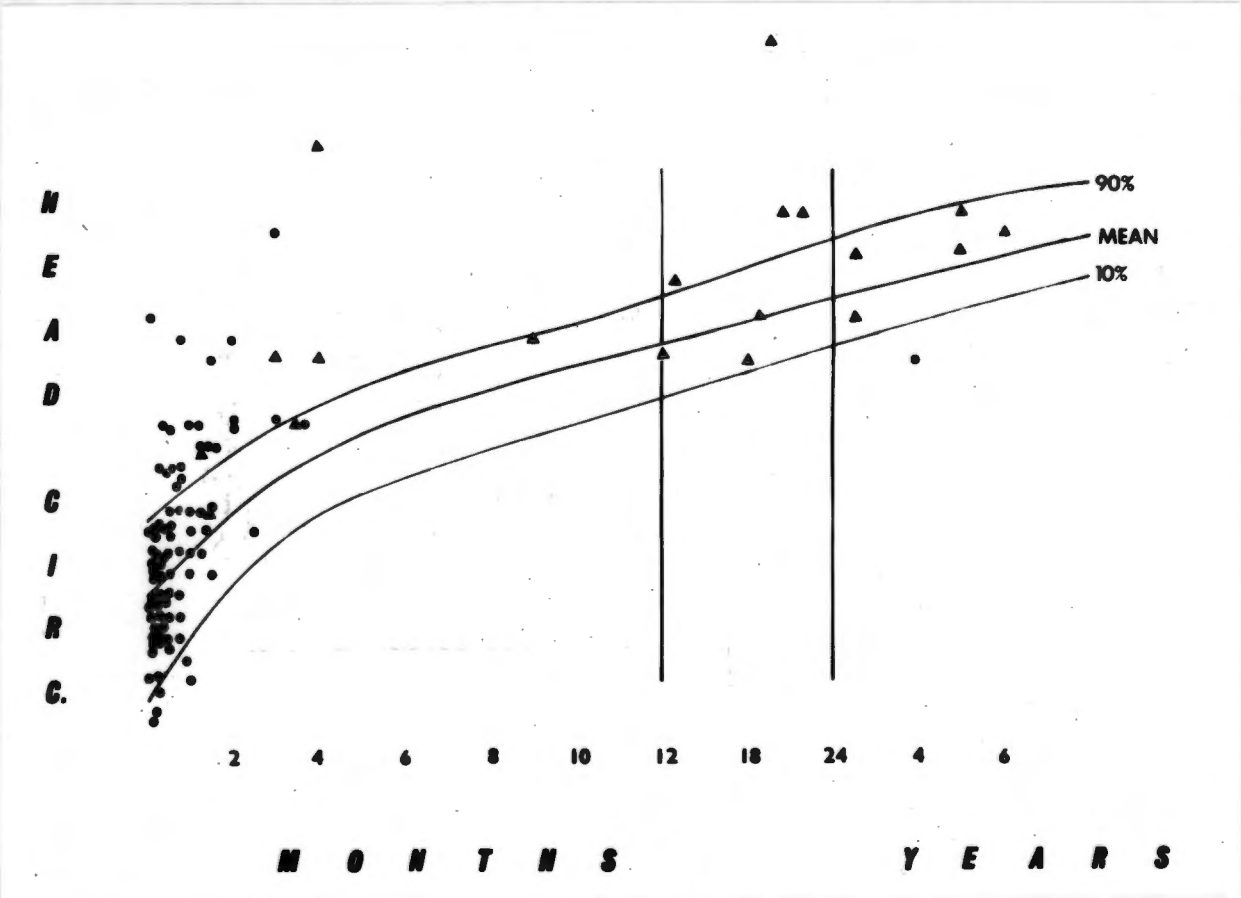
Group F - moderate herniation.

Group G - extreme herniation ("mountainous"). More than 50% of the cerebellar mass presented supratentorially (see Figure 29).

Head circumferences were measured at post mortem in each case. Figure 28 shows head circumferences against age, together with the mean, 10th. and 90th. percentiles; from this it is clear that there is a marked variation in head circumference measurement. This applies to the population as a whole, as well as to the individual age groups; it can be seen that the majority under the age of one month (neonatal group) have a head circumference below the 90th. percentile, and a few are below the 10th. percentile. Thus, the majority in the neonatal group have a head circumference within the normal range. On the other hand, those older than one month have circumferences that are mainly above the 90th. percentile; after twelve months the majority fall between the 10th. and 90th. percentile. In the latter group it is also

..../78

Figure 28

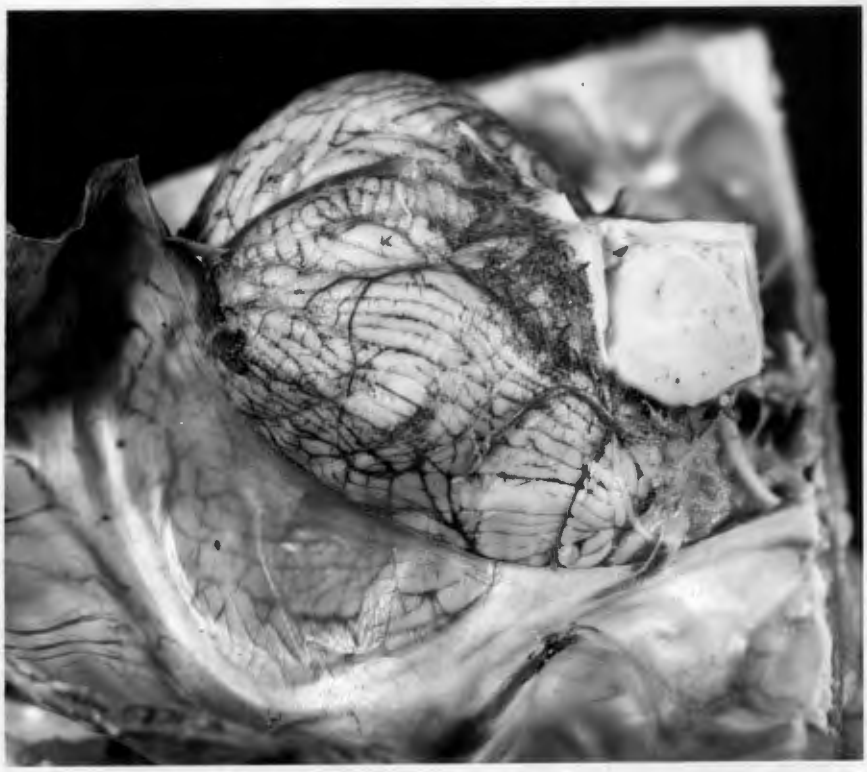


Head circumferences of children with meningomyelocele measured post mortem compared with mean of normal, 90th. and 10th. percentiles.

...../79

Figure 29

Showing enormous herniation of cerebellum through the tentorial hiatus.



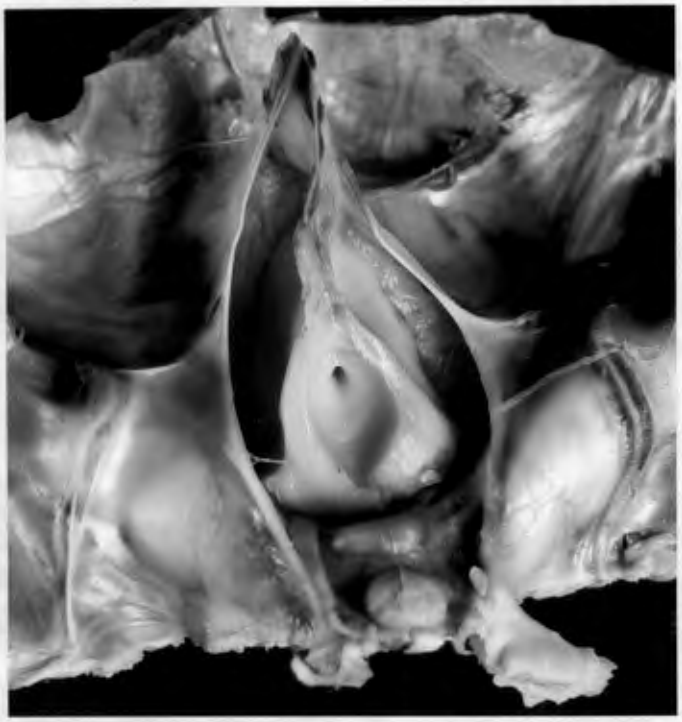
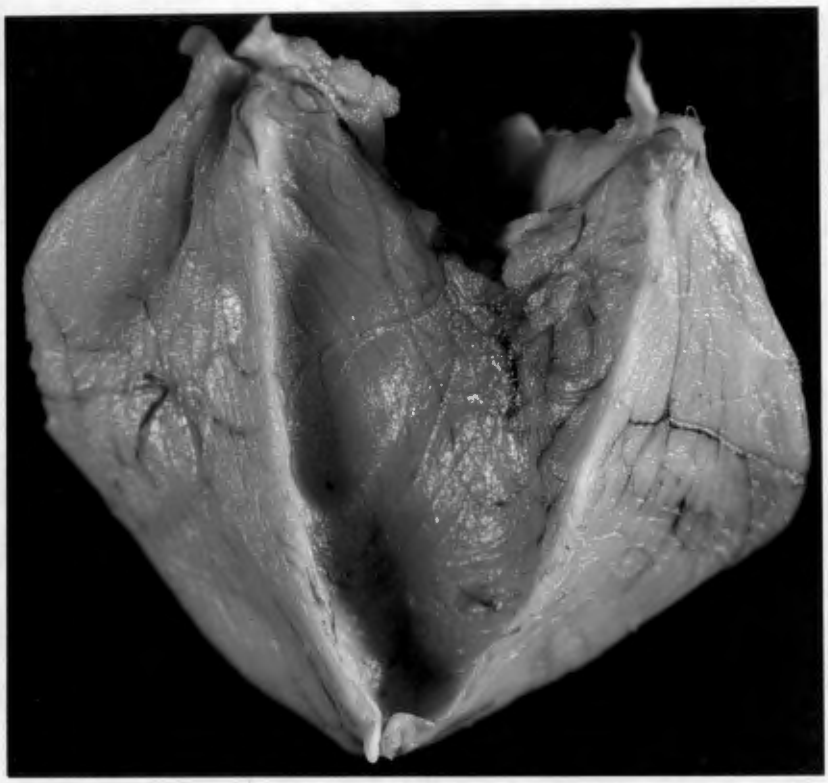


Figure 30

Showing midbrain and floor of the third ventricle depressed below the level of the free tentorial edge. This represents an example of an excavated superior surface. The aqueduct is clearly visible through the third ventricle.

...../80

Figure 31



Cerebellum from a child aged four weeks. There is a deep concavity in the area bordered by the free edge of the tentorium (head circumference 37cm., cerebellar weight 13gms.)

...../81

Figure 32

There is considerable flattening and excavation of the superior surface with atrophy of the cerebellar folia. Cerebellum from a child aged five years who suffered recurrent episodes of shunt blockage (head circumference 53cm., cerebellar weight 33 gms.)

...../82

Figure 33

Cerebellum from a child aged twenty-one months who died after a shunt crisis following a long period of adequate control of the hydrocephalus. There is a severe buckling deformity of the supratentorial hernia (head circumference 53cms., cerebellar weight 64gms.)

...../83

Figure 34

Cerebellum from a child aged twenty months who died after repeated episodes of shunt blockage. Note severe "lipping" of the lateral edge of the supratentorial component where it forms a deep groove over the free margin of the tentorium (head circumference 62cms., cerebellar weight 56gms.)

...../84

evident that all cases, except one, received decompression treatment for hydrocephalus. As the majority fell into the neonatal age group, it was decided to concentrate on this group for the purpose of correlating head circumference with such parameters as age, cerebellar weight and the type of cerebellar surface (elevation) (see Table 3). The table is divided into four - I. head circumference under 10th. percentile; II. head circumference between 10-50th. percentile; III. 50-90th. percentile; IV. above 90th. percentile. The head circumference was recorded in fifty-four neonates.

When the superior surface of the cerebellum with reference to "elevation" is considered, certain types appear to be more common in the neonatal group (see Table 4). Thus, of a total of fifteen cases showing concavity of the superior surface (i.e. superior surface type A), ten (70%) occurred within this age group; similarly, of a total of sixteen cases showing flattening of the superior surface (superior surface type B), eleven (69%) occurred within this group. These two superior surface types were more or less evenly distributed throughout the four neonatal groups shown in Table 3; these groups are also found in those with head circumferences above the 90th. percentile. It is therefore evident that flattening and depression of the superior cerebellar surface occurred despite a normal head circumference, and were also found in those with circumferences below the 10th. percentile.

The most common type of superior surface was group D, characterised by mild herniation through the tentorial notch; this formed about 50% of the whole series and included the majority up to the age of twelve months. Group D cerebellums most closely

Table 3

I.

P.M. No.	Age	Cerebellar Weight (Gms.)	Head Circumference (Cms.)	Superior Surface
5552	1d	9.5	31	D
4535	3d	7.9	29.5	B
4219	1m	10.3	31	D
4272	8d	3.7	30.5	A
4095	5d	7.9	31	B

II.

P.M. No.	Age	Cerebellar Weight (Gms.)	Head Circumference (Cms.)	Superior Surface
3292	24d	13.1	35	D
3459	19d	8.6	33	D
4661	12d	9.7	34	D
4736	3d	15.4	33	D
4787	5d	8.1	33.5	B
4788	2w	21.4	32.5	D
4295	10h	13.2	33	B
5785	2d	11	33	B
5388	4d	15.4	34	G
5629	3d	24.7	33	F
3765	9d	9.8	34	D
3858	12d	12.1	33.5	B
3104	4d	13.1	33	B
4539	10d	8.4	35	D
4589	8d	13.2	35	D
4665	19h	13.8	34	D
4666	22d	10.9	34	D
4678	7d	14.5	35	D
4635	2d	14.3	35	B
4316	17h	14.2	33	D

...../86

Table 3 (Contd.)

III.

P.M. No.	Age	Cerebellar Weight	Head Circumference	Superior Surface
		(Gms.)	(Cms.)	
3485	13d	12.5	38	D
3755	18d	14.2	36	A
3617	2w	18.1	38	D
3849	4w	13.1	37	A
4720	1d	13	36	D
4789	15d	16.9	37	D
4913	1d	17.6	36	B
4918	1m	10	39	B
4380	1m	18.6	38	D
4299	6d	12.7	36	A
4227	15d	14.8	38	D
5655	3d	11	36	D
5112	2d	16.7	36	D
4477	3w	21.6	39	D
4580	2w	15.6	39	A
4230	2d	17	36	D
4276	1m	22.9	36	A
4294	6d	14.8	38	A
4173	3w	13.8	37.5	D
5101	5d	20	38	D

IV.

P.M. No.	Age	Cerebellar Weight	Head Circumference	Superior Surface
		(Gms.)	(Cms.)	
3336	8d	14.9	41	A
3287	2w	11	43	A
4248	3w	23	40	D
5793	25d	16.9	47	D
4133	12d	10	43	A
4471	22d	12.8	40	D
4245	2d	5.1	48	B
4320	1m	18.7	43	D
4315	25d	21.6	41	F

...../87

Table 4

	0-1 mo	1-12 mo	>12 mo
A	10	4	1 (1)
B	11	5	0
C	0	1 (1)	0
D	39	9 (1)	3 (2)
E	0	0	1 (1)
F	2	2 (2)	2 (2)
G	1	3 (3)	6 (6)

Shows the number of cases in various superior surface elevation groups according to age. (Number of cases with shunt-treatment shown in parenthesis)

...../88

approximated the superior surface of the normal human cerebellum, the difference being that, in the abnormal cerebellum, the convex surface protruded through the tentorial notch.

Those cerebellums showing moderate (group F) to extreme (group G) supratentorial herniation (sixteen cases in all), were more common in the post neonatal group. The largest number of group G cases were among those older than twelve months. Except for one case, all group G cases had shunt treatment (see Table 4).

Of the two cases showing unusual abnormalities (C and E), one (C) was found in a child aged nine months and the other (E) in a child aged twenty-one months. Both children had terminal events complicated by recurrent shunt crises. The only case older than twelve months with a concave surface also had repeated terminal shunt crises (see Figure 32).

Although no direct measurement of ventricular size was performed, it was noted that apart from those cases in whom the head circumferences were increased and who showed obvious reduction in cortical thickness and ventricular dilatation, evidence of hydrocephalus was also discernible in those with a normal head circumference. This occurred particularly as mild to moderate dilatation affecting the occipital poles of the lateral ventricles.

The association between hydrocephalus and normal skull circumferences in children with meningomyelocele is well-described. Peach (1965) found that the majority of his cases had a normal skull circumference but, despite this, 75% showed clinical evidence of hydrocephalus in that the fontanelles were enlarged and the sagittal sutures were widened; also, in nineteen of the twenty cases which he studied, the ventricles showed moderate to severe

...../89

dilatation. MacFarlane and Maloney (1957 noted a similar discrepancy between skull size and hydrocephalic ventricles.

According to Cameron (1957), cranial expansion is retarded in these cases and there may even be microcephaly; his cases all showed severe internal hydrocephalus and two of the neonatal cases had head circumferences more than two standard deviations below the normal mean. He favoured the explanation of a fistulous escape of spinal fluid from the ventricles through the central canal of the cord into the amniotic sac; he argued that if ventricular volume was not maintained, regular expansion of the skull will not take place.

The explanation offered by Gardner (1968) for the "normal head" in association with the hindbrain malformation was as follows: Hydrodissection of the spinal subarachnoid space causes the ruptured and tethered spinal cord to protrude, forming the sac of the "myelocele". The pressure of the subarachnoid fluid may rupture the attenuating sac with relief of the hydrocephalus. During delivery the squeezing of the aftercoming hydrocephalic head may rupture not only the myelocele but also a previously unperforated rhombic roof.

It has been known for some time that hydrocephalus in these cases common commences after birth; the usual impression is that it coincides with surgical closure of the spinal lesion (Patten, 1953). One explanation for this (Wealthall, 1973) suggests that the meningomyelocele sac acts as a "pressure dampening system" within the spinal theca. Repair of the back lesion by removing this auxilliary to the normal pulsation-

...../90

absorption mechanism provokes hydrocephalus. He argues that this effect is nullified when the hindbrain deformity becomes established. This hypothesis, however, fails to take into account that the malformation is already established at birth in many cases of meningomyelocele and any pressure wave would almost certainly be arrested at the level of the deformity.

Our observations tend to support those of Lorber (1961) and Peach (1965) that head circumference is not a reliable indicator of ventricular size and it would appear that hydrocephalus is probably already present at birth in many children with meningomyelocele despite their normal head size. Of the sixty-three children who died within the first month of life, nine could be considered as having definite hydrocephalus based on a head circumference measurement. The remainder had circumferences within the normal range apart from five who were below the 10th. percentile. None of the sixty-three cases were shunt treated.

Beyond the neonatal age clinically obvious hydrocephalus appears to affect the majority up to the age of twelve months, beyond which normal head circumference again appears to be the rule. The ability of the skull bones to expand more freely in response to enlarging ventricles during the first twelve months seems to be the obvious explanation. This unlimited expansibility of the skull persists so long as the sutures remain ununited; left untreated, the hydrocephalus will progress. However, in most of the older children, shunt treatment would usually have been in progress for some time and control of

...../91

hydrocephalus would inevitably have facilitated some degree of fissural fusion; if acute hydrocephalus now supervenes, the situation would be equivalent to that found in the adult with a rigid cranial vault. Blockage of the Holter valve is a common complication in these children.

This would explain some of the unusual deformities found superimposed upon the supratentorial hernia in the older age groups (Groups C and E). This is seen in the form of buckling, mushrooming and also excavation deformities found in this part of the cerebellum in those children in whom the terminal event is determined or accompanied by acute and recurrent shunt blockage; this probably occurs in those where fissural fusion has become established and where the supratentorial cerebellar projection bears the full brunt of any acute rise in intracranial pressure. Thus the state of the sutures appears to have a decided effect on the type of supratentorial herniation.

In a previous section it was shown that there is an overall progressive increase in weight of the cerebellum in the different age groups studied (Part 1); it is evident in these cases that cerebellar growth can only take place through the tentorial notch; the size of the small posterior fossa remains relatively constant and, as seen previously, there is an apparent progressive shortening of the cerebellar "tail" with age.

Supratentorial herniation, thus, is probably related to the ability of the skull bones to expand; this, in turn, permits dissipation of any raised intracranial pressure. Flattening and excavation of the superior surface appears to result from a

...../92

direct encroachment of the overlying cerebral cortex through the tentorial notch. A similar situation occurs in hydrocephalus without meningomyelocele (Gilles and Kassiner, 1976); in such cases hippocampal herniation is common. The main difference is that in the "Arnold-Chiari" malformation the tentorium cerebelli is hypoplastic giving rise to a large tentorial notch; this permits a greater surface area of cerebral cortex to contact the upper surface of the cerebellum. The frequency with which superior surface groups A and B occur among neonates with normal and even low head circumference measurements may be viewed as indirect evidence of the presence of hydrocephalus in these groups.

Although herniation of cerebral cortex into the posterior fossa secondary to a prenatal hydrocephalus is one likely explanation for flattening and excavation of the cerebellar surface, there are two other possibilities to be considered. First, overgrowth of cerebral tissue as suggested by Barry, Patten and Stewart (1957) may be expected to produce a similar effect; but there are strong arguments against this hypothesis as discussed previously.

The second possibility is the hydrodynamic theory as proposed by Cameron (1957); this presupposes a fistulous communication between the central canal and the amniotic cavity. The resultant pressure differential between amniotic fluid and ventricular fluid causes a prolapse of the hindbrain into the foramen magnum. This theory is compatible with an association between the hindbrain malformation and a small head.

...../93

This theory is associated with the finding of hydromyelia of the central canal of the spinal cord; this is found in only a small number of cases (Cameron, 1957) and only involves certain levels of the cord. The development of a cervico-medullary kink commonly found in the deformity could lead to the central canal being obstructed at this level. Failure to find a patent central canal does not, of course, exclude its existence at an earlier stage in development of the deformity.

The question to be asked is: does some limiting factor exist in the intrauterine environment which prevents the skull bones from being thrust apart in response to the enlarging ventricles? One explanation may be found in recent experiments carried out on hydrocephalic cats (Hochwald, Epstein, Malham and Ransohoff, 1972 and 1973). Adult cats were made hydrocephalic by intracisternal injection of Kaolin. Acute hydrocephalus was followed, after a period, by a decrease in intraventricular pressure; this was attributed to transventricular absorption of cerebrospinal fluid. In this situation the intact skull limits the extent to which the ventricles dilate; beyond a certain point increased intraventricular pressure will initiate transventricular cerebrospinal fluid absorption and the hydrocephalus will become compensated.

When craniectomy was performed before or after hydrocephalus was induced, the ventricle dilated progressively. As the unsupported brain is not sufficiently elastic to resist deformation from the increased ventricular pressure, the hydrocephalus became decompensated.

...../94

Compressive head wrapping in infants with hydrocephalus is said to produce a similar situation to that seen in the hydrocephalic cat with an intact skull (Epstein, 1973; Epstein, Hochwald, Wald and Ransohoff, 1975).

Is it possible that the "latent" hydrocephalus frequently seen in infants at birth with meningomyelocele represents a type of compensated hydrocephalus? Is it possible that the limiting factor operating inutero is the normal pressure exerted by the amniotic fluid which, in turn, buttresses the foetal skull and so prevents its expansion?

Fishman and Greer (1963) demonstrated an increase in brain water content in experimental hydrocephalus. Similar studies have shown transventricular absorption of cerebrospinal fluid when intraventricular pressure reaches a certain threshold in hydrocephalic cats (Sahar, Hochwald, Sadik and Ransohoff, 1969). Is it possible that the increased cerebral hemisphere weights reported by Potter (1961) and Emery (1964) in children with meningomyelocele is due to increased water content?

...../95

PART 4

THE PATHOLOGY OF THE CENTRAL LOBULES

Chiari (1895), in his description of the types of deformity of the cerebellum, drew the important distinction between the deformities seen in adults (distortion and dislocation of the tonsils), and those in infants associated with meningomyeloceles (distortion and herniation of the central lobes). The latter is probably related to the fact that the central lobules of the cerebellum develop before the lateral lobules and it is likely that the movement of the central lobules forms the key to the understanding of most of the cerebellar abnormalities associated with meningomyelocele.

Thus, a detailed study of the changes that occur in the central lobules of the cerebellum was thought worthwhile.

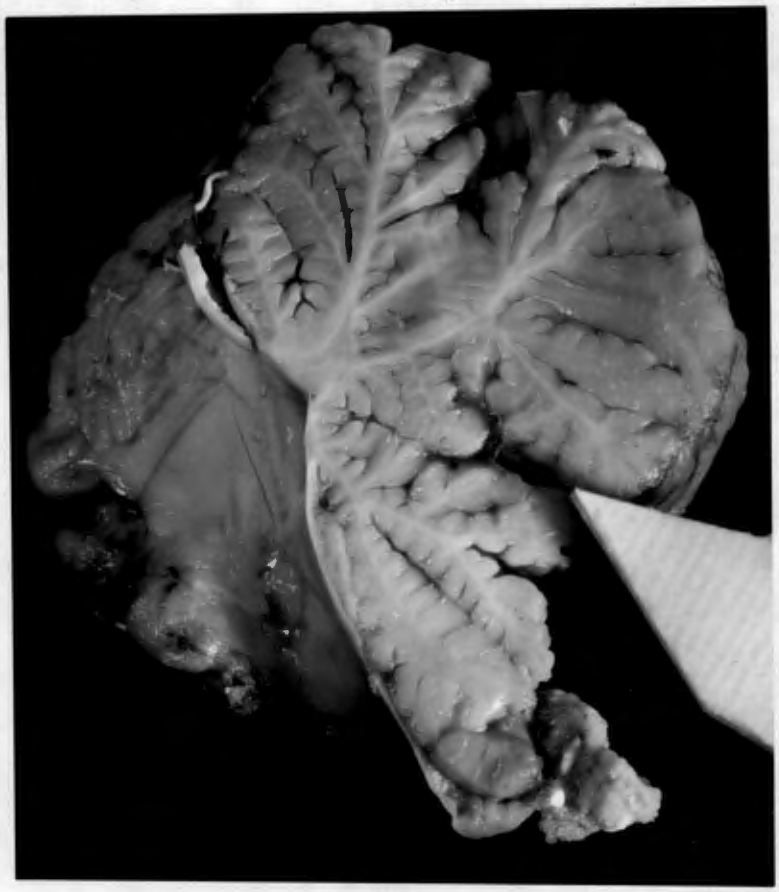
Overt hypoplasia of the cerebellar folia was seen in many of the specimens studied (see Figure 35a); these were confined to the younger group and more commonly involved the upper lobules. One case showed a small cystic cavity within the dislocated segment and was associated with gross evidence of chronic necrosis in this area (see Figure 35b); there was no evidence of communication between the cyst and the fourth ventricle.

Macroscopic evidence of acute necrosis was seen in 20% of cases and was usually seen in association with the folia of the upper central lobules and in the area adjacent to the posterior lip of the foramen magnum (see Figure 36).

When the weight of the cerebellum was related to the length of the dislocated segment, an inverse relationship was apparent (Figure 37). There was a diminution in the length of the tail corresponding to children with larger cerebellums and also in

..../96

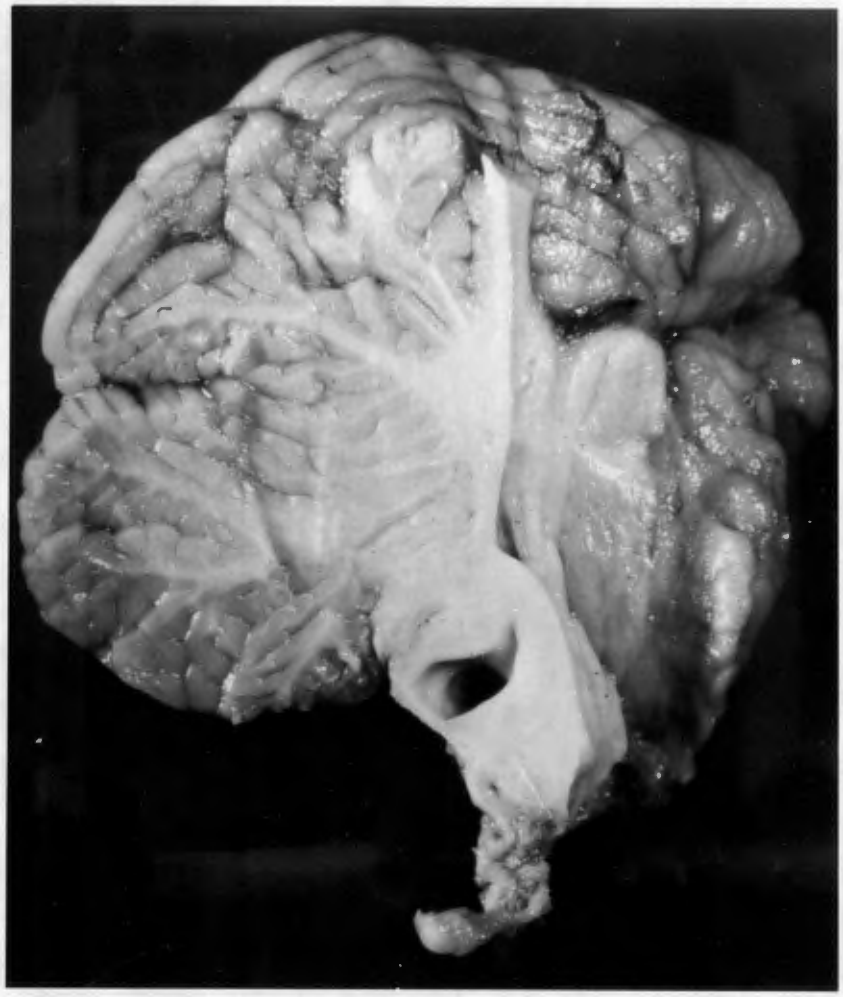
Figure 35a



Mid-sagittal view to show a marked degree of cerebellar hypoplasia. Arrow indicates level of prepyramidal fissure.

...../97

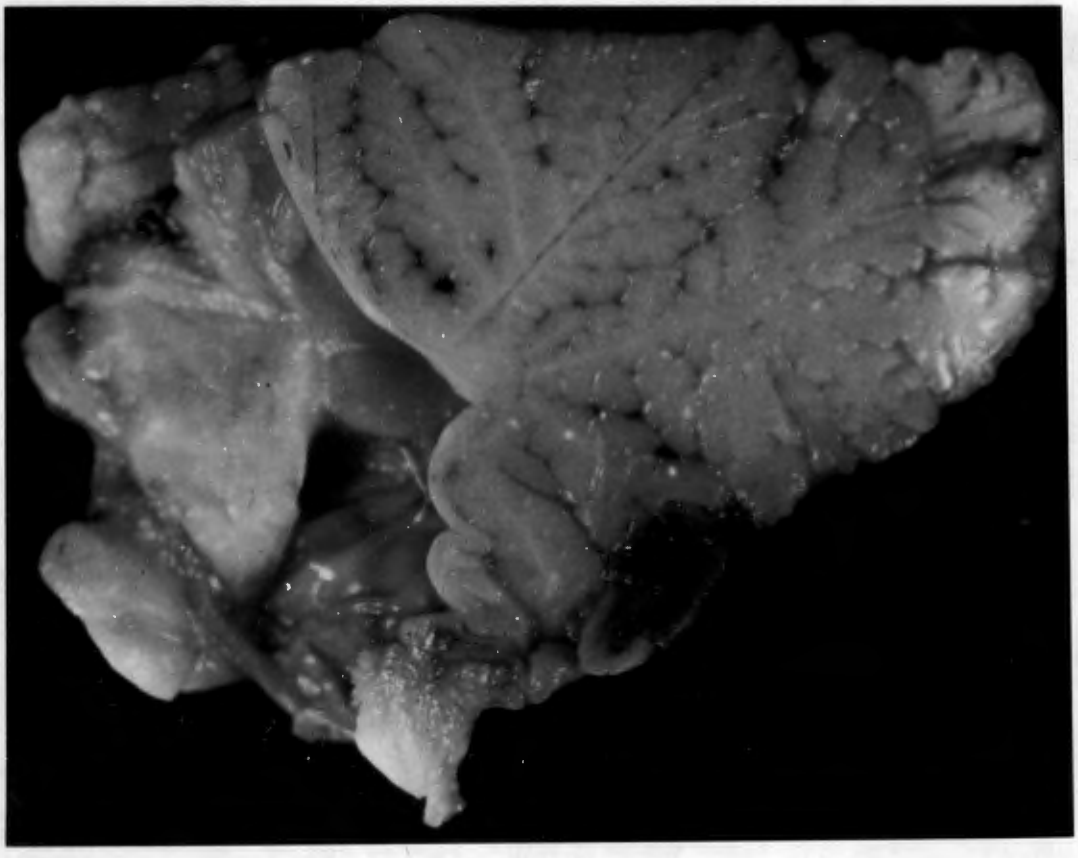
Figure 35b



Shows a small cyst within the cerebellar "tail", the latter showing evidence of "long-standing" necrosis. (This mid-sagittal view also shows depression of the superior vermis and is an example of group G described in Part 3)

...../98

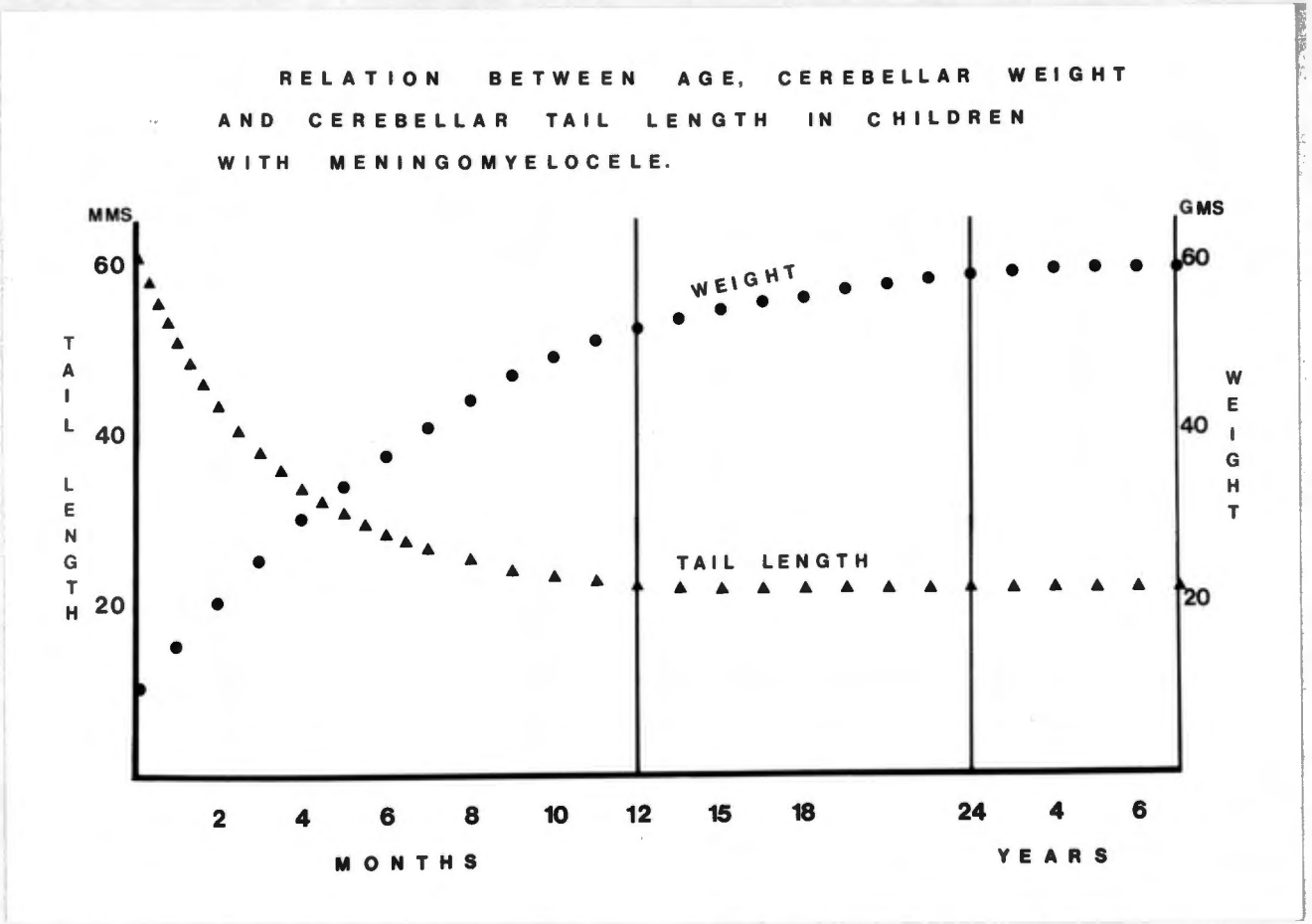
Figure 36



An area of acute necrosis involving the pyramid. Such areas of acute necrosis were frequently seen adjacent to the posterior lip of the foramen magnum.

...../99

Figure 37



Cerebellar 'tail' length, cerebellar weight and age in children with meningomyelocele.

association with increased survival time.

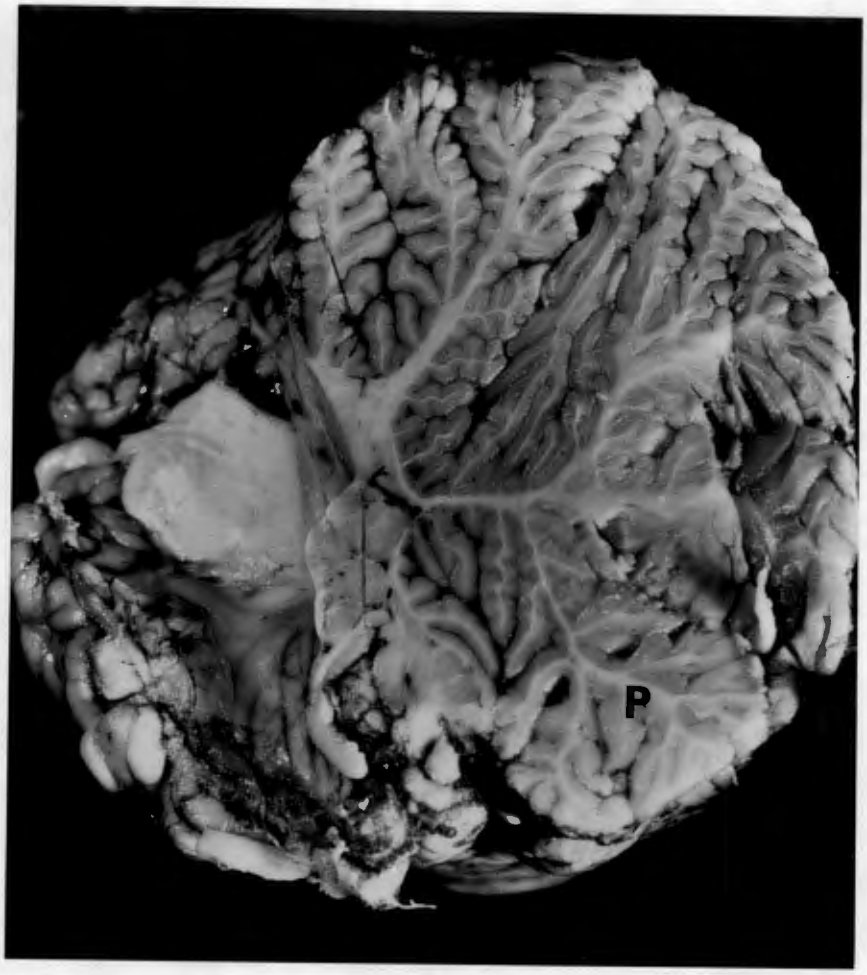
The length of the cerebellar component in the upper cervical canal ranged from 0mm. to 68mm. There were ten children in whom the cerebellum showed no tissue below the foramen magnum. Five of these had received decompression treatment with a Holter valve, and they comprised 25% of the shunt-treated group. These invariably belong to the older age group and one of the striking features of the specimens was necrosis with severe loss of tissue in the caudal area; the nodule, uvula,and sometimes the pyramid, were usually absent or deficient (see Figure 38). Compared with the younger age group which were characterised by longer dislocated cerebellar segments, although macroscopic evidence of necrosis was frequently present, the tissue comprising the caudal lobules was relatively well preserved (see Figure 39).

The remaining five children showing no infraforaminal dislocation of cerebellar tissue formed 6% of the untreated group; neither loss of tissue or necrosis was a significant feature.

Acute Necrosis

Of the 100 specimens, thirty-three showed histological evidence of acute necrosis (Figures 40 and 41), mainly confined to the upper central lobules. Acute necrosis was associated with two distinct clinical groups. The first group of twenty-six children were all under the age of one month, fourteen being between the age of birth and one week, six between one and two weeks, and six between two weeks and one month. The

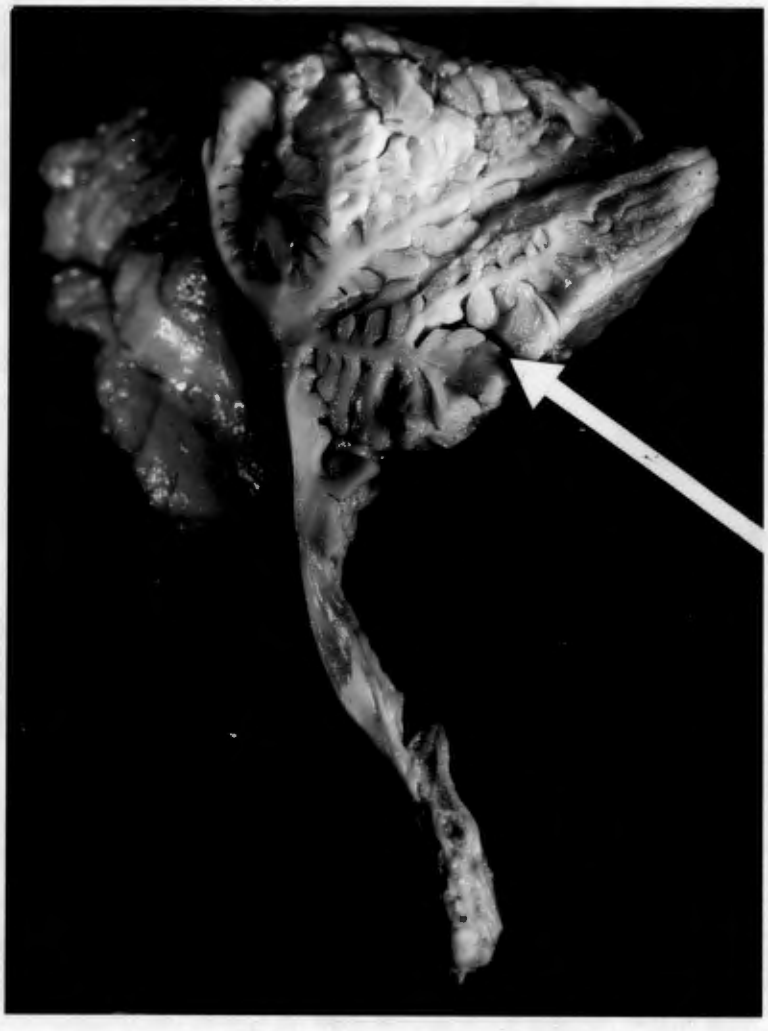
Figure 38



Mid-sagittal view of cerebellum from a child with meningomyeloceke at age eighteen months. Decompression with a Holter valve was performed at three months. Although the pyramid (P) appears to be comparatively normal, the nodule and uvula show marked atrophy and tissue loss.

...../102

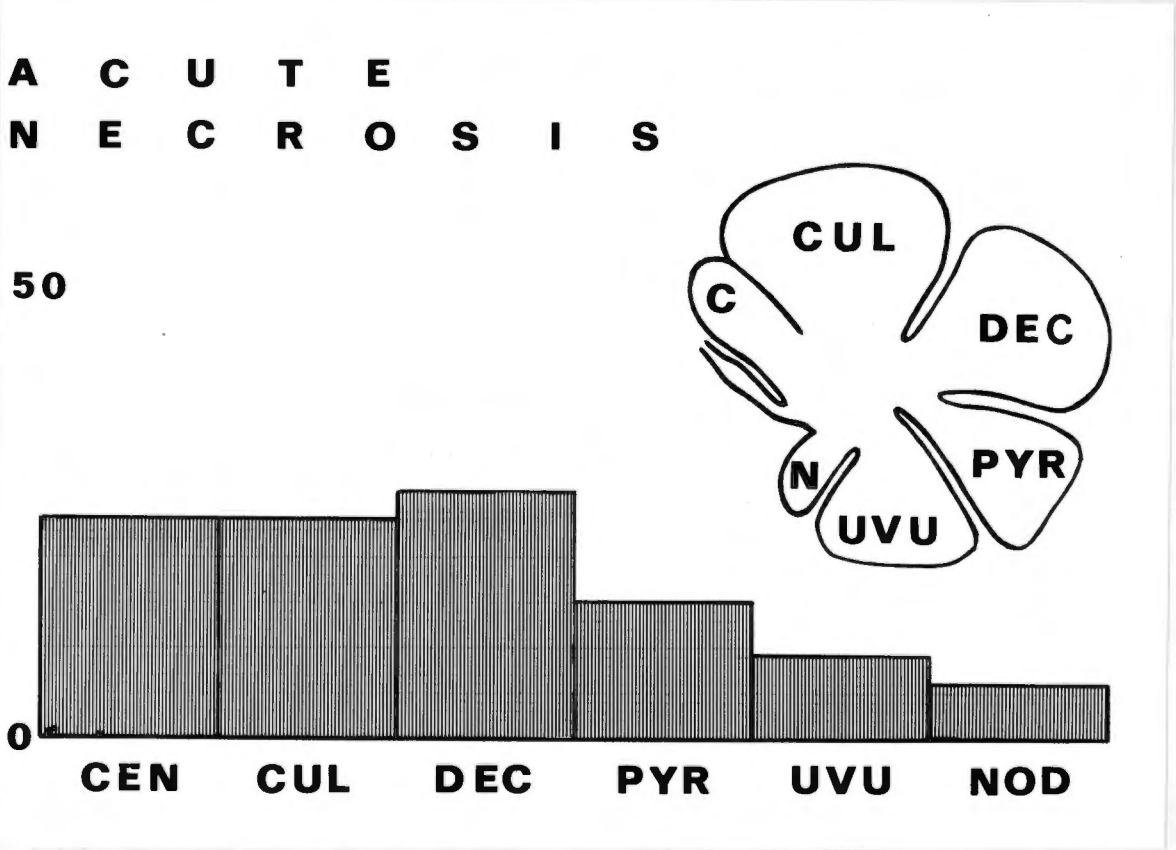
Figure 39



Mid-sagittal view of cerebellum from a child with meningomyelocele, soon after birth. Arrow shows the pre-pyramidal fissure. The nodule and the uvula are necrosed and elongated but there is no marked tissue loss. The pyramid appears to be comparatively normal.

...../103

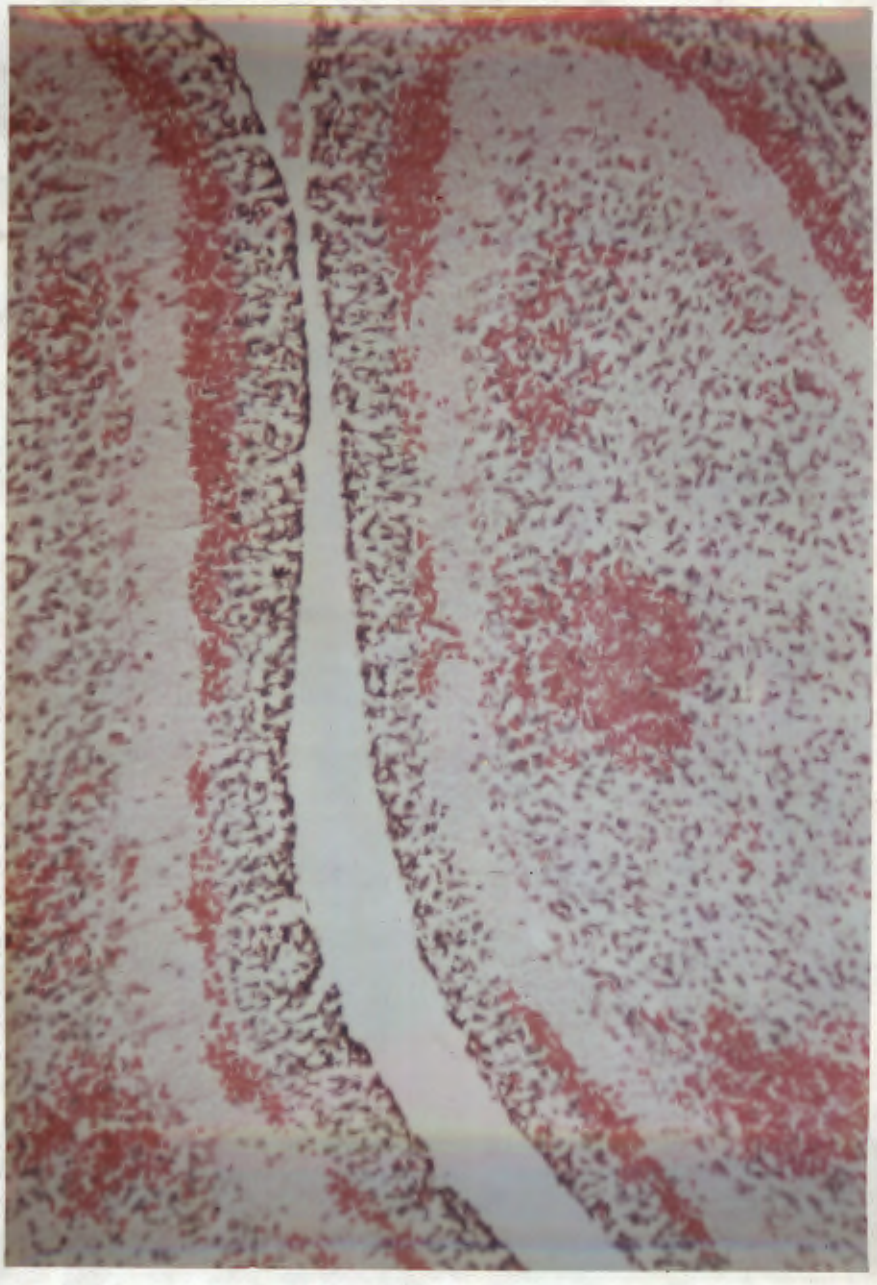
Figure 40



Distribution of acute necrosis in

the central lobules of the cerebellum.

Figure 41



Showing acute necrosis with recent haemorrhage in the cortex and internal granular layer.

...../105

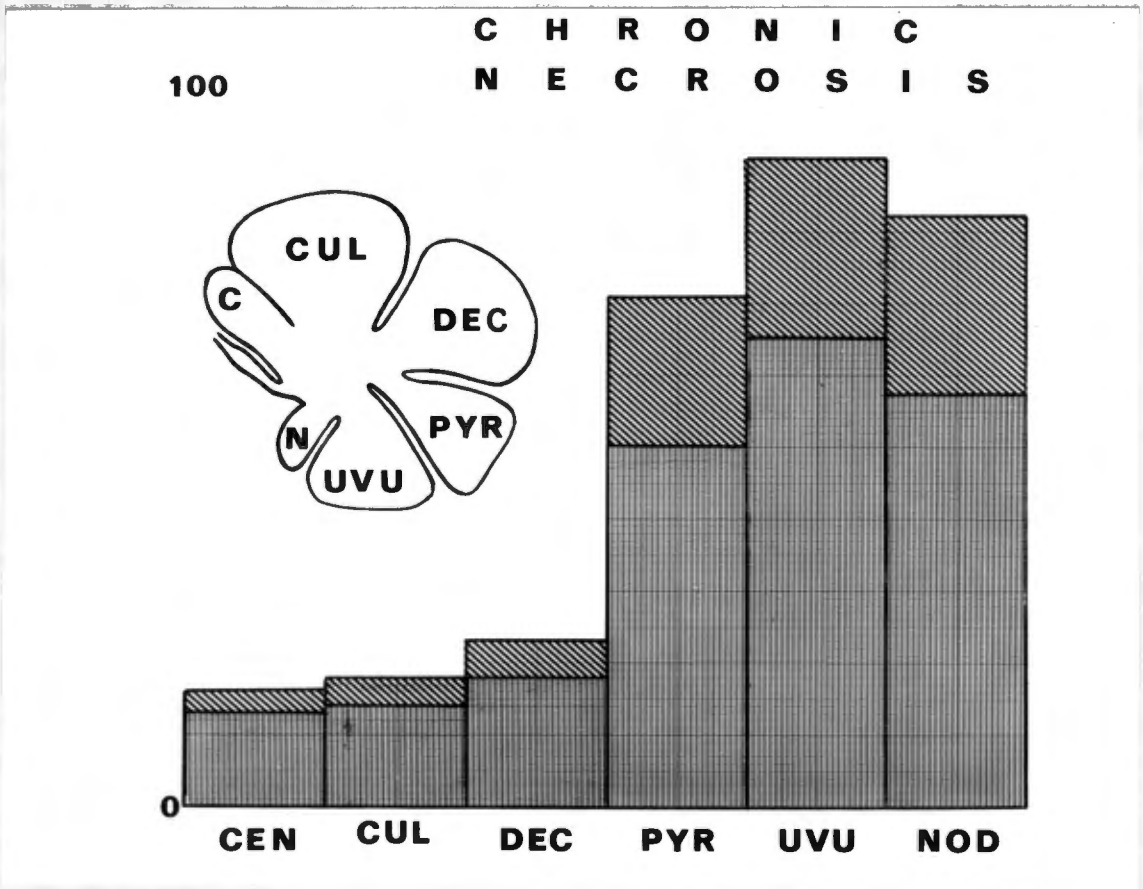
second group were six older children with a recently introduced Holter valve. The interval between the introduction of the shunt and death varied from one day to one week. There was no overlap in age distribution between the two groups. The remaining child, who showed both acute and chronic necrosis, had been treated with a valve for many months; the course had been complicated by recurrent blockage and frequent revisions, one of which precipitated the terminal state.

Old Necrosis

Histological evidence of long-standing necrosis was found in all of the 100 specimens examined. Thirteen cases showed diffuse, chronic necrosis which affected all of the lobules. In general, the distribution of chronic necrosis was chiefly within the pyramid, uvula and nodule (Figure 42). The principal feature of chronic necrosis was the loss of cellularity of the internal granular layer and Purkinje cell layer (Figures 43a and 43b). These changes sometimes affected very local areas of the cortex and were more liable to affect the ridges of the folia than the deeper interstices. Individual folia were frequently affected, particularly in the pyramid, and probably corresponded to areas where the cerebellum had apparently been in direct contact with the posterior margin of the foramen magnum or the floor of the posterior fossa. These lesions were similar to those described by Cameron (1957). In a few cases the nodule seemed to have necrosed almost completely, there being merely small areas of ependyma and central nervous tissue, with ghost-like areas of depopulated cerebellar cortex. Small fragments of

...../106

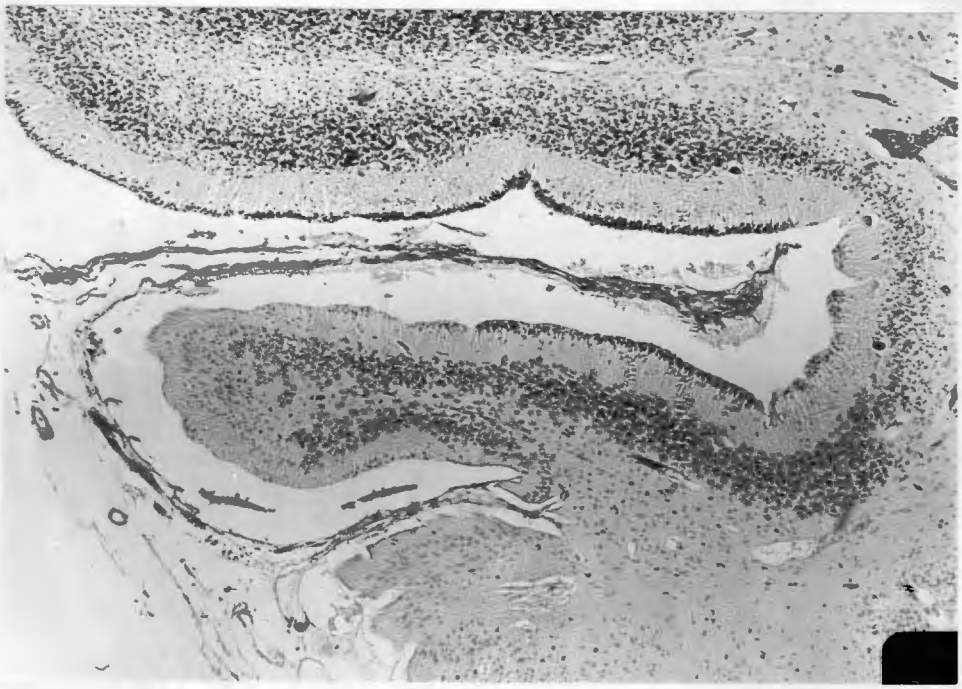
Figure 42



Distribution of chronic necrosis in the central lobules of the cerebellum.

...../107

Figure 43a



Photograph of section showing chronic necrosis, more marked in the lower part of the field. There is loss of differentiation of the layers composing the cortex with only a few Purkinje cells remaining.

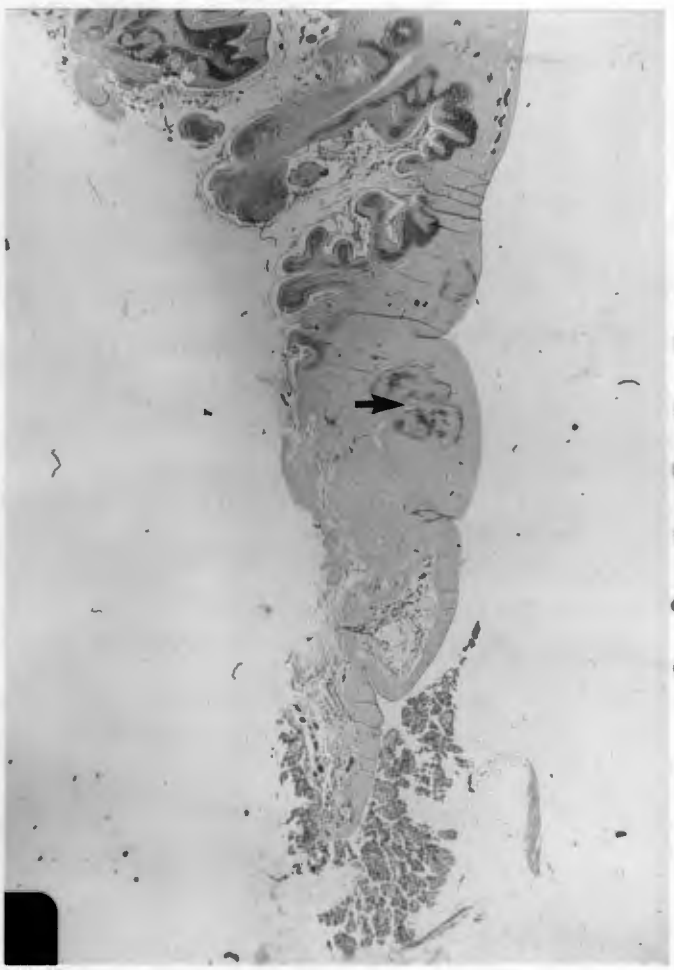


Figure 43b

Showing chronic necrosis in the dislocated segment of the cerebellum. Choroid plexus is seen at the caudal end. Foci of dysplasia are also present (arrow).

...../108

folia indicated the tissue origin.

Purkinje Cell Loss

This was only considered to be significant when less than half the normal population of Purkinje cells appeared to be present (compare Figs. 45a and 45b); this occurred in some part of the section in eighty-three of the 100 cases studied.

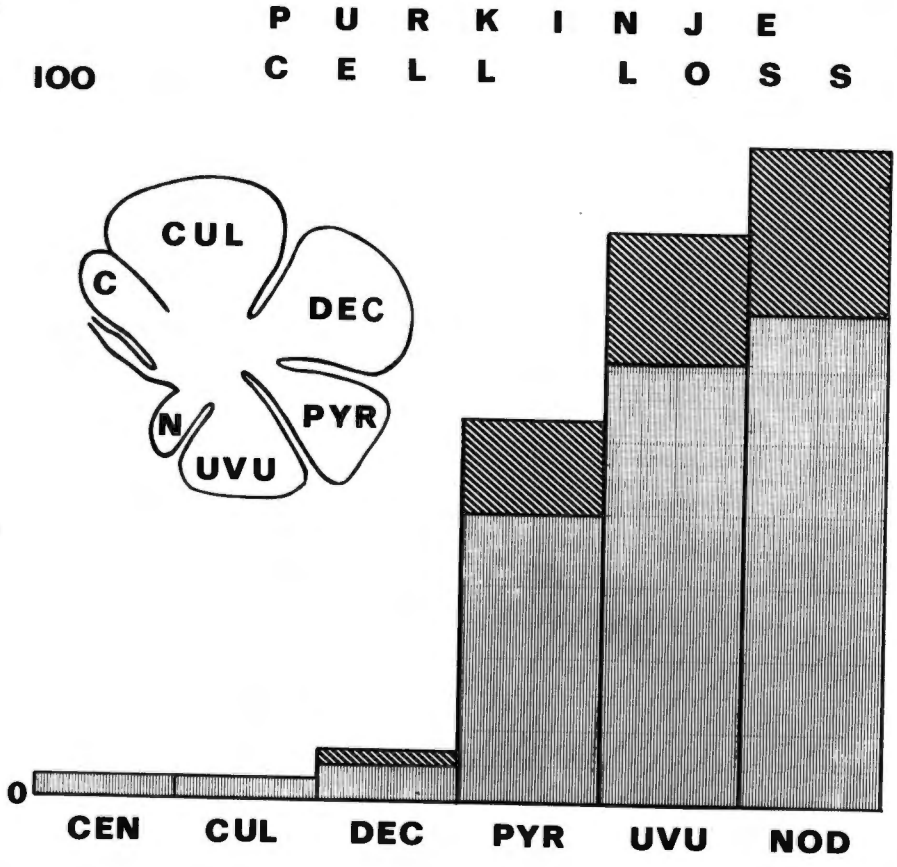
The distribution of Purkinje cell loss is shown in Figure 44 and principally affected the same lobules as did chronic necrosis. However, Purkinje cell loss and chronic necrosis do not necessarily go hand-in-hand; there were a number of cerebellums in which there had been extensive Purkinje cell loss with little gross cortical atrophy.

Dysplasias

A variety of abnormal structural formations in tissues were noted, especially related to the nodule and in the central areas related to the inferior velum. These areas have been described by others as 'heterotopic folia' (Peach, 1965) and 'internal microgyria' (Crome, 1952). The essential features of these abnormalities seemed to be an abnormal arrangement of the tissues in their local growth; therefore, the more conventional term of dysplasia of the developmental pathologist has been used.

Dysplastic changes, the most difficult to define, occurred in seventy of the 100 cases (Figure 46). About a quarter of the most grossly deformed cerebellums contained a central mass of dysplastic tissue lying just above the roof of the fourth ventricle and near the roots of the nodule and uvula. This area of dysplastic tissue usually appeared to be caudal or anterior to

Figure 44



Distribution of marked Purkinje cell loss in the central lobules of the cerebellum.

...../110

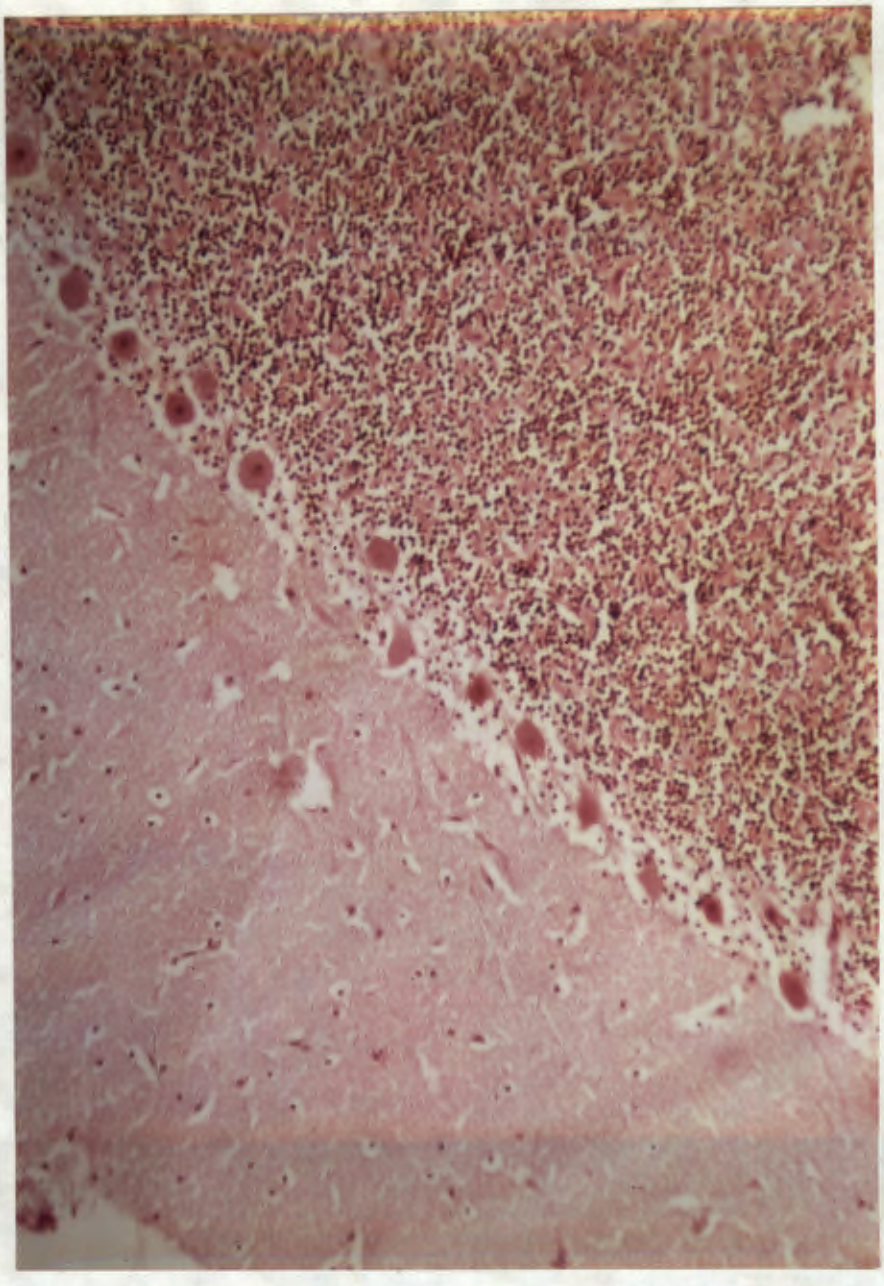
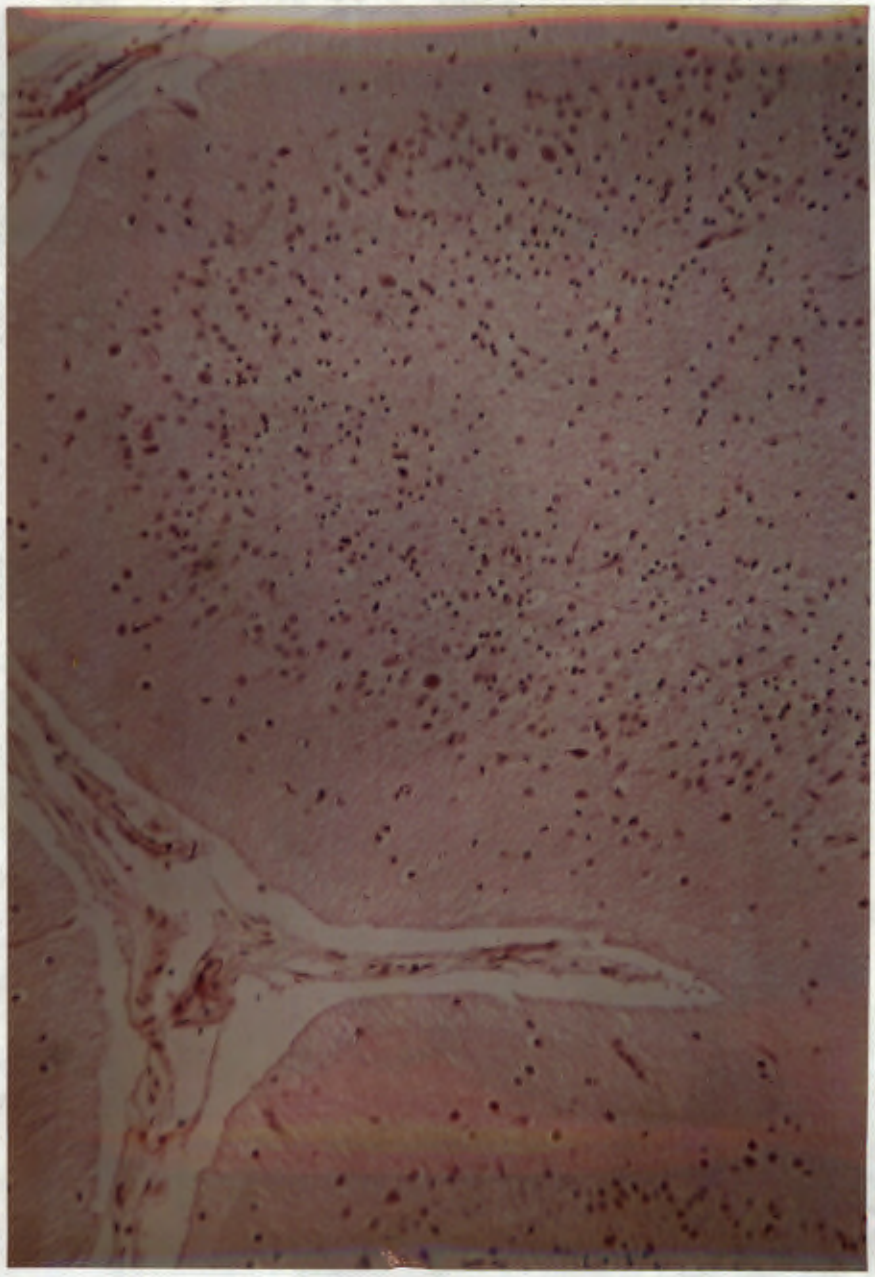


Figure 45a

Showing relatively normal run of Purkinje cells.

...../111

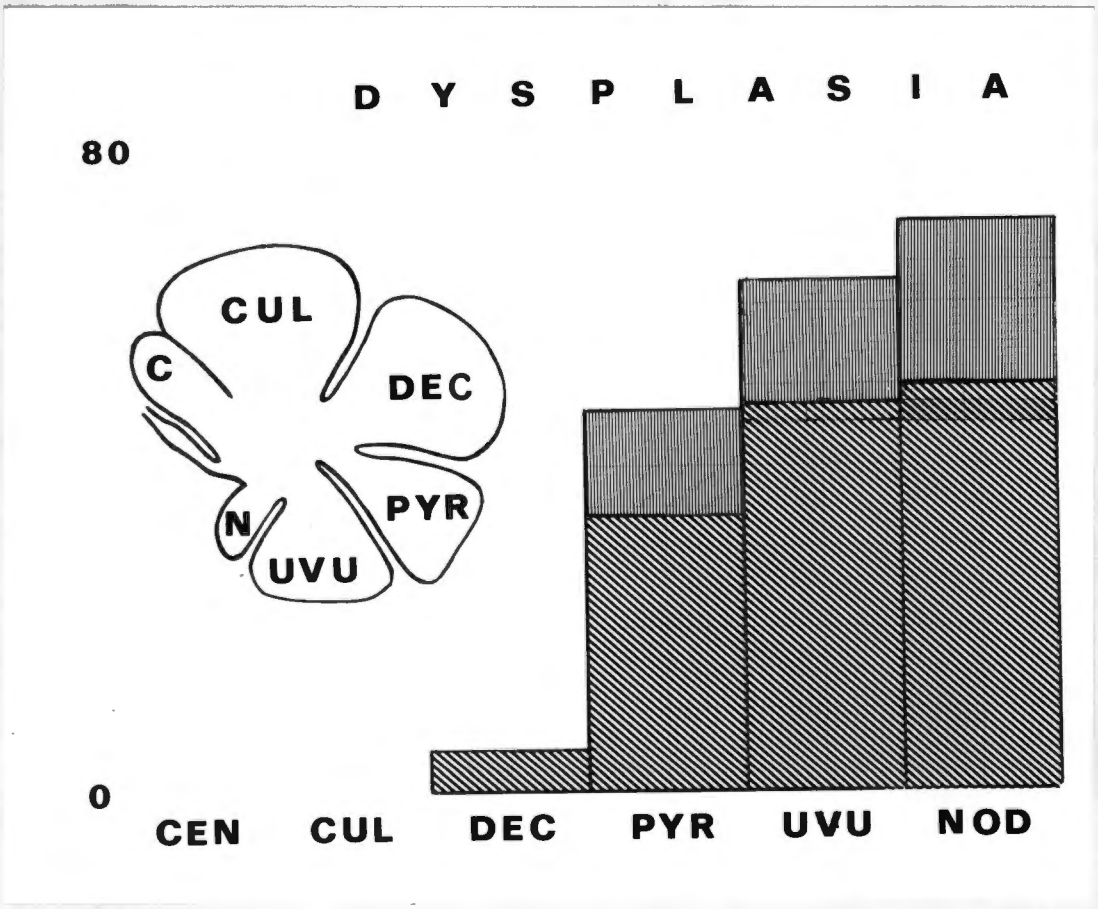
Figure 45b



Showing severe loss of Purkinje cells with associated chronic necrosis involving all layers of the cortex and internal granular layer.

...../112

Figure 46



Distribution of dysplastic change in the central lobules of the cerebellum.

...../113

the central group of ganglion cells which were usually present in normal sections from the same area.

The most characteristic dysplastic lesions consisted of irregular masses of Purkinje cells and what appeared to be a mixture of internal granular cells and strands and foci of molecular layer tissue (Figure 47). These areas very rarely showed calcification or evidence of old haemorrhage and necrosis. We prefer to use the term 'dysplasia' rather than 'heterotopic folia', as this tissue is abnormal and there is no true folium formation.

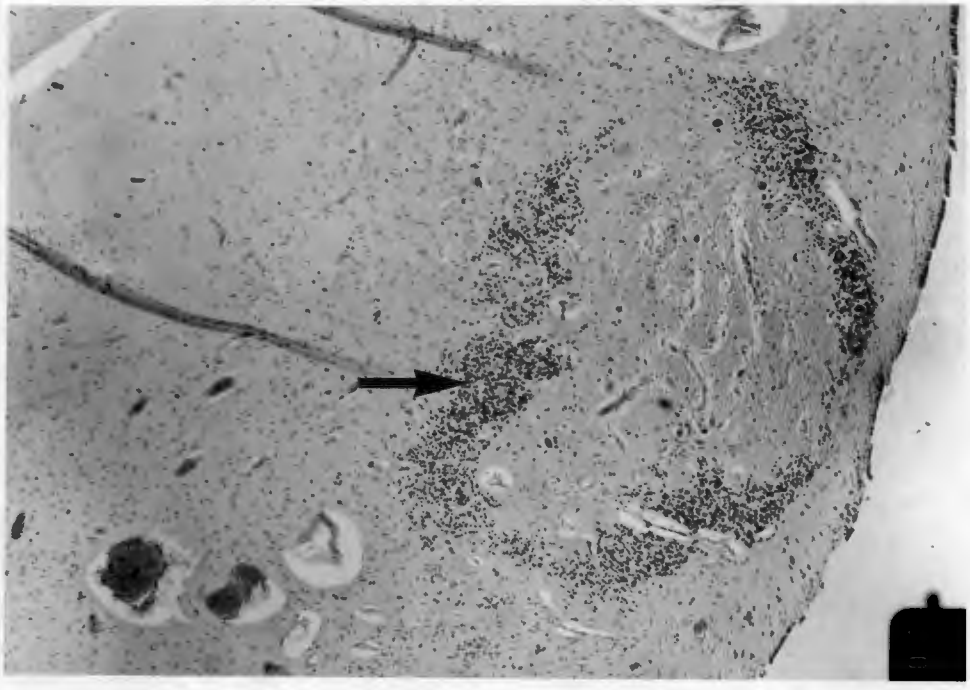
Cystic Degeneration

Slit-like cavities occurred in eight midline sections (see Figure 48). These were not lined with ependyma and occasionally contained groups of lipid-laden cells.

These cavities all occurred within the folia and showed branching into others. The appearance was of a degeneration of the centres of the white cores of the folia running into the hilum of the cerebellum, but not necessarily communicating with the fourth ventricle. Some of these cysts contained many compound granular cells but none were filled with blood. We did not examine serial sections to trace the ramifications of these lesions, but from our midline study were not impressed by their linking with the fourth ventricle, nor with evidence of any associated dilatation of the fourth ventricle. The lining of the roof of the fourth ventricle in most of these children appeared to be very well organised with cuboid and even columnar ependyma. However, this did not apply to four children who

...../114

Figure 47



Photograph of section showing area of dysplastic change (arrow) in the roof of the fourth ventricle; the latter with the ependymal lining is seen on the right.

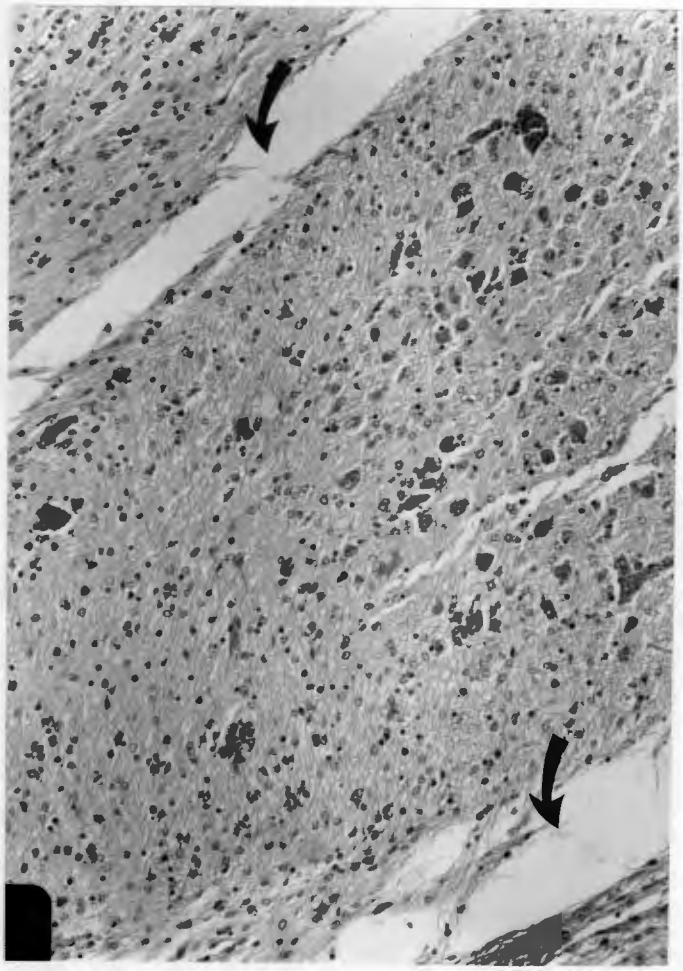


Figure 48

Photograph of section showing clefts (arrows) in the white matter of the cerebellum. Purkinje cells representing dysplastic change are also seen in the centre of the field.

..../115

showed gross dilatation of the fourth ventricle (this finding will be discussed in detail later).

Haemosiderin-laden macrophages within white matter cores were a striking finding in some cases (see Figure 49).

Discussion

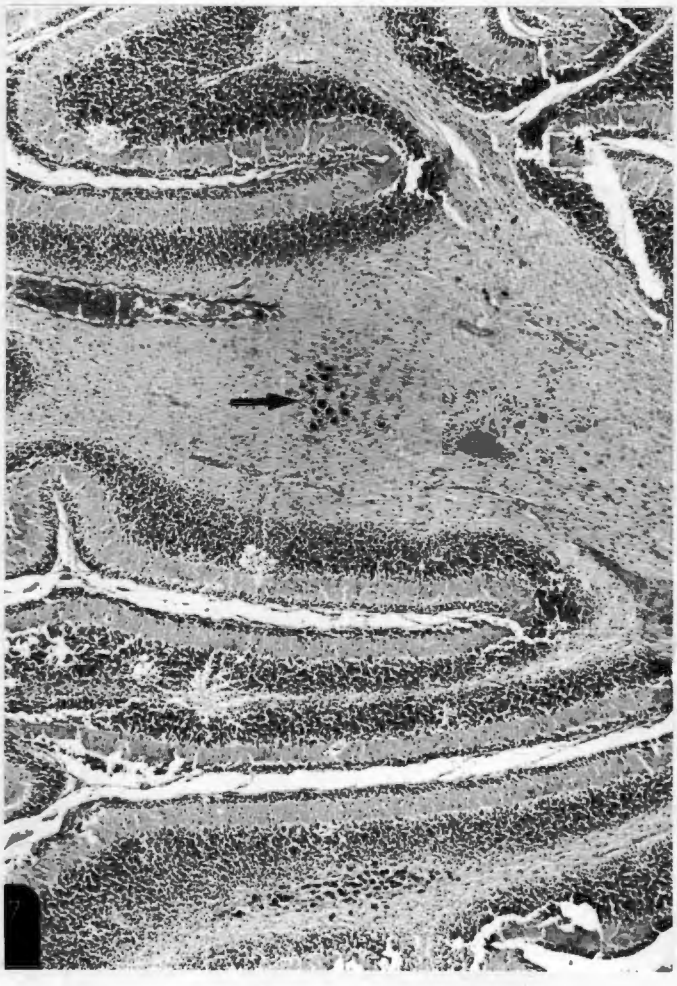
The findings reveal a varying pattern of necrosis, dysplasia and acute degeneration. Most of these lesions have already been noted by previous observers (Schwalbe and Gredig, 1907; Ingraham and Scott, 1942; Lichtenstein, 1942; Feigin, 1956; Cameron, 1957; Peach, 1965), but the purpose of this study of a large number of deformed cerebellums was to see if the lesions formed any distinct pattern which would help our understanding of the underlying condition.

The most frequent abnormality was necrosis, chiefly involving the caudal lobules. As will be seen from Figure 40, the extent of the necrosis was directly related to the position of the lobule. Within the 100 organs examined, there were none with a remaining normal nodule, whereas in most cases, the lingula and central lobules were probably within normal limits for the age of the child. This finding suggests that the deformities within the cerebellum were probably secondary and were notlikely to be due to any primary general cerebellar condition. The areas of chronic necrosis, while affecting the caudal lobules, were not confined to the lobules that were dislocated at the time of death.

When the extent of the cerebellar herniation into the neck was measured (see Figure 37), a progressive diminution with age with found. Interpretation of these data is not easy as one is

.....416

Figure 49



Showing foci of haemosiderin-laden macrophages (arrowed) within the white matter cores of the cerebellar folia.

...../117

dealing with a necropsy series and it could quite justifiably be argued that the longer-surviving children were those less deformed at birth. This is undoubtedly a factor, but there is further evidence within the skull which indicates that the growth of the cerebellum continues in children in whom the hydrocephalus has either undergone arrest or has been stabilised with a Holter valve. The direction of growth alters from a caudal to a cranial direction: this can be seen clearly in the way in which the cerebellum in older children very frequently herniates upwards through the tentorium (see previous section). The occurrence of old focal necrosis in the pyramid suggests that at an earlier stage this part of the cerebellum was in very firm contact with the foramen magnum and that this had later been relieved. Also, in a number of children, there is direct evidence that there had been very extensive necrosis of the nodule and, in some instances, complete disappearance of this lobule which seems to be independent of shunt treatment.

It is evident, therefore, that there is a reduction in the cerebellar dislocation following birth. Three factors are involved: 1) the severity of the condition related to mortality;

2) alteration in the direction of cerebellar growth;

3) necrosis and atrophy of the herniated tissue.

Apart from simple necrosis, the next most frequent observation was areas of dysplasia, particularly affecting the tissues just deep to the surface of the fourth ventricle and near the roots of the nodule, pyramid and uvula. These lesions have been discussed by Lichtenstein (1942) and Cameron (1957),

and our observations confirm the suggestion by Cameron that they are probably not primary developmental disorders but are due to interference with cortical development of the lobules of the cerebellum which are growing while being squashed into the vertebral canal. These areas of dysplasia are almost invariably associated with chronic necrosis of the overlying lobular folia.

As well as cortical atrophy and necrosis, there are areas in which the white matter of the folia have undergone degeneration, forming branch-like cavities within the white matter of the folia and, on occasion, forming fairly definite irregular cysts. Feigin (1956) also noted cystic cavities replacing much of the white matter within the caudal part of the cerebellum in one of his cases. In his study of twenty-six full cerebellums, Cameron (1957) found such lesions in 54% of his cases. Such lesions were found in 8% of the single sagittal sections of the cerebellum. In no instance was this cystic change associated with normal overlying cerebellar cortex. Cameron considered that these cavities communicate with the fourth ventricle. Although serial sections were not performed to follow the extent of these lesions, the impression here is that they are frequently widely separated from a diminished fourth ventricular cavity and that they require further study. While frequently there is evidence of old haemorrhage near some of these cysts, their contents rarely suggest that they are caused by haemorrhage. They usually contain, if anything, small groups of compound granular cells only and are not lined by ependyma.

...../119

The pattern of acute necrosis in the cerebellum does not coincide with that of chronic necrosis. Acute necrosis was found in two groups of children, one consisting of children under the age of one month and the other consisting of children who had suffered alteration in pressure on the cerebellum following a very recent operation for decompression.

The drop in cellularity in the cerebellar cortex is a subject for further study, but the more gross Purkinje-cells loss forms a pattern that is undoubtedly related to the chronic cortical necrosis. In addition, however, there is probably an overall reduction in Purkinje cells related to the same factors- such as chronic hypoxia or congenital heart disease - which produce a similar loss in other children. The relatively low Purkinje cell loss in the most normal lobules of the cerebellum in our children suggests that the original number and distribution of these cells was probably genetically normal. The general counts of the cells in the most sheltered lobules of the cerebellum (the lingula, central lobe and culmen) are such that one would not normally expect them to be associated with any clinically observable cerebellar lesions.

The results of this study support the impression that the areas of dysplasia found in these cerebellums are secondary and due to dislocation and interference with growth of the most caudal lobules of the cerebellum. Areas of necrosis above the foramen magnum are clearly compatible, in many instances, with mechanical influences; those in the dislocated segment probably result from vascular insufficiency consequent to constriction

..../120

at the level of the foramen magnum as well as a direct squeezing effect. Further, in surviving children, parts of the cerebellum which have not undergone necrosis appear to be capable of normal growth. Other observations suggest that further damage to the cerebellum in the form of acute necrosis is liable to occur around the time of birth, and in association with periods of blocked shunt and acute decompression procedures; this is most probably associated with acute pressure changes.

Summary

Deformities were present in all to varying degrees. There was necrosis and atrophy of the most caudal lobules of the cerebellum, particularly the nodule, and there was evidence that the nodule could completely disappear in some cases.

Following birth andttreatment of surviving children, the pressure on the caudal lobules diminished and the surviving and residual parts of the cerebellum, i.e. the more cranial lobules, appear to develop in a normal way. Dysplastic areas in the cerebellum seem to be secondary to attempts at growth under abnormal pressures. Areas of acute necrosis are related to very recent alterations in position and pressure within the fourth ventricle, either related to birth or to recent bouts of intracranial hypertension or possibly hypotension.

The findings support the impression that some of the deformities usually described as Cleland or Arnold-Chiari malformations are due to secondary states.

ADDENDUM to Part 4

Recently, Emery and Gadsdon (1975), using some of the material studied in this thesis, showed the cell and DNA complement of the declive and central lobule to be only slightly reduced compared with other lobules; the pyramid, uvula and nodule showed the greatest decrease in cell and DNA content.

The method used was a computerised analysis of a television image of neurones in standardised sections. The findings suggested to them that the central lobules of the cerebellum are probably genetically normal but have irregular degeneration and arrest of growth, probably the effect of pressure at the foramen magnum.

..../122

PART 5

"SPLIT CEREBELLUM", "SYRINGOCERBELLA"

AND FOURTH VENTRICULAR DILATATION

Previous studies have usually dealt with small numbers of children with meningomyelocele and it is not unexpected that when a larger population is involved, unusual variations of the hindbrain malformation should come to light; these unusual abnormalities might offer important clues to pathogenesis which have evaded a more general approach.

Results

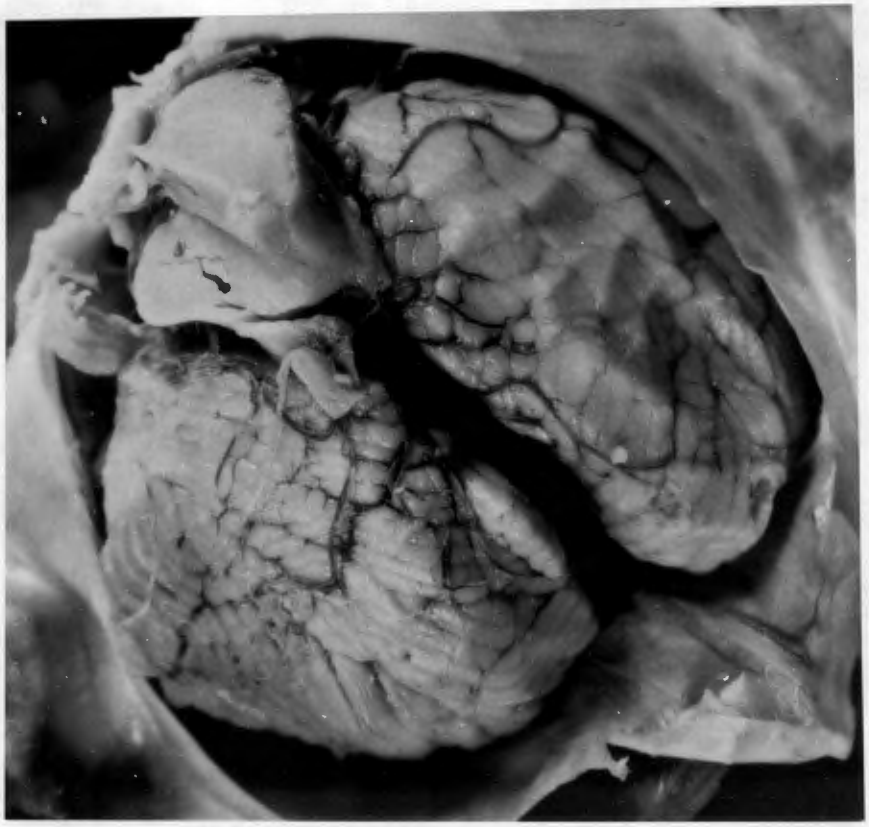
One child was born with a large lumbosacral meningomyelocele and lived for four years. There was no clinical evidence of hydrocephalus and intelligence was assessed as being relatively normal. He died from renal failure.

The tentorium cerebelli was markedly hypoplastic and there was a large tentorial hiatus (see Figure 50a). The superior surface showed wide separation of the hemispheres, viewed from above (see Figure 50b). A midline sagittal view (see Figure 50c) showed the limits of attachment of the hemispheres to be markedly reduced; the vermis was considerably hypoplastic. The superior medullary velum was still intact with an attached but dislocated central lobule. The cerebellum weighed 62 gms. (normal for age = 140 gms.). The caudal central lobules were absent; there was no cerebellar tissue in the upper cervical canal. The vermis in this area showed old necrosis which was confirmed microscopically. A relatively normal cerebral cortical mantle and small lateral ventricles confirmed the absence of associated hydrocephalus; the head circumference was, in fact, below the 10thl percentile. This cerebellum is referred to in the text as the "split cerebellum".

Another cerebellar specimen showed marked irregular cavitation

...../123

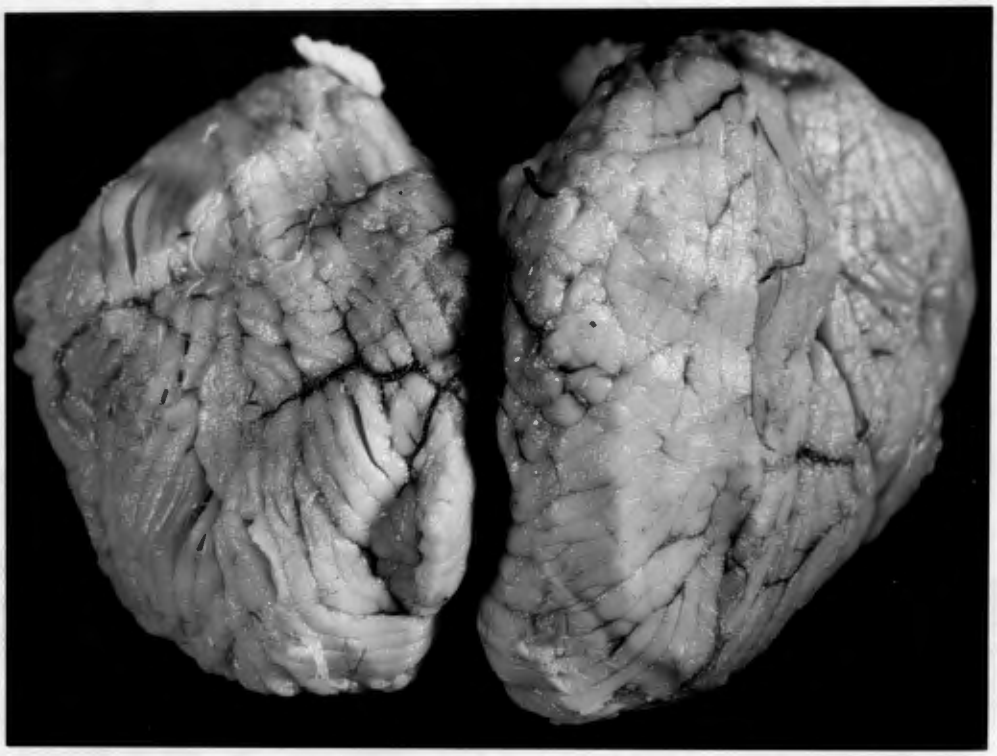
Figure 50a



Shows a cerebellum with marked separation of the hemispheres. The superior vermis is absent. There is severe hypoplasia of the tentorium cerebelli.

...../124

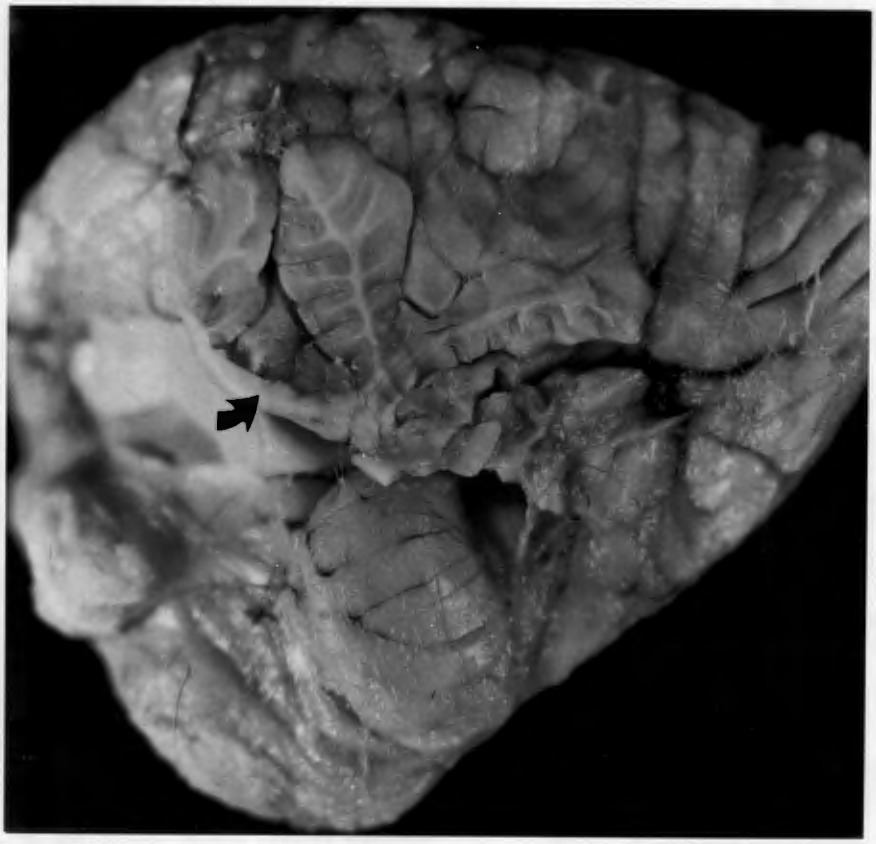
Figure 50b



Same cerebellum as is shown in Figure 50a, after removal from the posterior fossa.

..../125

Figure 50c



Mid-sagittal view of the same cerebellum as is shown in Figures 50a and 50b, showing the limits of attachment of hemispheres with a comparatively intact superior medullary velum (arrow) and marked hypoplasia of the superior and posterior vermis. A cerebellar 'tail' is absent.

...../126

within the organ; the cavity communicated with the fourth ventricle through a small aperture in the roof of the ventricle (see Figures 51a and 51b). There was extensive destruction of cerebellar tissue.

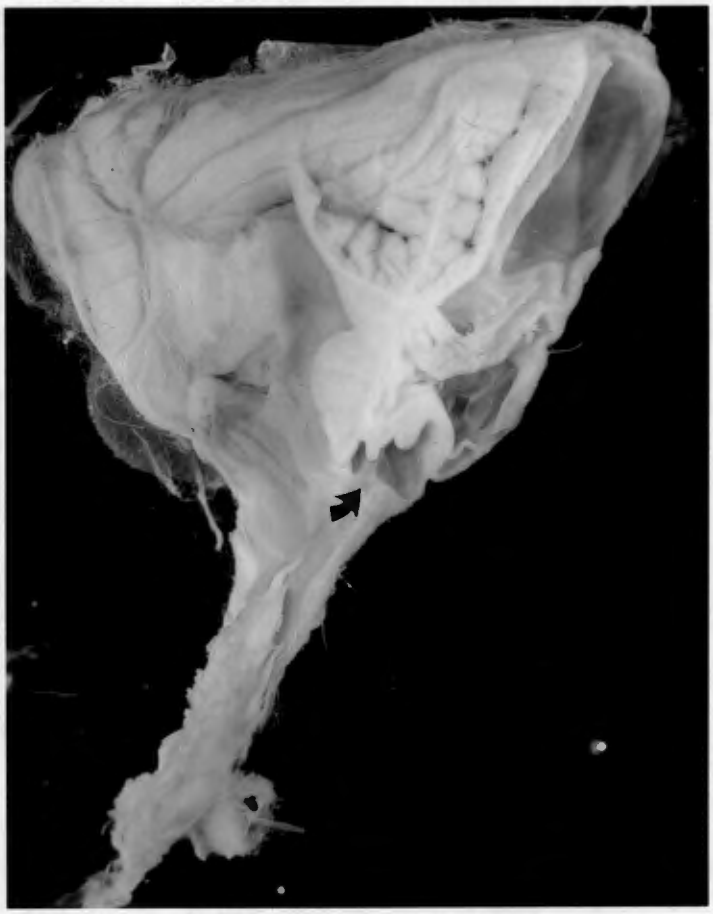
Cystic dilatation of the fourth ventricle was found in 6% of this series. In one case the fourth ventricle was enormous (see Figure 52a), the cyst extending through the tentorial opening (see Figure 52b). Lesser degrees of this anomaly were more commonly encountered (see Figures 53-55). All cases had marked forebrain hydrocephalus and there was usually severe loss of cerebellar tissue as evidenced by reduction in organ weight; histology of the midline lobules showed varying degrees of acute and chronic necrosis. Impaction of cerebellum into the foramen magnum with narrowing or obliteration of the caudal part of the fourth ventricle was usually present.

The Split Cerebellum

The 'split cerebellum' is one of the more interesting changes encountered in this series of children with meningomyelocele. The absence of hydrocephalus in one such case is particularly interesting and implies a relatively normal circulation of cerebrospinal fluid; the absence of a "cerebellar tail" is noteworthy. Previous reports have already alluded to necrosis in the dislocated segment of the cerebellum in this hindbrain malformation; it is likely that resorption of the "tail" following necrosis largely contributed to this defect, possibly resulting in a re-establishment of the cerebrospinal fluid pathway.

When the whole series is considered, changes described on

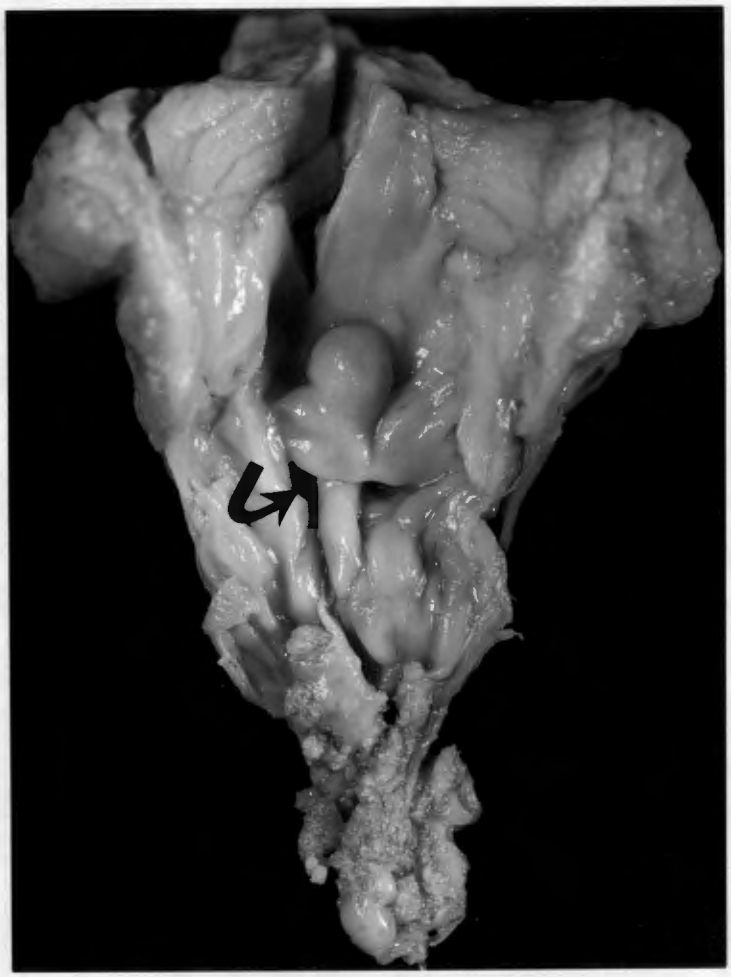
Figure 51a



Mid-sagittal view of cerebellum showing a multilocular cyst replacing much of the lobular tissue in the dorsal area. One of the locules communicates with the fourth ventricle (arrow).

...../128

Figure 51b



Ventricular surface of the same specimen as Figure 51a, showing an elliptical opening (arrow) in the roof of the fourth ventricle. A bulbous protrusion of the nodule is seen immediately above the opening.

...../129

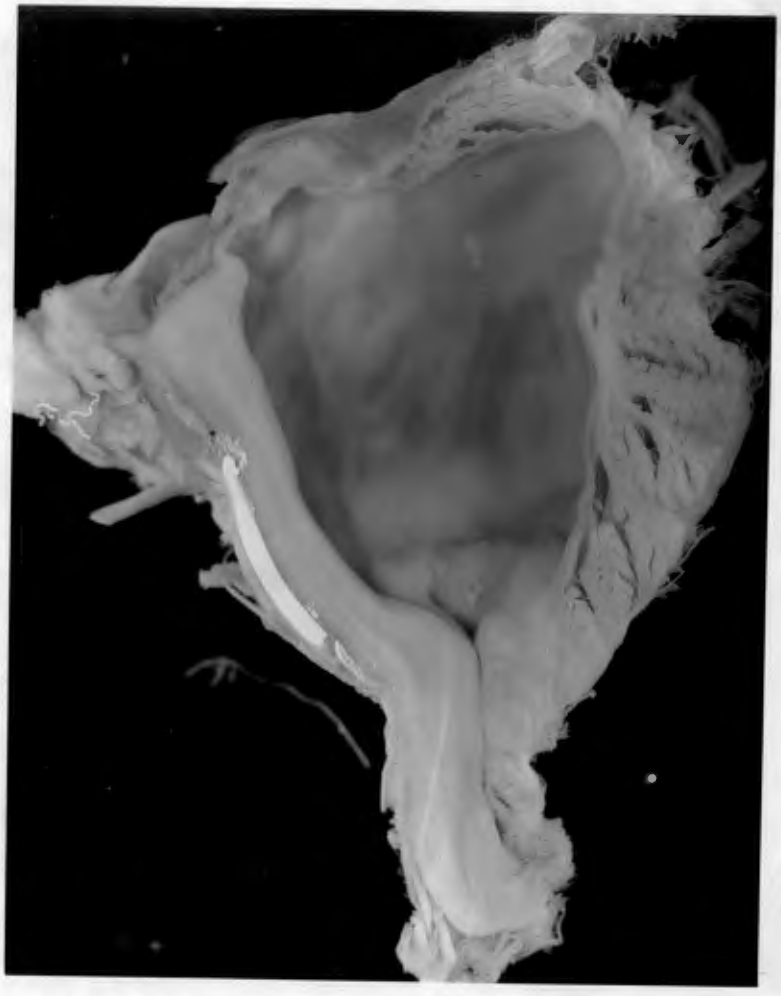


Figure 52a

Shows severe dilatation of the fourth ventricle with complete obstruction in the caudal part. (The basilar artery contains radio-opaque material).

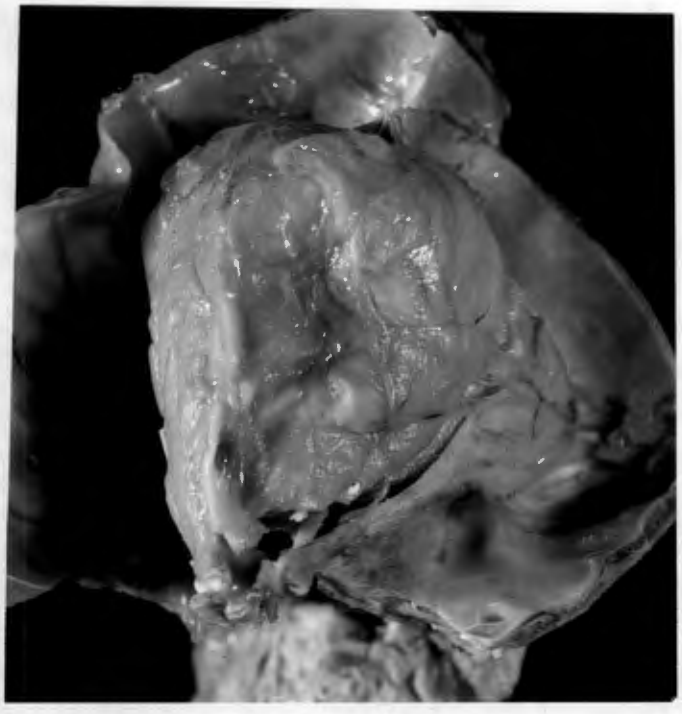


Figure 52b

Same specimen as in Figure 52a to show cystic extension of the fourth ventricle through a large tentorial hiatus.

...../130

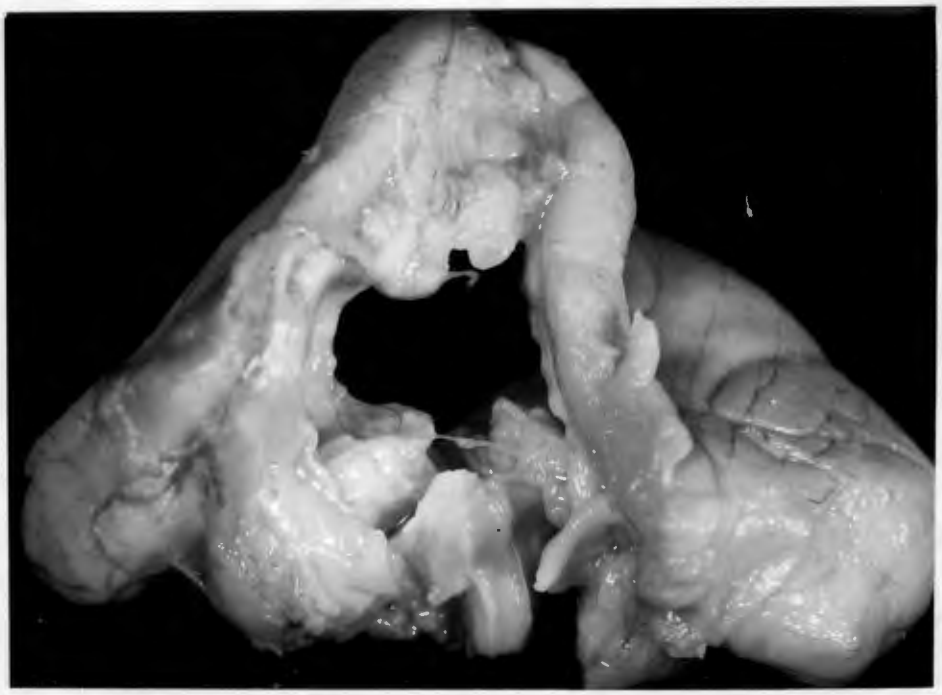


Figure 53

Anterior view of cerebellum from a typical case of fourth ventricular dilatation.

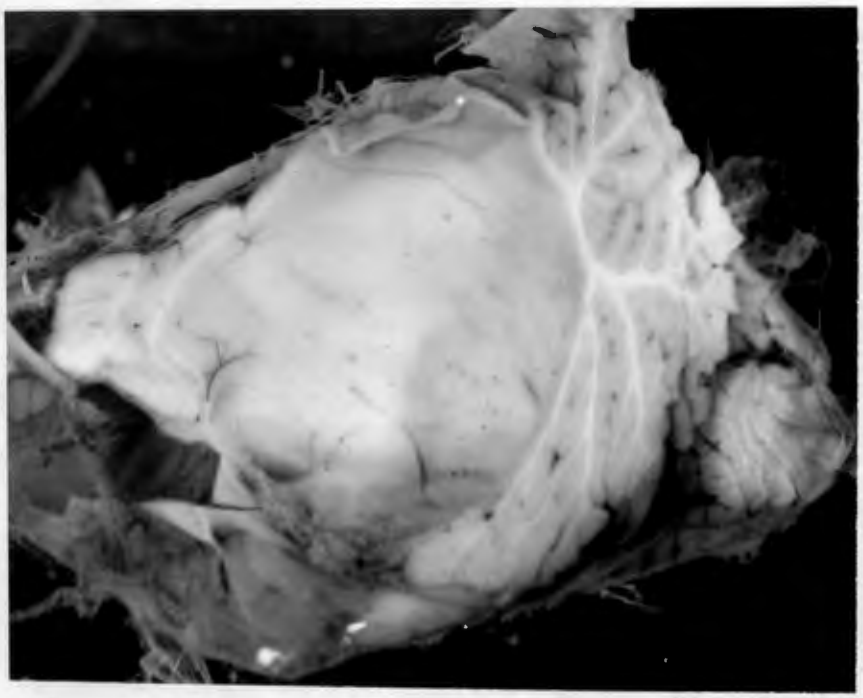


Figure 54

Mid-sagittal view of the cerebellum with fourth ventricular dilatation: the cerebellar lobules are compressed and poorly differentiated. The "cyst" is lined by ependyma and the floor contains choroid plexus.

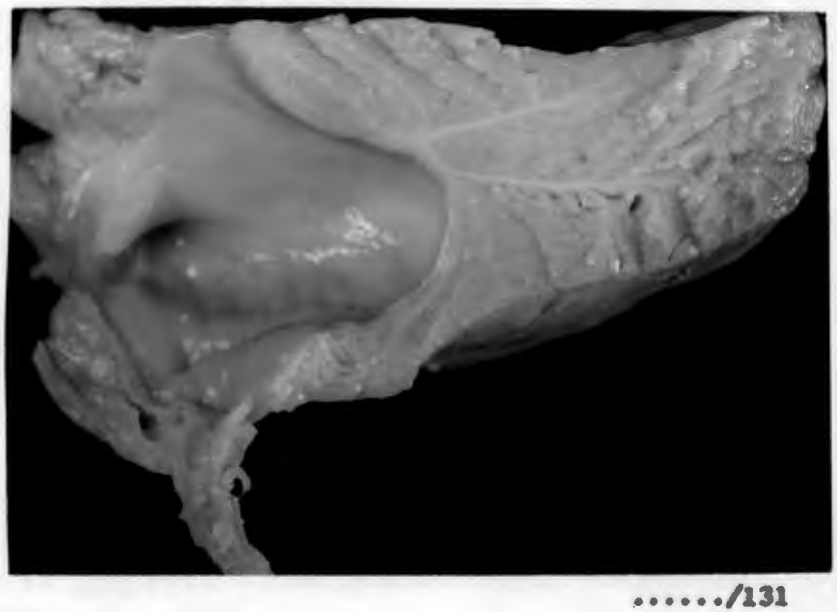


Figure 55

Cystic dilatation of the fourth ventricle with caudal extension of cerebellar tissue containing choroid plexus.

...../131

the superior surface in these cerebellums are found to form what appears to be continuum with wide separation of cerebellar hemispheres at one end; at the other end the superior surface is found to be comparatively normal. This implies that the 'split cerebellum' is an integral part of a spectrum of cerebellar changes found in the malformation and does not represent an isolated anomaly.

A comparison has already been drawn between the cerebellum in the hindbrain malformation and its normal early foetal form. Cameron (1957) compared the surface morphology of the cerebellum with that of an embryo of about the 100mm. stage. Cleland (1883) described a beak-like deformity of the midbrain resembling the early embryonic tectal plate. Daniel and Strich (1958) emphasised failure of the pontine flexure to develop; they also suggested a failure of the foetal cerebellum to evaginate that accounted for the intraventricular position of the cerebellar "tail" found in many of their cases. It is mainly for these reasons that the pathogenetic theory of primary developmental arrest has gained support. However, it is important to note that there does not appear to be any suitable equivalent for the "split cerebellum" in the stages of normal prenatal cerebellar development.

Hydrocephalus is not an invariable accompaniment of meningomyelocele. In Lorber's series of 172 cases of meningomyelocele and encephalocele (1961), twenty-two cases followed for eight months or more showed no evidence of hydrocephalus. The cerebellar deformity described, and its suggested mode of pathogenesis, might conceivably explain the

...../132

absence or arrest of hydrocephalus encountered in some of these cases.

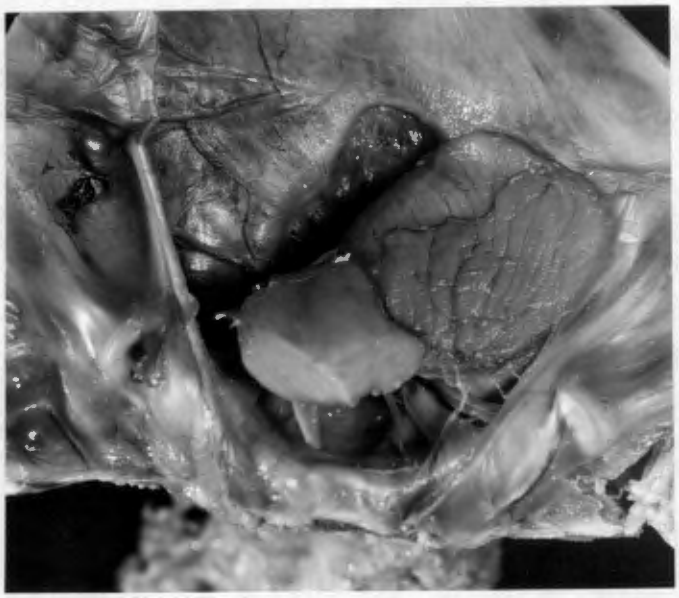
A "tail" was present in the remainder of the cerebellums with wide separation of the hemispheres and an absent superior vermis. A single cerebellar hemisphere was present in the posterior fossa in one case (see Figure 56); although it was difficult to precisely identify the tissue in the cervical canal, it was felt that the missing hemisphere had prolapsed through the foramen magnum and that this did not represent a true agenesis. This case was not included in the series of a hundred cerebellums studied and is mentioned here out of interest.

Certain anatomical features common to both the Dandy-Walker malformation and the "Arnold Chiari" malformation have previously been discussed (Gardner, Abdullah and McCormack, 1957; Gardner, Smith and Padget, 1972). These include: uncompensated hydrocephalus, either communicating or non-communicating, hydromyelia, syringomyelia, meningomyelocele, thickening of meninges at the level of the foramen magnum, dislocation of the caudal portion of the fourth ventricle into the cervical canal, and closure of the foramen of the fourth ventricle by membranes that represent persisting portions of the embryonic rhombic roof.

The pathology of the Dandy-Walker malformation is well-documented (Dandy, 1921; Taggart and Walker, 1942). In short, the essential features are dilatation of the fourth ventricle, wide separation of the cerebellar hemispheres, which are usually hypoplastic. The vermis is deficient or absent. The Dandy-Walker malformation occurs both in adults and children and there is

...../133

Figure 56



Showing severe hypoplasia of the tentorium cerebelli and absence of the right cerebellar hemisphere.

...../134

usually forebrain hydrocephalus.

To explain the pathogenesis of the Dandy-Walker malformation it would be helpful to briefly consider the work of Weed (1917) on the embryology of the cerebrospinal spaces in man. He divided the embryonic roof of the fourth ventricle into the area membranacea superior (AMS) and the area membranacea inferior (AMI), the two areas being separated by choroid plexus. The AMS, which is initially a permeable membrane, soon thickens to form the vermis resulting in the superior and inferior medullary velum; the AMI, caudal to the choroid plexus, is the future site of the foramen of Magendie.

It has been stated (Gardner, Smith and Padget, 1972) that in the Dandy-Walker malformation the bulging occurs in that portion of the AMS between the cerebellar anlage and the choroid plexus; they explain failure of normal cerebellar development being secondary to the fourth ventricular hypertension.

As in the Dandy-Walker malformation, the vermis in the "split-cerebellum" may also be considered hypoplastic and it is tempting to invoke a similar pressure effect.

However, this aertiology seems difficult to reconcile with the morphology of the "split-cerebellum" and, in my opinion, the more likely explanation for the deficient vermis in the latter anomaly is cerebellar growth in a rigid, small posterior fossa. Escape of the enlarging cerebellum through a patent tentorium is probably limited by early forebrain hydrocephalus. As already suggested (Part 3, page 68), the longitudinal midline fissure which typifies this malformation is probably due to a

passive process, the result of regional growth differences, the wide separation of the cerebellar hemispheres probably being a function of a very early embryological onset.

Encroachment of the midbrain on the antero-superior surface of the cerebellum subsequent upon forebrain hydrocephalus by preventing forward/inward migration of the superior lobules, is probably an additive factor. In normal early cerebellar development, the vermis represents a considerable area of the superior surface and this is already evident during the first half of the fourth month (Langelann, 1919). It is conceivable that any abnormal moulding influence exerted on the superior surface when the vermis is relatively prominent would have its main effect on this structure.

Cavities in the Cerebellum

Cavities have been described in the medulla and pons in children with meningomyelocele (Lichtenstein, 1949); He suggested a pathogenetic process of liquefactive necrosis due to ischaemic change. In the cervical cord the syringomyelic cavity may communicate with the central canal and in the medulla, it may communicate with the fourth ventricle. Impaction of the neuroaxis into the foramen magnum was held to be responsible for the vascular obstruction.

In keeping with current terminology, i.e. syringo-bulbia and syringomyelia, it might be appropriate to label this deformity "syringocerebella". As the cerebellum largely depends on the vertebrobasilar system of arteries for its vascular supply, a similar mechanism of pathogenesis might

apply here. At the same time, foraminal impaction might be expected to obstruct cerebrospinal fluid flow and accumulation of fluid in the fourth ventricle might be a contributory factor by causing dissection of fluid into the cerebellar substance.

Cameron (1957) first drew attention to slit-like cavities in the cerebellar substance; these were also found in this study and are described in the section dealing with the pathology of the central lobules; it was not agreed that they necessarily communicated with the fourth ventricular cavity. It is possible that such slit-like cavities might predispose to grosser degrees of cavitation described above.

Cystic Dilatation of the Fourth Ventricle

There has been occasional reference to fourth ventricular dilatation in the hindbrain malformation associated with meningomyelocele (Verbiest, 1953); this author found one such case in a series of pneumoencephalographs in children with meningomyelocele. In the usual description of the malformation the fourth ventricle is narrow and elongated, often reaching into the upper cervical canal. Unfortunately, this is still regarded as the sine qua non of the diagnosis of the deformity. Cystic expansion of the fourth ventricle might be explained by a limited capacity of the lateral ventricles to distend in the presence of obstructive hydrocephalus; at a critical point any further increase in volume of cerebrospinal fluid is accommodated in the fourth ventricle.

Conclusions

In some centres diagnosis of an "Arnold-Chiari" malformation relies on radiological demonstration; to avoid confusion radiologists must be made aware of these uncommon but important variations of the fourth ventricle. The finding of a dilated fourth ventricle might easily be mistaken for a Dandy-Walker malformation which occasionally occurs in children with meningomyelocele (Gardner, 1959); however, the low insertion of the tentorium cerebelli and associated transverse sinus, irrespective of the degree of fourth ventricular dilatation, should provide reliable evidence that one is dealing with an "Arnold-Chiari" malformation. Increasing awareness of the hazards of current methods of treatment of hydrocephalus might conceivably, in the near future, lead to more direct approach on the hindbrain to relieve hydrocephalus in children with meningomyelocele. Knowledge of the many variants of cerebellar morphology that may be encountered in this condition would be helpful.

These unusual deformities might be considered compatible, directly or indirectly, with the effects of hydrocephalus. Deformities of superior vermis and grosser ones involving the whole cerebellum suggest a different time relationship with the onset of hydrocephalus; while cystic dilatation of the fourth ventricle and cavitation of the cerebellum might be regarded largely as a late effect, defects of superior vermis would imply that hydrocephalus operates early during cerebellar development, at a time when the lobules are more malleable and most susceptible to moulding influences.

...../138

This part of the study does little in contributing towards solving the controversial issue of pathogenesis and describes what appears to be largely secondary changes in the morphology of the cerebellum in this hindbrain malformation.

...../139

PART 6

THE VENTRICULAR SURFACE

(Roof of the Fourth Ventricle)

Past reference to the roof of the fourth ventricle has been infrequent and usually brief; the number of cases studied from this aspect has been relatively small. According to Cameron (1957), the ependymal surface of the nodule in the abnormal cerebellum, normally very small and confined to the median dorsal recess, was very elongated and formed the roof of the caudal extension of the fourth ventricle. Daniel and Strich (1958) also noted the 'tail' to be covered by ependyma on its ventral aspect and sometimes also the dorsal part of its lower-most aspect.

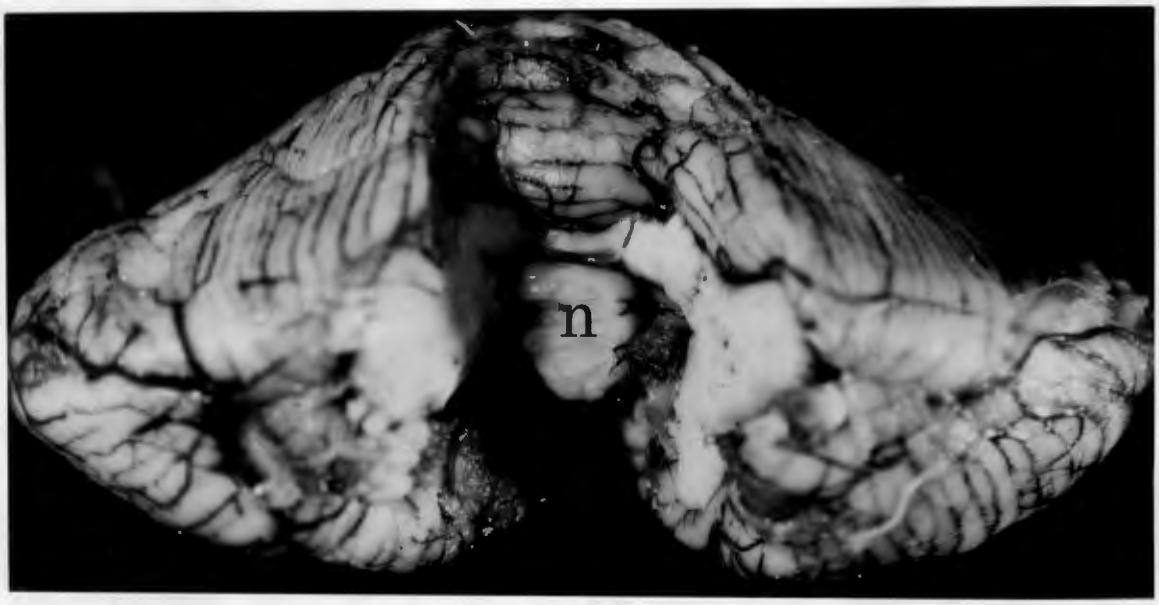
In this study three structures on this surface of the cerebellum are worthy of comment; these include:

1. the nodule
2. the inferior medullary velum
3. the flocculus.

In Part 2 the nodule was frequently mentioned as forming the apex of the dislocated cerebellar segment. On the ventral surface the nodule is usually found to be elongated, and sometimes it is discontinuous; the caudal end is frequently tipped by a tuft of choroid plexus, a feature previously noted by Cameron (1957). The dorsal median recess in the deformed cerebellum is characteristically shallow, i.e. the angle between the superior medullary velum and the inferior velum is abnormally obtuse. The nodule traverses the distance between the dorsal median recess and the most caudal end of the 'tail'. Thus, of all the caudal lobules, the nodule is seen to be the most severely deformed (compare Figure 57 with Figure 58).

...../140

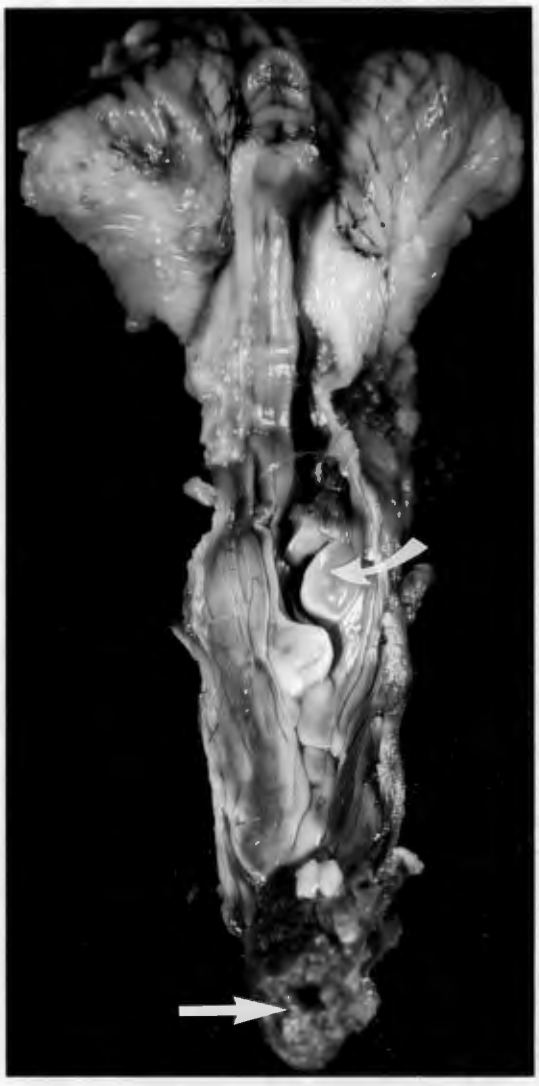
Figure 57



Ventricular surface of normal cerebellum from a newborn (n = nodule)

Figure 58

Ventricular surface of a cerebellum from a newborn who died on the first day with meningomyelocele. There is marked elongation and widening of the medullary velum. The nodule (curved arrow) is tortuous and elongated. Choroid plexus (straight arrow) is seen at the caudal end.



...../141

The inferior medullary velum is almost invariably considerably expanded and firmly adherent to the attenuated underlying structures; (this is in marked contrast to the normal inferior medullary velum). It is important to reiterate that the choroid plexus was invariably attached to the caudal end as this indicates unequivocally that we are dealing with Weed's area membranacea superior.

When the flocculus is considered it is evident that this lobule varied considerably in its attachment to the cerebellum. Figure 59 shows diagrammatically the different sites of attachment of the flocculus (Figures 60-63 show examples of each group).

In Group A the position corresponded with that in a normal cerebellum.

Group B shows the flocculus to be slightly displaced and to assume a position between the normal and the level of the foramen magnum.

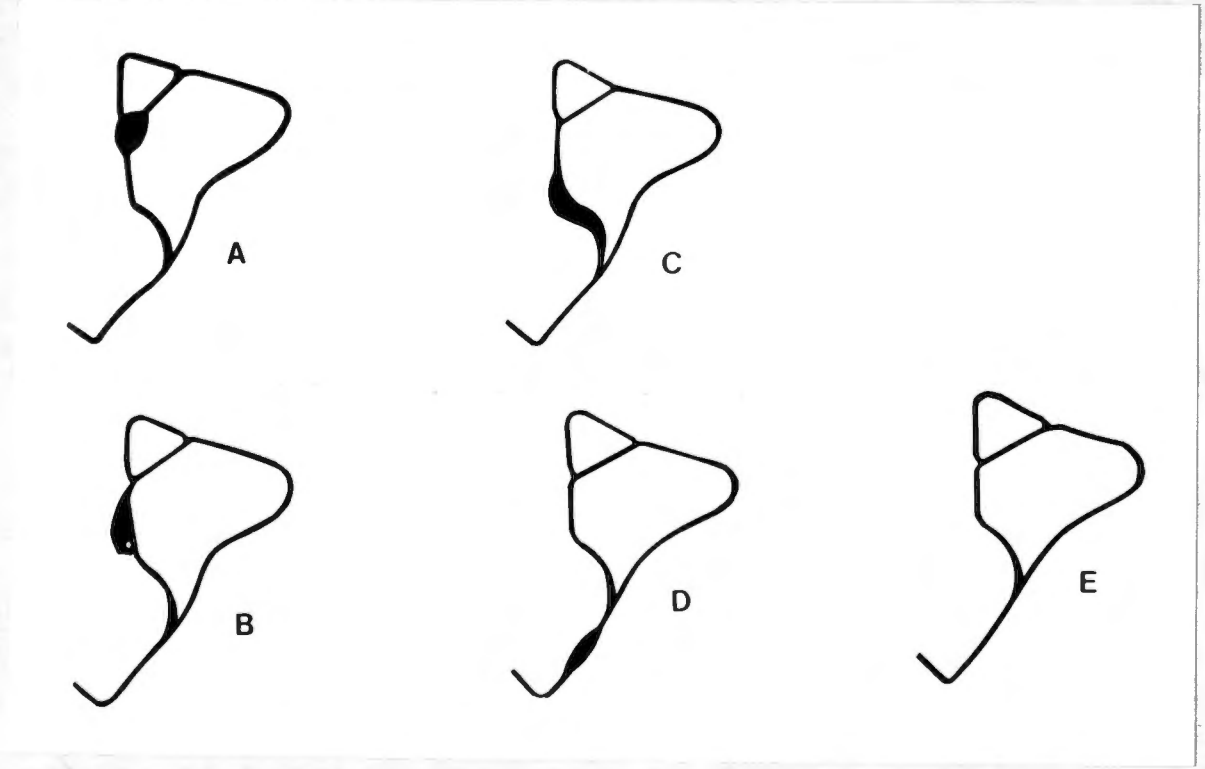
In Group C the flocculus is at the level of the foramen magnum and in Group D it forms part of the dislocated segment of the cerebellum; in the latter it is found below the level of the foramen magnum.

In the remaining cerebellums the flocculus could not be identified (Group E).

(It should be noted that, because of its ventral position, the flocculus was not included when the lobular composition of the dislocated segment of the cerebellum was discussed in Part 3).

When floccular position is compared with the length of the

Figure 59

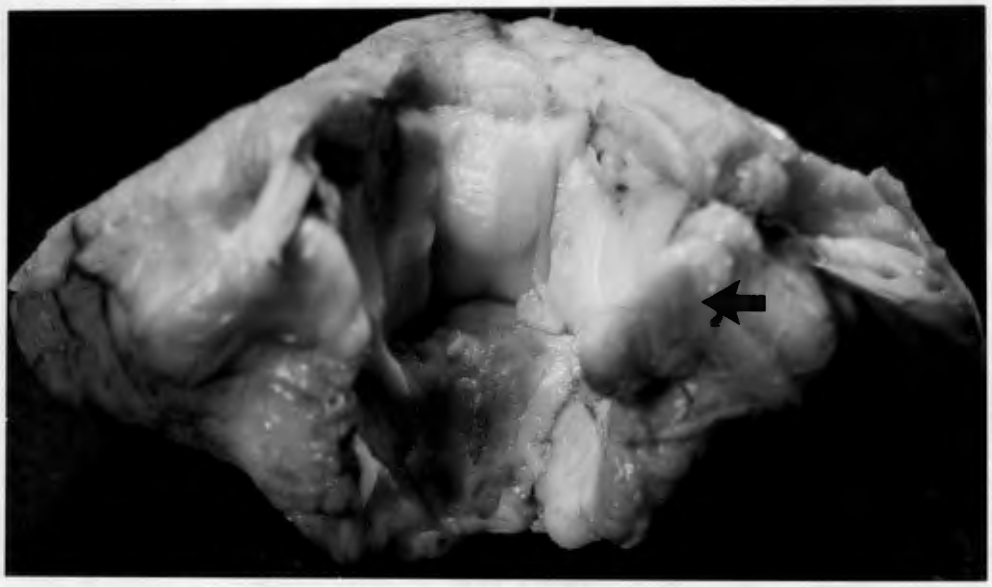


Diagrammatic representation showing different groups of floccular position.

Figure 60

The left flocculus (arrow) is seen in a normal position. Cerebellum from a child with a sacral meningomyelocele (age 1 month). There was no cerebellar displacement below the level of the foramen magnum.

Figure 61



Cerebellum from a child with meningomyelocele showing infraforaminal displacement of tonsils only. The left flocculus (arrow) shows mild caudal displacement.

...../144

Figure 62

Cerebellum from a child aged 5 weeks. The flocculus (arrow) is at the level of the foramen magnum and corresponds to Group C. The nodule, uvula and tonsils formed the cerebellar 'tail' in this case.

Figure 63

Cerebellum from a child aged 2 days. There was a marked degree of cerebellar displacement into the cervical canal. The flocculus (arrow) is infraforaminal and corresponds to Group D.

...../145

cerebellar 'tail' it is seen that, in many cases, the longer 'tails' are associated with the grosser degrees of flocculer displacement (see Table 5).

Table 5

Group	Number of Cases	Average 'tail' length in mms.
A	5	0
B	50	13
C	28	26
D	7	24
E	10	27

Showing the position of the flocculus in relation to cerebellar 'tail' length.

When interpreting this data it is important to take into account that the more complex cerebellar 'tails' often showed evidence of atrophy and necrosis so that the more marked degrees of flocculer displacement were, in some cases, associated with comparatively shorter 'tails'.

To explain some of the changes it is necessary first to consider the embryology of these lobules. Both the nodule and the flocculus develop from a single embryological nodule - the flocculer-nodular lobule (Langelaan, 1919). Also, the medullary velum forms an inseparable part of this lobule. More important, they are the first cerebellar lobules to develop. It follows, from the intimate embryological relationship of these lobules,

...../146

that they should respond together to any early disrupting influence.

The orderly displacement of these lobules would seem to be incompatible with pathogenetic theories implicating caudal displacement of hindbrain by forebrain. Clearly, other mechanisms must be searched for to explain this "well-organised" deformity. 'Traction from below' rather than 'pushing from above' would seem likely inview of the attenuated appearance of these ventral structures.

Above evidence shows that the nodule, flocculi and inferior medullary velum undergo an organised caudal displacement; this is probably related to their origin from a single embryological unit. From the position of the choroid plexus it is clear that we are dealing with Weed's area membranacea superior. It is noteworthy that on this surface of the cerebellum there was no buckling of tissue which one might expect had the disrupting influence been anything other than a direct traction from below. That these structures are the most severely deformed is probably related to the fact that they develop before the other lobules.

No quantitative methods were used when the foramina of Luschka and Magendie were studied. Some findings concerning this part of the malformation are, however, worthy of note. The foramina of Luschka are normally situated just inferior to the flocculi; in cases where the flocculi were displaced caudally, this normal anatomical relationship was maintained but the lateral foramina were invariably distorted and were

...../147

difficult to identify in many cases. When caudal displacement was moderate and the foramina of Luschka were still above the level of the foramen magnum, impaction of hindbrain tissue against the bony wall of the posterior fossa led to the impression that these foramina were obstructed. When caudal displacement of flocculi occurred into the cervical canal, the foramina were frequently obliterated or grossly distorted.

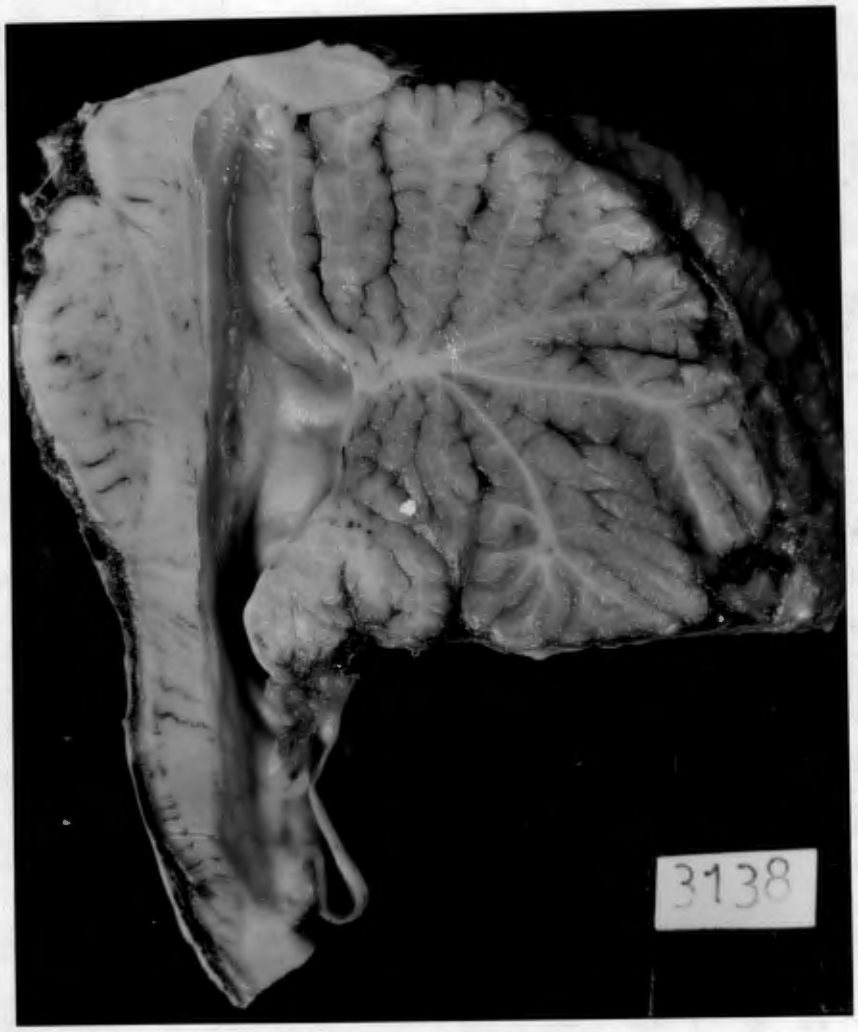
Essentially, four different situations were found when the foramen of Magendie was studied:

1. The foramen of Magendie was covered by a fine mesh of fibrous tissue. Fixative within the fourth ventricle was easily pushed out through the mesh by gentle pressure suggesting, at least, some degree of patency.
2. The caudal part of the fourth ventricle was exposed; these cases occurred more often in the older age group when there was usually necrosis and loss of tissue in the caudal part of the cerebellar dislocation.
3. A cystic extension of the fourth ventricle was present. These anomalies were found in 6% of the series; an example is illustrated in Figure 64.
4. Loose ragged membranes were present in the area of the foramen and suggested recent rupture of an intact membrane.

In my opinion it is not possible to assess the state of cerebrospinal fluid flow or the level of obstruction at post mortem by the appearance of the basal foramina alone; the fourth ventricle and the aqueduct must also be taken into consideration.

...../148

Figure 64



A mid-sagittal view of the hindbrain malformation showing a small caudal cystic prolongation of the fourth ventricle. Note also that the caudal lobules are necrosed.

...../149

Figure 64 shows unequivocally that, in some cases, the foramen of Magendie is imperforate; there can be little doubt that this represents a persistence of Weed's area membranacea inferior, and therefore part of the embryonic rhombic roof.

It is well known that hydrocephalus associated with meningomyelocele may be communicating or non-communicating (Russel and Donald, 1935); they were able to show in a series of ten cases with meningomyelocele, using dye and ink injections, the presence of non-communicating type in eight cases of hydrocephalus. In one of these the foramina of Luschka and Magendie were imperforate and in the other, there was atresia of the aqueduct.

In the series reported by Ingraham and Scott (1943), internal hydrocephalus was present in each of the twenty cases of the hindbrain malformation. All were associated with meningomyelocele. Assessment of the state of the basal foramina was made post mortem. Twelve cases were of the communicating type. In four cases the type of obstruction was not determined. They proposed that obstruction may be produced in several ways: the fourth ventricle or the foramina may be obstructed by squeezing in the upper cervical canal; the fourth ventricle may be patent but the subarachnoid space is obliterated at the level of the foramen magnum by pressure of the herniated hindbrain; there is free passage of cerebrospinal fluid into the spinal subarachnoid space but no egress into the posterior fossa. This results in communication hydrocephalus. Their third explanation is the formation of a "plastic exudate" in the region of the

...../150

basal cisterns which they attribute to a type of aseptic meningitis.

Lichtenstein (1942) initially described associated aqueductal stenosis as being significant in the cause of the hydrocephalus. In a more recent series, an aqueductal abnormality was found in 50% of twenty cases of the "Arnold-Chiari" malformation (MacFarlane and Maloney, 1957). Emery, (1974) also found a high incidence of displacement, shortening and compression of the aqueduct but thought there was anatomical patency in all cases, but functional patency depended on the degree of lateral compression by dilated occipital poles.

Verbiest (1953), who carried out pneumo-encephalography in his cases, demonstrated the hindbrain malformation in eight out of eleven cases. In four cases in which this was successful, no communication was found between the fourth ventricle and the spinal subarachnoid space; the air remained in the fourth ventricle.

More recently, definite membranous coverings to the outlet of the foramina Magendie have been described. In some cases there may be a cystic prolongation of the fourth ventricle (Gardner, 1959; Peach, 1964; Emery and MacKenzie, 1973). This anomaly was found in 25% of Peach's series, (although not all cases showed the cyst to be intact); it was only present in those cases showing a medullo-cervical dislocation.

Gardner (1959) held that these cysts represented persistence of the embryonic rhombic roof, a view that was supported by

...../151

Peach (1964). Blake (1910), described similar caudal protrusions from the fourth ventricles in advanced embryos of certain animal species. Wilson (1937) also found these pouches in human embryos and suggested that they were part of the normal development of the foramen of Magendie. However, Brocklehurst (1969), investigating development of the basal foramina in human embryos and foetuses, was of the opinion that the development was passive and did not entail preceding cyst formation and rupture. The study of Van Noytema and Van den Berg (1966), using a 140mm. embryo with 'spina bifida', has a special significance here; they found undue persistence of the embryonic roof in the embryo studied compared with an age-matched control. The association between atresia of the foramen of Magendie and the hindbrain malformation in the adult is well established (Gardner, 1957).

These cysts must be distinguished from diverticular prolongations of the fourth ventricle into the medulla; these have been referred to as syringomyelic-like cavities by Lichtenstein (1942) and are depicted in the paper by Emery and MacKenzie (1973). They were also noted occasionally in the present series.

The operative findings on exposure of the hindbrain malformation in a forty-six year old woman has been described as follows: "The impacted hernia moved sharply downward with each pulse systole and upward with its diastole" (Gardner, Smith and Padget, 1972). There was a translucent, cyst-like structure in the area of the foramen of Magendie. They state that the purpose of the operative procedure was to permit the 'partly imprisoned ventricular fluid pulse wave to escape freely into the cisterna magna'.

It is conceivable that an intact elastic membrane

...../152

continuously subjected to raised pressure, both static and pulsatile, may eventually distend and result in cystic diverticula found in the region of the basal foramen. A progressive extension of the cyst into the cervical canal would, by a process of simple traction, attenuate the medullary velum and attached lobules caudally. I would add that in the many cases of the hindbrain anomaly with severe dislocation of cerebellar tissue, the mechanism needs to commence early in cerebellar development to allow for the considerable degree of moulding that has to take place.

It is evident that these cysts may burst or perforate at any stage in the formation of the deformity and this would explain the marked variation in the degree of cerebellar displacement. It is not uncommon for the cerebellum to extend caudally beyond the medulla in some cases of the hindbrain malformation in children (Cameron, 1957; Peach, 1965). A mechanism, as postulated here, would easily explain a disproportionate displacement of cerebellum relative to the medulla.

Provided the central canal of the spinal cord retains some degree of patency at the time that these cystic extensions burst, it is quite possible for a negative pressure to be set up in the central canal; this may explain the finding of particulate matter derived from the amniotic fluid within the cord in certain cases of children with meningomyelocele (Jacobs, Landing and Thomas, 1961; Lichtenstein and Kirschbaum, 1941).

PART I

A REVISED PATHOGENETIC THEORY

In an early part of this study it was shown that cerebellar weight is uniformly diminished at birth. The reduction in weight is constant throughout the series despite prolonged shunt treatment; it is therefore apparent that these babies start life with a small cerebellum.

The central lobules of the cerebellum show definite patterns of atrophy and chronic necrosis, these changes being maximal in the caudal-most lobules. (Acute necrosis shows a reverse pattern in that the upper-most lobules are involved.) It is important to point out that the supra-foraminal central lobules and those below the foramen magnum are all involved, the former, however, to a much lesser degree; although one cannot be too dogmatic, it is probable that such changes also involve the adjacent lateral lobules within the posterior fossa. It is normally held that the changes in the cerebellar tail are the result of an impaired blood supply secondary to squashing in the upper cervical canal. Similar changes are found in the supra-foraminal part of the cerebellum and this is usually most marked in those lobules abutting against the wall of the bony compartment, especially the pyramid.

The cause of the acute necrosis in the upper lobules is less clear-cut but would seem to be associated with acute alterations in cerebrospinal fluid pressure incurred during delivery and introduction of shunting devices.

The chronic changes described favour a disruptive influence operating some time during intrauterine life and probably explains the hypoplastic appearance of the cerebellum noted at birth.

...../154

Conversely, it could be argued that the small cerebellum in these cases is not genetically based. Pathological insults directed at certain critical phases of brain development have already been referred to in Part 2. In the cerebellum the damage is most likely one of obstructed growth, and the effect would be greatest during the last trimester when glial proliferation is maximal. From the point of view of regeneration the brain is a non-replicator and this would go some way in explaining the permanency of the cerebellar weight reduction.

After birth there is a tendency for the cerebellum to grow out of the posterior fossa through the tentorial hiatus. The degree of cerebellar projection above the tentorium appears to be related to shunt treatment, the more marked degrees seemingly related to duration of treatment. At the same time, there is apparent shortening of the cerebellar tail; one possible reason for this is resorption of atrophic tissue and also overall elevation of the cerebellum in the posterior fossa. In spite of these changes, alleviation of obstruction to cerebrospinal fluid flow does not appear to be the rule; this is probably associated with aqueductal and fourth ventricular blockage.

The fissural patterns on the superior surface of the cerebellum are variable, the more complex patterns being associated with the smaller cerebellums. The impression is that the size of the cerebellum is determined by the size of posterior fossa in which it grows. For instance, the abnormal fissuring has been interpreted as an effort by the cerebellum to effect as great an external surface area as possible following growth in a

confined space; the upper surface grows inwards - this is strong evidence that the tentorial hiatus is obstructed during foetal life and the most likely explanation for this obstruction is an early foetal forebrain hydrocephalus.

Flattening of the superior surface (a defect of elevation, as opposed to a fissural anomaly) is common in the neonatal period and is probably due to increased intracranial pressure; This occurs despite a normal head circumference measurement in many of the cases and raises the possibility of a compensated hydrocephalus in such cases. The implication is that free expansibility of the skull is somehow or other restricted inutero despite the presence of foetal hydrocephalus. If this is the case, could the reason be amniotic fluid pressure?

Previous descriptions of the malformation seem to have overlooked a feature of the cerebellum which, in my opinion, argues conclusively against the several popular theories of pathogenesis; this is the frequent considerable elongation and displacement of the organ into the cervical canal, usually composed of several lobules. The tendency in the past has been to grossly underestimate or entirely overlook this aspect; the dislocated segment has far too long been referred to simply as cerebellar vermis. It is difficult to link any of the popular theories of pathogenesis with this severe cerebellar deformity; even the advantages of the popular hydrodynamic hypotheses seem to fall short in fully explaining this particular part in the cerebellar deformity.

The important question is: what causes the cerebellar "tail"

to elongate to this remarkable degree? Gardner has suggested that, with rupture of the caudal part of the embryonic neural tube, there is a sudden reduction in intraluminal pressure. The enlarging choroid plexus continues to transmit cerebrospinal fluid pressure waves (Bering phenomenon) in the presence of a caudally opened neural tube; the tendency would be to accelerate the posterior migration of the primitive transverse sinus and attached tentorium, resulting in an abnormally small posterior fossa. The hindbrain enlarging in the small posterior fossa obstructs the fourth ventricle - obstructive hydrocephalus occurs. This leads to caudal displacement of hindbrain. However, the degree of displacement from this mechanism is unlikely to be very significant and would not easily explain those cerebellums with marked infraforaminal elongation.

It is useful to separate changes described in the cerebellum into two categories; 1) those compatible with an onset during early prenatal life; and 2) those changes occurring at the later foetal stage and post-natal life. Although the timing is different the common denominator would seem to be forebrain hydrocephalus. In the first instance hydrostatic forces are applied to an organ which is rapidly developing and plastic and therefore easily deformable. Certain structural alterations occur but the basic integrity of the organ is preserved; tissue necrosis is not a feature (there is "bending" with little "breakage").

Later, a relatively mature but less deformable cerebellum emerges which is subject to the same extrinsic forces; this

maturity involves gross structure and also the cellular level. We are now dealing with a comparatively rigid organ in a bony compartment pounded by hydrostatic forces acting from above the tentorium. Structural changes are now minimal (the organ is less deformable), tissue necrosis becones a dominant feature ("breakage" is important, "bending" is minimal).

Although these later changes are significant in explaining some of the cerebellar features of this malformation, they do not really contribute much to our understanding of pathogenesis. The pathogenetic issue is better resolved by pinpointing and analysing changes which are recognisably early ones and those which occur later. The former applies to such alterations occurring on the superior surface, particularly abnormal fissuring, and elongation and displacement of ventral structures such as the nodule, inferior medullary velum and flocculi. The association between hydrocephalus, cystic prolongation of the rhombic roof, and caudal displacement of the flocculo-nodular unit is clearly important in this context; it is a good example of the extraordinary malleability of an early developing organ in response to an adjacent disruptive force. Unfortunately it can only be regarded as one unit in what is clearly a highly complex pathogenetic system.

In Part 6 I discussed the ventricular surface of the cerebellum in this malformation. The elongated medullary velum and nodule were emphasised and the significance of the flocculus as a marker of this elongation was pointed out. It was then implied that these three ventral structures were

...../158

displaced together; the reason was their close embryological relationship, the nodule, velum and flocculi originating from the same phylogenetic lobe. It can also be deduced that such displacement must have occurred at a relatively early stage inutero for such malleability to have been possible.

Cystic prolongation of the imperforate rhombic roof has received little attention in the past. When these cysts have been observed there has been a tendency to regard them in isolation; it is proposed here that these cysts are primarily responsible for the cerebellar malformation. There are several explanations for failure of the rhombic roof to perforate: the membrane might be intrinsically abnormal and this might fit in with Gardner's idea that the rhombic roof "forgets to become adequately permeable". Caudal displacement of the rhombic roof could obliterate the space necessary to allow the membrane to distend so that a physiological rupture does not take place. A third possibility is a lowered cerebrospinal fluid pressure in the fourth ventricle due to an early fistulous escape of fluid through a patent central canal into the amniotic fluid; thus the pressure is lost that is normally required to disrupt the embryonic roof and form the basal foramina.

Whatever the reason for the persistence of the rhombic roof it is clear that, in many instances, these intact membranes undergo cystic prolongation, the cysts pointing caudally, down the cervical canal, dorsal to the cervical spinal cord and beyond the most caudal end of the cerebellum. When the central

...../159

canal of the cord becomes obstructed (presumably) in the region of the cervico-medullary kink), any build up of pressure in the fourth ventricular system is likely to exert itself directly onto the intact rhombic roof. If this is allowed to go unchecked it is reasonable that such membranes will distend and eventually become cystic. The Bering phenomenon is probably of paramount importance in potentiating this process.

The strategic position of these cysts in relation to the fourth ventricle, and more specifically to the ventral aspect of the cerebellum, can be clearly seen; any progression of these cysts during the foetal period will inevitably cause traction on the flocculo-nodular unit. During early foetal life with its property of increased organ malleability, gross degrees of structural deformities can easily result. The cystic prolongation of the fourth ventricle is, in fact, similar to an intestinal hernia; if left untreated, continued intra-abdominal pressure inevitably leads to progression of the condition. (Another analogy would be a leading point in an intestinal intussusception).

It is only by appreciating the importance of these cysts, their relation to the roof of the fourth ventricle, the hydrostatic forces to which they are subject, including the Bering effect, can we fully appreciate the most important single factor in the pathogenesis of the cerebellar deformity in this malformation, i.e. <u>complex</u> dislocation of the cerebellar "tail" into the upper cervical canal.

It is evident that many of these cysts rupture before

...../160

birth; this is supported by the frequent finding of what appears to be ragged membranes at the lower end of the cerebellum in this series. Gardner thought that they rupture at the time of birth due to pressure on the head as it passes through the birth canal. Intact cysts were found in six cases in the present study and they have been reported by a number of other authors. Whatever the timing of rupture it is clear that when this happens a potentially very significant disruptive mechanism is "switched off". Further investigation of this part of the malformation is only possible by studying fetuses with myeloceles following termination of pregnancy, preferably by hysterotomy. This will preclude pressure changes secondary to normal delivery and if this is the usual mechanism of rupture these cysts will be found intact. Such fetuses could become more readily available as selective terminations of pregnancy become more common, based on serum and amniotic fluid α-fetoprotein estimations.

Another merit of this pathogenetic hypothesis is that it will explain a communicating hydrocephalus in the presence of a fully developed hindbrain malformation; when the cyst ruptures there is a clear route for ventricular fluid into the spinal subarachnoid spaces; this occurs despite the presence of significant infraforaminal dislocation of cerebellum.

The theory of developmental arrest is based mainly on the many structural similarities between the normal early

hindbrain and those present in the malformation. Major degrees of elongation and displacement of the caudal lobules are not seen in normal early development and this, in itself, is strong argument against this hypothesis.

Some of the features of the malformation resembling those normally found in embryonic and fetal life include the intraventricular position of the choroid plexus, failure of the pontine flexure to develop, the beak-like deformity of the midbrain and the overall configuration of the cerebellum resembling that found in the embryo.

All these features may, however, be explained on the basis of simple mechanical factors. "Squashing" of the midbrain between the distended third ventricle and the pons probably leads to beaking over the superior surface of the cerebellum. Failure of the rhombic roof to perforate and its possible causes have already been discussed. Preservation of this membrane will inevitably result in persistence of an intraventricular choroid plexus. For the same reason the caudal end of the cerebellum will not rotate upwards and the embryonic configuration would persist. Crowding of hindbrain structures in the small posterior fossa with elongation of the fourth ventricle would easily explain failure of the pontine flexure to develop.

Thus, the considerable displacement of the cerebellar lobules into the cervical canal would not be compatible with a concept of development arrest; the evidence is strongly in favour of this part of the deformity being a

...../162

secondary manifestation. I have also referred to the occasional occurrence of the "split" cerebellum and other abnormal fissuring on the superior surface of the cerebellum. It has been shown that these changes represent part of a continuum of cerebellar changes and is not an isolated anomaly. There is no counterpart for this anomaly in any of the stages of normal cerebellar development.

Theories proposed by Williams are based on the assumption that the hindbrain malformation develops at, or soon after, birth; this, however, is negated by the fact that the malformation is already well established at birth; (one of the stillborn neonates in this series had a severe deformity in which the cerebellum extended 5.4 cm. into the cervical canal). Moreover, it is well known that the deformity occurs as an entity in early prenatal life. Williams' theory is based on the idea that cerebrospinal fluid by-passes the malformation in a caudal-cephalad direction, a concept which he supports with intraspinal and intra-ventricular pressure studies during crying, feeding and other neonatal movements. It is difficult to envisage this direction of cerebrospinal fluid flow, especially in the presence of severe malformations; it is, of course, impossible to accept this idea in those cases with imperforation of the rhombic roof.

The hindbrain structures are sometimes easily dislodged upward through the foramen magnum in the post mortem state using slight digital pressure; this could easily alter intraventricular pressure without necessarily altering

intraventricular fluid volume. I would suggest that cephalad displacement of hindbrain secondary to raised intraspinous pressure consequent upon crying and other manoeuvres in the neonate would account for the pressure changes recorded by Williams in the presence of the hindbrain malformation.

Certain difficulties in accepting the "overgrowth theory" as a valid concept have already been mentioned. Barry and colleagues (1957) believed that the cerebellum was hypoplastic at birth and explained this on the basis of a differential growth between cerebrum and cerebellum during the latter part of intrauterine life. Presumably he meant that overgrowth of cerebrum compressed the cerebellum to the extent that the latter, in spite of intrinsic overgrowth, appears hypoplastic at birth. However, if the cerebellar deformity were due to neural overgrowth, one would expect the longer cerebellar "tails" to occur in those cerebellums which are heavier. However, this does not appear to be the case when the data in Figure 4 is considered.

Another criticism of this theory is the paradox between the small posterior fossa and neural overgrowth of the hindbrain. Barry's description of the hindbrain malformation in a young foetus suggests that neural overgrowth must have commenced at an early stage, that is, before migration of the transverse sinuses is complete; surely such overgrowth would inevitably result in a migrational arrest of the venous sinus and comparatively large posterior fossa.

It is perhaps timely to redescribe the sequence which

...../164

results in the movement of the cerebellum in the posterior fossa based on a proposed new concept of pathogenesis. As suggested by Gardner, there is a sudden reduction in intra-ventricular pressure due to rupture of the neural tube (usually at the caudal end); this results in an unopposed Bering effect, followed by exaggerated posterior migration of the transverse sinus. This leads to a small posterior fossa. The cerebellum now grows within a small confined space. Cerebellar morphology itself is probably minimally altere at this stage.

Due to one of the reasons given above, the foutth ventricular exit foramina fail to develop; the central canal of the cord, at first patent, becomes inadequate as an effective fistulous escape for cerebrospinal fluid from the ventricular system. This might be related to the development of the "kinking" at the cervico-medullary junction. Increased pressure within the fourth ventricle results in diverticulum (cyst) formation of the unperforated rhombic roof. The diverticulum is only able to extend in a caudal direction; the result is traction on the early prenatal ventral lobules - there is elongation of the medullary velum and nodule with proportional displacement of the laterally placed flocculi.

Varying degrees of fourth ventricular narrowing occurs; this is probably mainly because of crowding of hindbrain structures in the small posterior fossa but also due to fourth ventricular elongation. Forebrain hydrocephalus is compounded. The midbrain becomes compressed between a distended third ventricle and cerebellum; this "concertina effect" causes beaking of the

...../165

midbrain with distortion of the aqueduct; obstruction would be potentiated at this level but this seems to be uncommon (Emery, 1974). Obstruction to the flow of cerebrospinal fluid within the fourth ventricle may be minimal or absent, in which case the hydrocephalus is communicating in type, provided that the foramina are patent.

Gardner suggested that the imperforate rhombic roof might rupture during the process of birth. However, many cases in this study showed no evidence of cysts or their remnants, although it is possible that they might have existed well before birth; resorption of residual membrane following early rupture is possible. Another theory is that fourth ventricular extension into the substance of the medulla in some cases (syringobulbia) could, in itself, have produced the same effect as suggested for these cysts; this assumes that the foramina are imperforate or obstructed. However, syringobulbia was not very common and it is more likely that cysts develop and rupture at different times inutero and this would account for the wide variation in the complexity of the deformity.

This wide variation in the gross morphology of the cerebellum has been emphasised; it is suggested that the milder types were probably similar to the malformation seen in the adult, for which there is also some evidence of a congenital origin. The pathogenesis is therefore likely to be related. In these adult cases an imperforate rhombic roof and some cerebellar deformation are usual and internal hydrocephalus is also sometimes seen. It would seem that neural tube rupture is not essential for the pathogenesis of this mild deformity. Gardner suggested that,

...../166

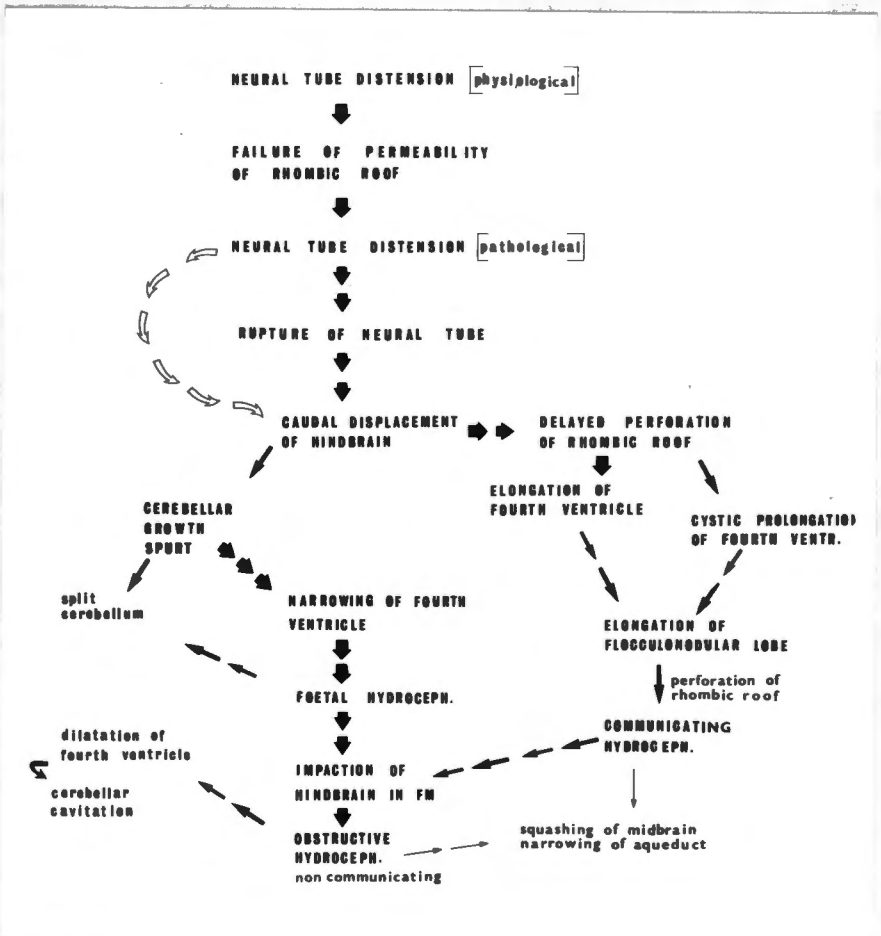
in these cases, the permeability of the rhombic roof during early foetal life is only partially disturbed. Neural tube distension, although not sufficient to rupture the neural tube, would be sufficient to produce some degree of foetal hydrocephalus; the immature hindbrain could be caudally displaced so that the future cisterna magna is reduced; thus the space necessary for membrane distension and basal foramina formation is not available. The hydrocephalus, however, becomes compensated, but may be reactivated in later life.

With regard to pathogenesis, the conclusion of this study may be summarised as follows (see Figure 65): the early lesion is a caudal displacement of hindbrain following rupture of the early neural tube; in accordance with Gardner's theory, this rupture is consequent upon early neural tube distension due to some disturbance in the permeability of the primitive rhombic roof. This early displacement is probably mild and usually just sufficient to obliterate the cisterna magna; the basal foramina therefore do not develop. Due to the more caudal position of the cerebellum, the migration of the tentorium cerebelli is greater than normal; this determines the small posterior fossa. Ventricular-amniotic fistulous escape of cerebrospinal fluid is limited to the early part of the development of the malformation but becomes progressively less effective.

A secondary hydrocephalus commences due to the persistence of the rhombic roof; the inferior medullary velum distends caudally to form a cystic "pocket". This results in a pulsation-traction system; the early ventral lobules elongate with expansion of the medullary velum and elongation of the nodule.

...../167

Figure 65



A schematic representation of the proposed inter-related foetal events causing the cerebellar malformation.

...../168

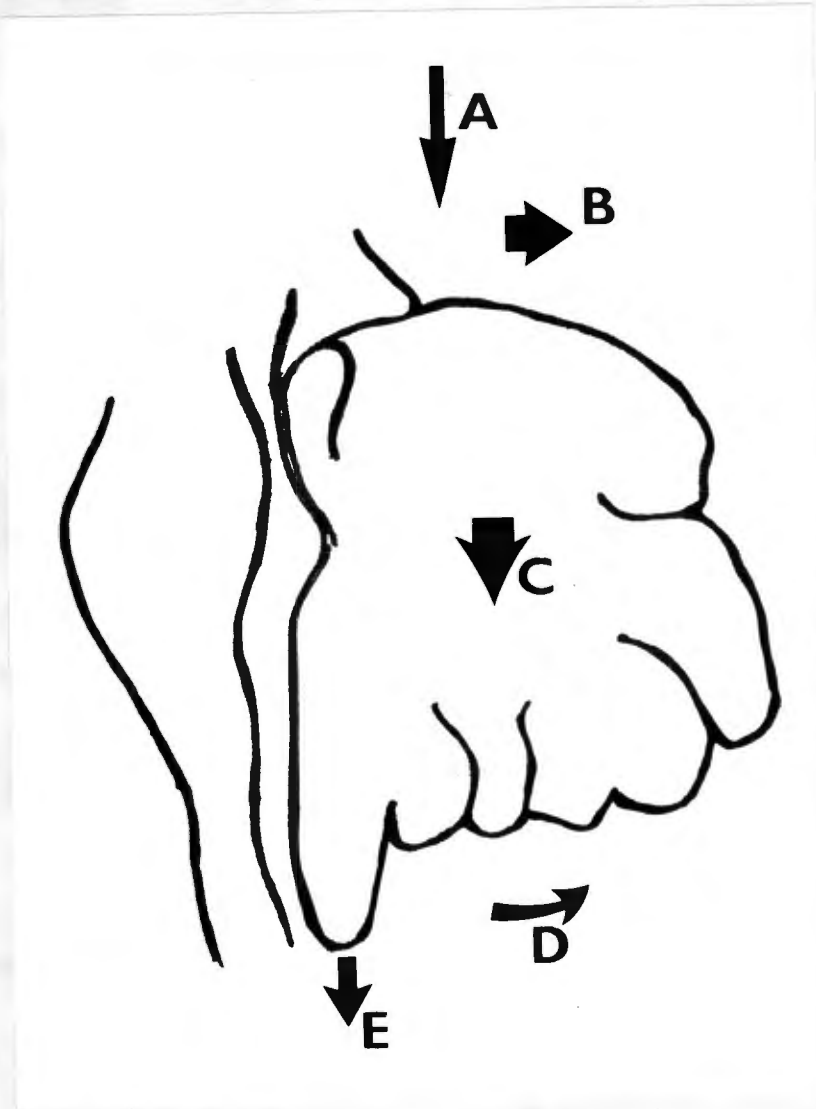
The "cyst" ruptures, presumably at varying stages in the development of the deformity and traction on the cerebellum then ceases. This stage in the genesis of the deformity is associated with elongation and narrowing of the fourth ventricle; some degree of aqueductal narrowing due to distortion of the midbrain is also to be expected.

During the second trimester cerebellar growth is slow but constant; however, there is probably no, or very little, emergence of cerebellar tissue above the tentorium cerebelli, the latter being probably hypoplastic at an early stage. This tentorial exit is blocked by the hydrocephalic occipital lobes and the result is development of the cerebellum in a small, rigid, mainly bony compartment. The organ appears to grow into itself, producing aberrant fissures mainly on the upper surface.

The growth spurt of the organ commences at the end of the second trimester; this growth is obstructed in the small posterior fossa. Both the infraforaminal part of the cerebellum and the portion above the foramen magnum are damaged by pressure and ischaemia; the result is necrosis and atrophy of the more caudally placed lobules.

Figure 66

Component Forces Acting in Deforming the Cerebellum



A - the influence of forebrain hydrocephalus, which is a relatively late foetal event.

B - the superior surface is prevented from growing upward, forward and inward; it is proposed that this is primarily due to the impacted midbrain (secondary to A).

C - early caudal displacement of the cerebellum, probably occurring at the time of rupture of the neural tube.

D - prevention of inward rotation of the inferior cerebellar lobules secondary to persistence of the rhombic roof and a small or absent basal cistern.

E - elongation of the early ventral lobules; this follows failure of perforation of the basal foramina, cerebrospinal pulsation forces, cyst formation and caudal traction.

...../170

BIBLIOGRAPHY

APPLEBY, A., FORSTER, J.B., HANKINSON, J. and HUDGSON, P. (1968): "The diagnosis and management of the Chiari anomalies in adult life", Brain, 91, 131-139.

ARING, C.D. (1938): "Cerebellar syndrome in adult with malformation of cerebellum and brain-stem (Arnold-Chiari deformity) with note occurrence of "Torpedoes" in cerebellum", J. Neurol. Psychiat., 1, 100-109.

ARNOLD, J. (1894): "Myelocyste, Transposition von Gewebskeimen und Sympodia", Beitr. Path. Anat., 16, 1-28.

BARROW, N. and SIMPSON, D.A. (1966): "Cranium bifidum. Investigation, prognosis and management", Aust. Paediatric Journal, 20, 10-26.

BARRY, A., PATTEN, B.M. and STEWART, B.H. (1957): "Possible factors in the development of the Arnold-Chiari malformation", J. Neurosurg., 14, 285-301.

BERING, R.A. (1955): "Choroid plexus and arterial pulsation of cerebrospinal fluid; demonstration of choroid plexuses as cerebrospinal fluid pump", Arch. Neurol. Psychiat., 73, 165-172.

BLAKE, J.A. (1910): "Roof and lateral recesses of the fourth ventricle, considered morphologically and embryologically", J. Comp. Neurol., 10, 79-98.

BLINKOV, S.M. and GLEZER, L.L. (1968): "The human brain in figures and tables - A Quantitative Handbook". New York: Basic Books. pp.152.

BOULTER, T.R. (1967): "The dysraphic states", Surg. Gynec. Obstet., 124, 1091-1100.

BOERMA, I. (1929): "Die Dynamik des Medullarrhrachulusses", Roux. Arch. Entw. Mech., 115, 601-607.

...../171

BROCK, D.J.H. and SCRIMGEOUR, J.B. (1972): "Early prenatal diagnosis of anencephaly", Lancet, ii, 1252-1253.

BROCKLEHURST, G. (1969): "The development of the human cerebrospinal fluid pathway with particular reference to the roof of the fourth ventricle", J. Anat., 105, 467-475.

BUEY, P.C. and LICHTENSTEIN, B.W. (1945): "Arnold-Chiari deformity in an adult without obvious cause", J. Neurosurg., 2, 245-250.

CARTANO de BARROS, M., FARIAS, W., ATAIDE, L. and LINS, S. (1968): "Basilar impression and Arnold-Chiari malformation", J. Neurol. Neurosurg. Psychiat., 31, 596-605.

CAMERON, A.H. (1957): "The Arnold-Chiari and other neuro-anatomical malformations associated with spina bifida", J.Path.Bact., 73, 195-211.

CARMEL, P.W. and MARKESBERY, W.R. (1970): "Arnold-Chiari malformation in an elderly woman", Arch. Neurol., 21, 258-262.

CARTER, C.O. (1971): "Genetics of common malformations", Recent Advances in Paediatrics, pp.546., Churchill Livingstone.

CHIARI, H. (1891): "Uber Veränderungen des Kleinhirns, des Pons und der Medulla oblongata in Folge von Congenitaler Hydrocephalie des Grosshirns", Deutsch. Med. Wschr., 27, 1172-1175.

CHIARI, H. (1895): "Uber Veränderungen des Kleinhirns, des Pons und der Medulla oblongata in Folge von congenitaler Hydrocephalie des Grosshirns", Deutsch. Akad. Wiss., Wien, 63, 71-116.

CLAIREAUX, A. (1970): "The first week of life", British Births,1970, 1, 235-253.

CLELAND, J. (1883): "Contribution to the study of spina bifida, encephalocele and anencephalus", J.Anat. Physiol., 17, 257-292.

...../172

CROME, L. (1952): "Microgyria", J. Path. Bact., 64, 479-495.

DANDY, W.E. (1921): "The diagnosis and treatment of hydrocephalus due to occlusions of the foramina of Magendie and Luschka", Surg. Gynec. Obstet., 32, 112-124.

DANIEL, P.M. and STRICH, S.J. (1958): "Some observations of the congenital deformity of the central nervous system known as the Arnold-Chiari malformation", J. Neuropath. Exp. Neurol., 17, 255-266.

DEPARTMENT OF HEALTH AND SOCIAL SECURITY, England (1973): "Care of the child with spina bifida".

DOBBING, J. (1970): "Under-nutrition and the developing brain: The relevane of animal models to the human problem", Amer. J. Dis. Child., 120, 411-415.

DOBBING, J. and SANDS, J. (1973): "Quantitative growth and development of human brain", Arch. Dis. Childh., 48, 757-767.

DODDS, G.S. (1941): "Anterior and posterior rhachischisis", Amer. J. Path., 17, 861-872.

ELLIS, R.S. (1920): "Norms for some structural changes in the human cerebellum from birth to old age", J. Comp. Neurol. Psychol., 32, 1-20.

EMERY, J.L. and REID, D.A.C. (1962): "Cerebral oedema and spastic hemiplegia following minor burns in young children", Brit. J. Surg., 50, 53-56.

EMERY, J.L., (1964): "Effects of continual decompression using Holter valve on weights of cerebral hemispheres in children with hydrocephalus and spina bifida cystica", Arch. Dis. Childh., 39, 379-382.

EMERY, J.L. (1965): "Intracranial effects of long-standing decompression of the brain in children with hydrocephalus and meningomyelocele", Dev. Med. Child Neurol., 7, 302-309.

EMERY, J.L. and Levick, R.K., (1966): "The movement of the brain stem and vessels around the brain stem in children with hydrocephalus and the Arnold-Chiari malformation", Dev. Med. Child Neurol., Suppl. 11, 49-60.

EMERY, J.L. (1967): "Kinking of the medulla in children with acute cerebral oedema and hydrocephalus and its relationship to the dentate ligaments", J. Neurosurg. Psychiat., 30, 267-275.

EMERY, J.L. and NAIK, D. (1968): "Spinal cord segment lengths in children with meningomyelocele and the 'Cleland-Arnold-Chiari' deformity", Brit. J. Radio., 41, 287-290.

EMERY, J.L. and LENDON, R.G. (1973): "The local cord lesion in neurospinal dysraphism (meningomyelocele), J.Path., 110, 83-96.

EMERY, J.L. and McKENZIE, N. (1973): "Medullo-cervical dislocation deformity (Chiari II deformity) related to neurospinal dysraphism (meningomyelocele)", Brain, 96, 155-162.

EMERY, J.L. (1974): "Deformity of the aqueduct of Sylvius in children with hydrocephalus and meningomyelocele", Dev. Med. Child Neurol., 16, Suppl.32, 40-48.

EMERY, J.L. and GADSDON, D.R. (1975): "A quantitative study of the cell population of the cerebellum in children with meningomyelocele", Dev. Med. Child Neurol., 17, Suppl. 35, 20-25.

EPSTEIN, F. (1973): "Neonatal hydrocephalus treated by compressive head wrapping", Lancet, i, 634-636.

...../174

EPSTEIN, F., HOCHWALD, G.M., WALD, A. and RANSCHOFF, J. (1975): "Avoidance of shunt dependency in hydrocephalus", Dev. Med. Child Neurol., 17, Suppl. 35, 71-77.

FEIGIN, I. (1956): "Arnold-Chiari malformation with associated analagous malformation of the midbrain", Neurology, 6, 22-31.

FEREMBACH, D. (1963): "Frequency of spina bifida occulta in prehistoric human skeletons", Nature, 199, 100-101.

FISHMAN, R.A and GREER, M. (1963): "Experimental obstructive hydrocephalus", Arch. Neurol., 8, 156-161.

FOWLER, I. (1953): "Responses of chick neural tube in mechanically produced spina bifida", J. Exp. Zool., 123, 115-152.

GARDNER, W.J. and GOODALL, R.J. (1950): "The surgical treatment of Arnold-Chiari malformation in adults", J. Neurosurg., 7, 199-206.

GARDNER, W.J., ABDULLAH, A.F. and McCORMACK, L.J. (1957): "Varying expressions of embryonal atresia of fourth ventricle in adults. Arnold-Chiari malformation, Dandy-Walker syndrome, "arachnoid" cyst of cerebellum and syringomyelia", J. Neurosurg., 14, 591-607.

GARDNER, W.J. (1959): "Anatomic abnormalities common to myelomeningocele of infancy and syringomyelia of adulthood suggest a common origin", Cleveland Clin. Quart., 26, 118-133.

..../174a

GARDNER, W.J. (1959): "Anatomical features common to the Arnold-Chiari and Dandy-Walker malformations suggest a common origin", Cleveland Clin. Quart., 26, 206-222.

GARDNER, W.J. (1964): "Diastematomyelia and the Klippel-Feil syndrome. Relationship to hydrocephalus, syringomyelia, meningocele, meningomyelocele and iniencephalus", Cleveland Clin. Quart., 31, 19-43.

GARDNER, W.J. (1968): "Myelocele: Rupture of the neural tube", Clin. Neurosurg., 15, 57-79.

GARDNER, W.J., SMITH, L.S. and PADGETT, D.H. (1972): "The relationship of Arnold-Chiari and Dandy-Walker malformations", J. Neurosurg., 36, 481-486.

GILLES, F.H. and KASSINER, M. (1976): "Hydrocephalus", Human Pathology, 7, 123-126.

GOLDSTEIN, F. and KEPES, J.J. (1966): "The role of traction in the development of the Arnold-Chiari malformation", J. Neuropath. Exp. Neurol., 25, 654-666.

GRAY'S ANATOMY (1967): 34th. Ed., Ed. by DAVIES, D.V. and COUPLAND, R.E., Longmans.

..../175

GUNBERG, D.L. (1954): "Spina bifida and herniation of hindbrain in the offspring of Trypan Blue injected rats", Anat. Rec., 118, 387

GUNBERG, D.L. (1956): "Spina bifida and the Arnold-Chiari malformation in the progeny of Trypan Blue injected rats", Anat. Rec., 126, 343-349.

HALL, P., KALSBECK, J., CAMPBELL, R. and MULLER, J. (1975): "Hydrosyringomyelia and myelodysplasia: Experimental and clinical investigations", Dev. Med. Child Neurol., 17, Suppl. 35, 158

HOCHWALD, G.M., EPSTEIN, F., MALHAN, C. and RANSCHOFF, J. (1972): "The role of the skull and dura in experimental feline hydrocephalus", Dev. Med. Child Neurol., 14, Suppl.27, 65-69.

HOCHWALD, G.M., EPSTEIN, F., MALHAN, C. and RANSCHOFF, J. (1973): "The relationship of compensated to decompensated hydrocephalus in the cat", J. Neurosurg., 39, 694-697.

HURTHAU, E.F. (1950): "Arnold-Chiari malformation", J. Neurosurg., 7, 282-284.

INGRAHAM, F.D. and SCOTT, H.W. (1943): "The Arnold-Chiari malformation: A study of 20 cases", New Eng.J.Med., 229, 108-114.

JACOBS, E.B., LANDING, B.H. and THOMAS, W.(1961): "Vermicomyelia: Its bearing on theories of genesis of Arnold-Chiari complex", Amer. J. Path., 39, 345-353.

KRUYFF, E. and JEFFS, R. (1966): "Skull abnormalities associated with the Arnold-Chiari malformation", Acta Radio. (Diagn.), 5, 9-24.

LANGELAAN, J.W. (1919): "On the development of the external form of human cerebellum", Brain, 42, 130-170.

...../176

LARSELL, O. (1947): "The development of the cerebellum in man in relation to its comparative anatomy", J. Comp. Neurol., 87, 85-129.

LAURENCE, K.M. and MARTIN, D. (1959): "A technique for obtaining undistorted specimens of the central nervous system", J. Clin. Path., 12, 188-190.

LAURENCE, K.M. (1971): "Congenital abnormalities in infancy", by NORMAN, A.D., 2nd.Ed., Blackwell Scientific Publications, pp.62.

LEMIRE, R.J., SHEPARD, T.H. and ALVORD, E.C. (1965): "Caudal myeloschisis (lumbo-sacral spina bifida cystica) in a five millimetre (Horizon XIV) human embryo", Anat. Rec., 152, 9-16.

LICHTENSTEIN, B.W. and KIRSHBAUM, J.D. (1941): "Foreign body giant cell granuloma of the spinal cord associated with spina bifida", Amer. J. Path., 17, 873-877.

LICHTENSTEIN, B.W. (1942): "Distant neuro-anatomic complications of spina bifida (spinal dysraphism)", Arch. Neurol., Psychiat., 47, 195-214.

LIGHTOWLER, C.D.R. (1971): "Meningomyelocele: The price of treatment", B.M.J., ii, 385-387.

LOGUE V. (1971): "Syringomyelia: A radiodiagnostic and radiotherapeutic saga", Clin. Radiol., 22, 2-16.

LORBER, J. (1961): "Systematic ventriculographic studies in infants born with meningomyelocele and encephalocele" Arch. Dis. Childh., 34, 381-389.

LORBER, J. (1971): "Medical and surgical aspects in the treatment of congenital hydrocephalus", Neuropädiatrie, 2, 239-246.

...../177

MacFARLANE, A. and MALONEY, A.F.J. (1957): "The appearance of the aqueduct and its relationship to hydrocephalus in the Arnold-Chiari malformation", Brain, 80, 479-491.

MacKENZIE, N. and EMERY, J.L. (1971): "Deformities of cervical cord in children with neurospinal dysraphism", Dev. Med. Child Neurol., 13, Suppl.25, 58-67.

MALIS, L.I., COHEN, I. and GROSS, S.W. (1951): "Arnold-Chiari malformation", Arch. Surg., 63, 783-798.

MARGOLIS, G. and KILHAM, L. (1969): "Experimental virus-induced hydrocephalus. Relation to pathogenesis of the Arnold-Chiari malformation", J. Neurosurg., 31, 1-9.

MARIN-PADILLA, M. (1966): "Study of the vertebral column in human craniochachischisis", Acta Anat., 63, 32-48.

McCONNELL, A.A. and PARKER, H.L. (1928): "A deformity of the hindbrain associated with internal hydrocephalus. Its relation to the Arnold-Chiari malformation", Brain, 81, 415-429.

McLETCHIE, N.G.B., PURVES, J.E, and SAUNDERS, R.L. de C.H. (1954): "Genesis of gastric and certain intestinal diverticula and enterogenous cysts", Surg. Gynec. Obstet., 99, 135-141.

MORGAGNI, J.B. (1769): "The seats and causes of diseases investigated by anatomy", translated by Benjamin Alexander, 3, A. Millar and T. Cadell, London, pp.751-755.

NAIK, D. and EMERY, J.L. (1968): "The position of the spinal cord segments related to the vertebral bodies in children with meningomyelocele and hydrocephalus", Dev. Med. Child Neurol., 10, Suppl.16, 62-68.

...../178

OGRYZLO, M.A. (1942): "The Arnold-Chiari malformation", Arch. Neurol. Psychiat., 48, 30 46.

PADGET, D.H. (1957): "Development of cranial venous system in man from viewpoint of comparative anatomy", Carnegie Inst. Wash. Publ. 611, Contrib. Embryol., 36, 79-140.

PADGET, D.H. (1968): "Spina bifida and embryonic neuroschisis - A causal relationship", The Johns Hopkins Medical Journal, 123, 233-252.

PADGET, D.H. (1970): "Embryonic neuroschisis and mal-development", J. Neuropath. Exp. Neurol., 29, 192-216.

PADGET, D.H. (1972): "Development of so-called dyseraphism, with embryologic evidence on clinical Arnold-Chiari and Dandy-Walker malformations", Johns Hopkins Med. J., 130, 127-165.

PATTEN, B.M. (1953): "Embryological stages in the establishment of myeloschisis with spina bifida", Amer. J. Anat., 93, 365-395.

PEACH, P. (1964): "Cystic pmlongation of fourth ventricle", Arch. Neurol., 11, 609-612.

PEACH, P. (1964): "Arnold-Chiari malformation with normal spine", Arch. Neurol., 10, 497-501.

PEACH, P. (1965): "Arnold-Chiari malformation", Arch. Neurol., 12, 527-535.

PEACH, P. (1965): "Arnold-Chiari malformation: Anatomic features of 20 cases", Arch. Neurol., 12, 613-621.

PENFIELD, W. and COBURN, D.F. (1938): "Arnold-Chiari malformation and its operative treatment", Arch. Neurol. Psychiat., 40,328-336.

POTTER, E.L. (1961): "Pathology of the fetus and infant", 2nd. Ed., Chicago: Year Book Medical Publishers, pp.430.

...../179.

RUSSEL, D.S. and DONALD, C. (1935): "The mechanism of internal hydrocephalus in spina bifida", Brain, 58, 203-215.

RUSSEL, D.S. (1949): "Observations on the pathology of hydrocephalus", London: H.M.Stationery Office (Spec. Rep. Ser. Med. Res. Council. No. 265).

RYDELL, R.E. and PULEC, J.L. (1971): "Arnold-Chiari malformation, neuro-otologic symptoms", Arch. Otolaryng., 94, 8-12.

SAHAR, A., HOCHWALD, G.M., SADIK, A.R. and RANSCHOFF, J. (1969): "Cerebrospinal fluid absorption in animals with experimental obstructive hydrocephalus", Arch. Neurol., 21, 638-644.

SCHWALBE, E. and GREDIG, M. (1907): "Uber Entwicklungsstörungen des Kleinhirns, Hirnstamms und Halsmarks bei Spina bifida", Beitr. Path. Anat., 40, 133-194.

SHELLSHEAR, I. (1975): Personal Communication.

SHELLSHEAR, I. and EMERY, J.L. (1975): "The tectum and aqueduct of Sylvius in hydrocephalus unassociated with meningomyelocele", Dev. Med. Child Neurol., 17, Suppl. 35, 26-34.

SMITH, J.P. (1974): "Paediatric neuropathology", McGraw-Hill Book Co., A Blakiston Publication, pp.5.

SWANSON, H.S. and FINCHER, E.F. (1949): "Arnold-Chiari deformity without bony anomalies", J. Neurosurg., 6, 314-319.

TENG, P. and PAPATHEODOROU, C.(1965): "Arnold-Chiari malformation with normal spine and cranium", Arch. Neurol., 12, 622-624.

TAGGART, J.K. and WALKER, A.E. (1942): "Congenital atresia of the foramens of Luschka and Magendie", Arch. Neurol., 48, 583-612.

VAN HOUWENINGE GRAFDIJK, C., (1932): "Over hydrocephalus", Diss. Med. (Leiden).

...../180

VAN HOYTEMA, G.J. and VAN DEN BERG, R. (1966): "Embryological studies of the posterior fossa in connection with Arnold-Chiari malformation", Dev.Med.Child Neurol., Suppl.11, 61-75.

VERBIEST, H. (1953): "The Arnold-Chiari malformation. Radiological examination with the 'Ziedses des Plantes' procedure", J. Neurol. Neurosurg. Psychiat., 16, 227-233.

WALLACE, S.J. (1973): "The effect of upper limb function on mobility of children with meningomyelocele", Dev. Med. Child Neurol., 15, Suppl. 29, 84-91

WARKANY, J., WILSON, J.G., and GEIGER, J.F. (1958): "Myeloschisis and myelomeningocele produced experimentally in the rat", J. Comp. Neurol., 109, 35-64.

WEALTHALL, S.R. (1973): "An investigation of factors involved in regulating ventricular size and production of hydrocephalus" (Casey Holter Memorial Prize Essay), Dev. Med. Child Neurol., 15, Suppl. 29, 1-11.

WEED, L.H. (1917): "Development of cerebrospinal fluid spaces in pig and man", Contr. Embryo.., 5, 7-116.

WEED, L.H. (1938): "Meninges and cerebrospinal fluid", J. Anat., 72, 181-215.

WILLIAMS, B., (1969): "The distending force in the production of communicating syringomyelia", Lancet, ii, 189-193.

WILLIAMS, B., (1971): "Further thoughts on the valvular action of the Arnold-Chiari malformation", Dev. Med. Child Neurol., 13, Suppl. 25, 105-112.

...../181

WILLIAMS, B., (1975): "Cerebrospinal fluid pressure-gradients in spina bifida cystica, with special reference to the Arnold-Chiari malformation and aqueductal stenosis", Dev. Med. Child Neurol., 17, Suppl. 35, 138-150.

WILSON, J.T. (1937): "On the nature and mode of origin of foramen of Magendie", J. Anat., 71, 28-33.

WINIEK, M., ROSSO, P. and WATERLOW, J. (1970): "Cellular growth of the cerebrum, cerebellum and brain stem in normal and marasmic children", Exp. Neurol., 26, 393-400.

YU, H.C. and DECK, M.D.F. (1971): "The Clivus deformity of the Arnold-Chiari malformation", Radiology, 101, 613-615.

..../182

GLOSSARY

SPINA BIFIDA - often used (erroneously) to denote any unfused condition of the neural arches. In the past this term has been commonly used synonymous with meningomyelocele.

SPINA BIFIDA OCCULTA - unfused condition of the neural arches. The spinal cord is usually normal. The only visible external abnormality may be localised superficial skin defects.

MENINGOCELE - spina bifida is accompanied by herniation of the meninges out of the spinal canal. The meninges are found directly on the surface or covered by normal or abnormal skin. The cord remains within the spinal canal, but may show a variety of malformations. Rarer than meningomyelocele, and affected children have a much better prognosis.

MYELOCELE - an area of unclosed neural plate is exposed at the site of the spina bifida.

MENINGOMYELOCELE - a myelocele which has become scarred over and epithelialised soon after birth. Gardner (1968) prefers to term myelocele rather than meningomyelocele because the neural tissue constitutes the primary component of the sac.

RACHISCHISIS - frequently used to cover the condition of myelocele with spina bifida (rachis is the Greek word for spinal column). Rachischisis is therefore more synonymous with myelocele.

...../183

HYDROCEPHALUS - dilatation of the ventricular system.

NON-COMMUNICATING HYDROCEPHALUS - (syn. obstructive hydrocephalus) hydrocephalus in which there is no egress of cerebrospinal fluid from the ventricles into the subarachnoid spaces.

COMMUNICATING HYDROCEPHALUS - hydrocephalus in which there is a free communicating between the ventricular system and the subarachnoid spaces. Classically occurs when there is over-production of cerebrospinal fluid or when the re-absorptive surfaces over the cerebral surfaces are obliterated.

CRANIUM BIFIDUM - congenital defect in the bones of the skull, usually in the midline; almost always accompanied by protrusion of meninges, containing fluid or neural tissue. The former is usually known as cranial meningocele, the latter as encephalocele. Anencephaly (syn. encercephalus) is a broader term which encompasses both these conditions.

HYDROMYELIA - over-distension of the central canal of the spinal cord. The central canal usually closes late in intra-uterine life. In the presence of "ventricular" hydrocephalus and inadequate permeability of the rhombic roof, the central canal becomes distended with cerebrospinal fluid; most likely to occur with failure of the basal foramina to form.

...../184

SYRINGOMYELIA - a localised distension of the central canal. The syrinx undergoes progressive enlargement because cerebrospinal fluid continues to enter.

DIASTEMATOMYELIA - a localised duplication of the spinal cord separated by tissue derived from mesoderm, bone or fibrous tissue.

CRANIOLACUNIA - (syn. craniofenestra, lückenschädel, lacunar skull deformity), these are localised areas of bony aplasia involving the membranous calvarium; tends to disappear during the first 2-3 months after birth. Gardner (1965) believes the cause to be pressure on the calvarium by an over-distended cerebral mantle.

DYSRAPHISM - failure of fusion of the parts along the dorsal midline.

DANDY-WALKER SYNDROME - congenital abnormality characterised by enormous dilatation of the fourth ventricle with separation and hypoplasia of the cerebellar hemispheres. Pathogenesis is discussed in the text. Usually associated with forebrain hydrocephalus and imperforation of the rhombic roof.

APPENDIX 1

Further Details of the 100 Cases Used During This Study

KEY

Cause of Death

V.	-	Ventriculitis
S.	-	Septicaemia
P.	-	Pneumonia
M.C.A.	-	Multiple Congenital Abnormalities
T.Pneumothorax	-	Tension Pneumothorax
Ac.I/C.H°tension	-	Acute Intracranial Hypertension
C.H.D.	-	Congenital Heart Disease
M.	-	Meningitis

Mode of Delivery

N.D.	-	Normal Delivery
C.S.	-	Caesarian Section
F.D.	-	Forceps Delivery
B.D.	-	Breech Delivery

Site of Back Lesion

T.	-	Thorax
L.	-	Lumbar
S.	-	Sacral

* Meningomyelocele not operated on.

No.	Mode of Delivery	Birth Weight (gms.)	Gest. Age (wks)	Site of Lesion.	Age at Death	Cause of Death
1	ND	3270	36	T/L	14/12	Renal failure (pyelo-nephritis)
2	ND	2490	FT	T/L	20/12	Ac.I/C.H°tension
3	ND	?	FT	T/L	17hrs	C.H.D.
4	ND	2880	39	T/L	29/12	S.
5	ND	?	?	L/S	2/7	M.C.A. *
6	ND	?	FT	T/L	5/52	Pulmonary abscesses
7	ND	3810	?	T/L	2/7	?
8	ND	3660	FT	L	25/7	S.
9	ND	3150	40	T/L	21/12	Ac.I/C.H°tension
10	ND	3520	?	T/S	6/7	V. and P.
11	ND	?	?	S	47/12	Post-op. Peritonitis
12	BD	2700	33	L/S	18/12	Ht.failure due to Pulm.Dis.
13	ND	3040	FT	L/S	2/12	V.
14	ND	3300	FT	T/L	1/12	M. *
15	ND	3150	41	S	12/7	S.
16	ND	3210	39	T/L	5/52	Ac.I/C.H°tension
17	ND	3180	?	T/L	1/12	Pulmonary Aspiration
18	ND	3010	?	L/S	10/52	V.
19	ND	?	?	L/S	4/52	Cerebral abscess
20	ND	2850	FT	T/S	1/12	V. and P.
21	ND	3000	40/41	T/L	6 yrs	Ac.I/C.H°tension
22	ND	3200	40	T/L	22/7	S.
23	ND	3645	?	L/S	7/7	S. and M.
24	BD	3720	40	T/L/S	14/52	?
25	CS	2700	FT	L/S	1/12	V.
26	FD	4140	?	T/L	9/52	S.
27	CS	?	?	T/L	5 yrs	Ac.I/C.H°tension
28	ND	2760	FT	T/L	4/52	V.
29	ND	3150	40	T	3/52	V.
30	ND	3060	?	T/L	3/52	?
31	ND	3090	?	T	19/12	Pulmonary embolisation
32	ND	3210	?	T/L	6/52	Pulmonary inhalation
33	BD	1650	Twin	L	9/7	P.
34	ND	3210	FT	T/L	19hrs	?
35	ND	4050	?	L	2/7	P.
36	ND	?	?	T/L	24/7	M.C.A. and S.
37	ND	4290	?	L	12/7	V.
38	CS	3150	FT	T/L	3/52	S. and P.
39	ND	3070	?	T/L	10hrs	Post-op. haemorrhage
40	ND	2280	?	T/L/S	1/7	?
41	ND	2250	?	T/L	5/7	M.C.A. and S.
42	ND	3090	?	L	2/52	?
43	ND	3150	38	T/L	18/7	S.
44	ND	3390	?	T/L	15/7	S. and P.
45	ND	3450	FT	L	6/7	P. and S.
46	ND	3150	FT	L	6/52	M.C.A.
47	ND	2700	FT	T/L	5/52	P.
48	ND	?	?	L	4/52	V.
49	ND	3070	FT	T/S	8/7	P.
50	CS	3930	?	T/L	14/7	V.

Contd.....

No.	Mode of Delivery	Birth Weight (gms.)	Gest. Age (wks)	Site of Lesion.	Age at Death	Cause of Death
51	ND	2520	37	T/S	6/52	V.
52	ND	3090	?	L/S	5/7	?
53	ND	2760	FT	T/L	6/7	S.
54	ND	?	FT	L/S	15/7	?
55	ND	?	?	T	3/7	M.C.A.
56	ND	3150	FT	T/L/S	3/12	?
57	ND	?	?	T/L	5/7	P.
58	ND	4500	FT	L	14/52	?
59	ND	3000	?	T/L	2/12	Bronchitis
60	ND	3150	FT	T/L	10/7	M.
61	ND	2295	38	T	15/7	S.
62	ND	3690	42	T/L	6/52	S.
63	ND	2700	?	L	2/52	?
64	ND	3150	?	L/S	10/7	S. and P.
65	ND	2700	?	T/L	2/7	T. Pneumothorax
66	ND	3150	?	L/S	3/7	P.
67	ND	3180	41	L/S	15/7	P.
68	ND	3480	FT	T/S	13/7	S.
69	ND	?	?	T/L	13/52	V.
70	ND	2160	36	T/L	19/7	V. *
71	ND	3090	FT	T/L	5/52	Bronchiolitis
72	ND	3040	FT	T/L	14/7	?
73	ND	2700	?	S	3/7	Wound sepsis
74	ND	3600	FT	T/L	3/52	V. and P.
75	ND	3150	FT	L	9/12	V.
76	ND	3450	FT	S	31/12	?
77	ND	2550	34	T/S	2/12	M.
78	ND	3000	?	T/L	5/52	Bronchiolitis
79	ND	3600	42	T/L	2/52	M.
80	ND	3670	44	L	2/52	V.
81	ND	2850	FT	L	3/52	Respiratory infection
82	ND	?	?	T/L	2/12	P.
83	ND	?(SB)	39	T/L	-	-
84	ND	2160	3587	S	3/12	M.C.A.
85	ND	4770	FT	L/S	1 yr.	P.
86	ND	3490	40	T/S	8/7	S.
87	ND	3090	?	T/L	2/7	Meconium aspiration
88	ND	3210	FT	T/S	1/12	S.
89	ND	2880	41.5	L/S	4/12	?
90	ND	2430	FT	T/L	12/7	Peritonitis
91	ND	?	?	T/S	1/7	M.C.A.
92	ND	3330	?	T/L	6/52	?
93	ND	?	FT	L	3/12	Intracardiac Thrombosis
94	ND	3150	FT	T/S	22/7	V.
95	ND	4050	FT	T/S	4yr. 10/12	Renal failure
96	ND	3040	FT	L	5/7	?
97	ND	2700	38	L	2/52	V. and S.
98	ND	3900	?	T/S	19/12	Ac.I/C.H°tension
99	ND	3210	FT	T/S	3/52	S.
100	ND	3490	FT	T/S	6/7	S.

...../188

Appendix 1 (Contd.)

In several cases the immediate cause of death was difficult to ascertain. These cases were usually regarded as belonging to Emery's type 1 "cot death". In the majority of cases the back lesion was operated on within twenty-four hours of birth. Occasionally, an infected meningomyelocele, or the severity of associated congenital abnormalities contra-indicated operative intervention. In several instances the associated multiple congenital abnormalities were held to be responsible for death.

Deaths due to acute intracranial hypertension usually occurred in the older age group and were invariably secondary to shunt blockage; this was occasionally the cause of death in the younger shunt-treated group.

Histology was performed in all cases; this either confirmed or permitted a change in the initial post mortem diagnosis.

Appendix 2

Curriculum Vitae

and Background Details

1. House Officer in General Medicine and Surgery, Livingstone Hospital (South Africa), January to December, 1966.

   Senior House Officer in Paediatrics, Livingstone Hospital (South Africa), January, to October, 1967.

   General Practise, Cape Town (South Africa), November, 1967 to April, 1968

   Medical Officer, Government of Botswana, May, 1968 to October, 1970.

   Senior House Officer in Paediatrics, The Royal Hospital, Wolverhampton (U.K.), January to December, 1971.

   Locum Registrar in Paediatrics, St. Stephen's Hospital, (London) and Leeds General Infirmary, February to May, 1972.

   Registrar in Paediatrics, The Children's Hospital, Sheffield, August, 1972 to October, 1974 (including nine months in paediatric pathology).

   Registrar in Pathology, City Hospital, Nottingham, November, 1974 to July, 1975.

   Senior Registrar in Pathology, Nottinghamshire Area Health Authority (Teaching), August, 1975 - present appointment.

2. The background work for this manuscript was performed in the Department of Pathology, Children's Hospital, Sheffield, England, during my tenure as Paediatric Registrar from August, 1972 to October, 1974; compilation of the manuscript was carried out during 1975 and 1976.

   Some of this work has already been published, reprints of

...../190

which are included in the pocket in the back cover. An abstract of part of the work presented before the Paediatric Pathology Society has been published as follows:

"Deformity of the lateral cerebellar lobes in children with meningomyelocele", Arch. Dis. Childh., (1974), 49, No.6, p.495.

Ten of the post mortems were performed entirely by myself; the rest were performed by various pathologists over the previous eight years. The skull and spinal columns of these cases were prepared and stored in formalin as described on page 20; dissection of these specimens, all measurements and drawing of all diagrams were performed by myself; some of the histological interpretation was done with the help of Professor J. L. Emery due to my inexperience at the time.

3. Degrees

M.B., Ch.B.,	-	University of Cape Town, 1965
D.C.H.	-	London, 1971
M.R.C.P.	-	London, 1972
M.R.C.Path.,	-	London, 1977

Reprinted from TERATOLOGY
Vol. 13, No. 3, June 1976

Cervical Dislocation of the Cerebellum in Children with Meningomyelocele

S. VARIEND AND JOHN L. EMERY
Department of Pathology, Children's Hospital, Sheffield, S10 2TH, England

ABSTRACT In a study of 100 cerebellums from children dying with meningomyelocele, the lobular pattern of the dislocated segment was identified and classified. There was a graded variation in the degree of cerebellar deformity ranging from complete absence of cerebellar tissue in the upper cervical canal to one in which the upper cerebellar lobules were displaced through the foramen magnum. Within this range there were 2 instances in which the cerebellar defect conformed to that found in the Chiari type 1 deformity, consisting of prolapse of tonsillar tissue only. During fetal life the lobular relation in the caudal aspect of the cerebellum undergoes considerable change and it is likely that the type of deformity present in the cervical canal is closely related to the stage of cerebellar development at which the alteration in growth has its inception. The evidence presented argues against the defect being of a primary developmental nature. The terms "Chiari type 1 deformity" and "Arnold-Chiari malformation" have outlived their usefulness and future descriptions of the cerebellum in children with hindbrain deformities should indicate the shape of the lobules and precise ones involved in the herniation.

In 1883 Cleland described a congenital anomaly of the brainstem in which the medulla was elongated, the 4th ventricle extended into the cervical canal, the midbrain protruded dorsally, and the inferior vermis of the cerebellum was displaced caudally. In 1891 Chiari described 3 types of hindbrain anomaly associated with the hydrocephalus. In his type 1 deformity he described caudal extension of the cerebellar tonsils and medial parts of the inferior lobes. This deformity was restricted to the cerebellum and in no way involved the pons or the medulla oblongata. His type 2 deformity, which he believed to be a severe form of type 1, was described in a girl with meningomyelocele and was similar to that described by Cleland but in which he also noted a dorsal protuberance at the junction of the medulla and cervical cord.

Arnold (1894) presented a less detailed description of the type 2 deformity, and Schwalbe and Gredig ('07), working in Arnold's laboratory, coined the term "Arnold-Chiari malformation" to designate the Chiari type 2 deformity. In many instances the Chiari type 2 deformity is completely associated with meningomyelocele and this relation is now well established. Russell and Donald ('35) stated that they doubted the existence of a type 2 deformity in the absence of meningomyelocele. The Chiari type 1 deformity, however, may be found in a wide range of conditions including cerebral tumors, platybasia (Peach, '64), and cerebral edema (Emery and Reid, '62).

In an effort to characterize the type 2 deformity further, a number of new neuroanatomical features have been described, and some have been reemphasized. These include over-riding of the medulla onto the cervical cord causing a characteristic kink (Schwalbe and Gredig, '07); cephalad course of the upper cervical

Received Oct. 14, '75. Accepted Dec. 1, '75.

nerve roots from their points of origin (Russell and Donald, '35); low insertion of the tentorium cerebelli resulting in a small posterior fossa (Penfield and Coburn, '38; Cameron, '57); "hypoplastic" appearance of the cerebellum (Schwalbe and Gredig, '07; Russell and Donald, '35); and analogous malformation of the midbrain (Feigin, '56). Certain radiological features of the skull have also been reported (Kryff and Jeffs, '66). However, it is now evident that of these features many may also be found associated with the Chiari type 1 deformity. For instance, caudal displacement of the pons and medulla has been reported with acute cerebral edema in children, even producing a kink in the region of the medullocervical junction (Emery, '67), and the peculiar course of the upper cervical roots has also been described with intracranial space-occupying lesions (Gardner and Goodall, '50) implying caudal displacement of the pons and medulla.

However, despite this rather significant overlap in features between these 2 hindbrain anomalies, attempts to categorize them into 2 distinct groups have continued to gain ground. Peach ('64) drew attention to the considerable confusion i the use of the terms "Chiari type 1 deformity" and the "Arnold-Chiari malformation," and quoted a number of reports in which the deformity had apparently been wrongfully designated the "Arnold-Chiari malformation" which were, in fact, examples of Chiari's first type. In an effort to clarify the situation he stressed the difference in morphology of the cerebellum in the two deformities, i.e., herniation of the cerebellar tonsils in the type 1 deformity and herniation of the cerebellar vermis in the type 2 deformity.

In Chiari's second report (1896) in which he described 24 cases of congenital hydrocephalus there were 7 instances of the type 2 deformity and these were all associated with meningomyelocele. Fourteen cases were of the type 1 deformity and it is interesting that among these there was 1 case of spina bifida. Furthermore, the cerebellar defect of the Chiari type 1 deformity has been reported in a child with meningocele, hydrocephalus, and elongated medulla and 4th ventricle (Russell, '49). Also, Cameron ('57) described 26 cases of myelocele and meningomyelocele, found 2 cases in which only the tonsils formed the cerebellar defect.

In the original report by Cleland and those by Chiari (1891), Lichtenstein ('42), Cameron ('57), Daniel and Strich ('58), and Peach ('65), the displaced segment of the cerebellum in the type 2 deformity was consistently referred to as "the inferior vermis" or "an elongation of the inferior vermis." Other authors have referred to it as a "tongue-like process from the inferior poles of the cerebellar hemispheres" (Ingraham and Scott, '43) or a "tongue of variable length consisting of cerebellar tissue" (Russell and Donald, '35). We thought it useful to record the actual cerebellar tissue that had herniated through the foramen magnum in a series of 100 necropsies on children dying with meningomyelocele.

MATERIALS AND METHODS

The brain was fixed in the skull prior to dissection. The upper cervical canal was opened and, with the neck in a midposition between full extension and full flexion, the distance between the foramen magnum and the lowest part of the cerebellum was measured with calipers. The fissural pattern and lobular arrangement of the dislocated segment of the cerebellum were mapped and photographed. The skull was then opened from above and, after removal of the cerebral hemispheres, the cerebellum was dissected free. A detailed examination was then made with regard to the fissural and lobular pattern of the posterior surface above the level of the foramen magnum. This area was similarly mapped and photographed. The whole cerebellum was weighed; the results of this have already been reported(Variend and Emery, '73). The lobules within the herniated part of the cerebellum were then

identified in relation to the rest of the lobules constituting the posterior surface of the organ. In this way we were able to confirm or change our initial assessment of the lobular composition of the intraforaminal portion of the cerebellum.

The study comprised 100 cerebellums from children with meningomyelocele. Their ages ranged from birth to 6 years and the causes of death varied from pulmonary to renal complications, ventriculitis to shunt crises. Twenty cases had received decompression treatment with a Holter valve for a period exceeding 2 weeks. Detailed descriptions of other deformities in the spinal cords of these cases have already been reported (Emery and Levick, '66; MacKenzie and Emery, '71; Emery and MacKenzie, '73; Emery and Lendon, '73).

RESULTS

Our cases were divided according to the extent of the cerebellar dislocation through the foramen magnum (fig. 1).

Group A (18 cases). The horizontal fissure was displaced into the upper cervical canal so that the dislocated segment of the cerebellum included the superior semilunar lobules, inferior semilunar lobules, biventral lobules, tonsils, pyramid, uvula, and nodule.

Group B (32 cases). All of the lobules below the level of the horizontal fissure were displaced into the cervical level. The horizontal fissure itself was still above the level of the foramen magnum. The dislocated segment of the cerebellum therefore included inferior semilunar lobules, biventral lobules, tonsils, pyramid, uvula, and nodule. This was the most common group encountered.

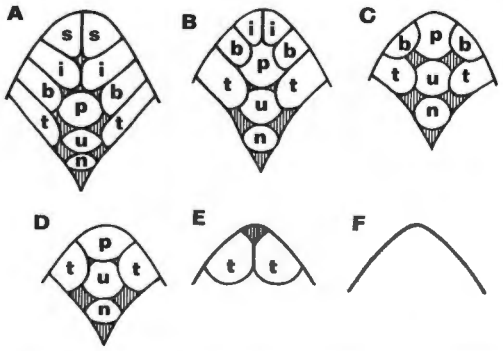


Fig. 1 Diagramatic representation of the various groups to show the pattern of the lobules in the dislocated segment. N, nodule; U, uvula; P, pyramid; T, tonsil; B, biventral lobule; I, inferior semilunar lobule; S, superior semilunar lobule.

Group C (20 cases). The biventral lobules together with the tonsils, pyramid, uvula, and nodule were displaced into the upper cervical canal.

Group D (14 cases). The tonsils together with the uvula and nodule were displaced below the level of the foramen magnum.

Group E (2 cases). The tonsils alone were displaced.

Group F (10 cases). No cerebellar tissue was found below the level of the foramen magnum. In some of these cases a close inspection often revealed cerebellar tissue approximating the foramen magnum from above but there was no displacement of tissue beyond this point. Of these 10 cases, 5 were in the untreated population and 5 in the shunt-treated group.

Minor degrees of asymmetry in the cerebellar hemispheres were common so that one side of the dislocation often involved more lobules than the other. Occasionally the asymmetry was more marked; in 1 case the right side showed tonsillar tissue only while the opposite side showed displacement up to the level of the inferior semilunar lobules. In this classification the highest level was taken into account so that the latter case was put into Group B. In some cases the infraforaminal lobules were clearly smaller than one would have expected for the age of the child and in comparison with the rest of the cerebellum and gave the impression of having undergone atrophy. This was especially so in the older shunt-treated group. In other cases atrophy appeared to have resulted in complete, or almost complete, loss of lobular differentiation so that any attempt to identify individual lobules in this region had to be abandoned. However, it was still possi-

ble to determine the level of cerebellar displacement as the lobular tissue above this level was relatively well preserved. In 4 cases the entire cerebellum had undergone such degeneration as to render them totally unsuitable for inclusion in our classification.

In some cases the degree of displacement was so extreme as to include lobules of the superior surface anterior to the superior semilunar lobules. Among the cases in Group A there were 9 in which the lobuli simplex were found in the upper cervical canal and 2 cases also showed the quadrangular lobules. Such severe cerebellar deformities can only really be appreciated by referring to figure 7, which classically shows the fissures of the superior surface passing almost directly to the foramen magnum so that the most anterior lobules of the superior surface are displaced through the foramen magnum.

DISCUSSION

We found a wide range of deformity in the cerebellar component of the hindbrain anomaly, and the common statement that the displaced segment of the cerebellum is

Fig. 2 Cerebellum from Group A showing the level of indentation of the posterior margin of the foramen magnum. The horizontal fissure has been displaced below this level so that the superior semilunar lobules are part of the dislocated cerebellar segment, together with the more caudal lobules.

simply an elongated inferior vermis is both vague and inaccurate. In 10% of our series no cerebellar tissue appeared in the upper cervical canal. The least severe cerebellar deformity showed displacement of the tonsils only, whereas the most complex deformity was associated with displacement of the horizontal fissure below the foramen magnum so that the superior surface of the cerebellum presented in the upper cervical canal.

There were 2 cases in which only tonsils were displaced; this is compatible with the cerebellar defect in the Chiari type 1 deformity. These individuals were 3 days and 31 months old. In each the nodule, as well as the other lobules, was easily identified and there was no question of loss of tissue.

It is impossible to explain the more complex deformities of the cerebellum simply on the basis of caudal displacement of a normal organ through the foramen magnum. As reported in the past (Variend, '74) the cerebellar lobules of the upper and posterior surfaces were displaced dorsally and caudally, espectively, which resulted in lobules being more concentrated in the caudal end of the organ, this is well illustrated in figure 2. Lack of depth of the posterior fossa associated with low insertion of the tentorium cerebelli was almost invariably present in the type 2 deformity and necessitated the cerebellum occupying a more caudal position relative to the foramen magnum. The two factors most likely to explain the infraforaminal component of the cerebellar deformity are, first the displacement of the lobules within the organ itself and second the displacement of the cerebellum relative to the posterior fossa. The complex nature of the cerebellar deformity has not been alluded to before in any detail, except perhaps by Margolis and Kilham ('69) who described a similar malformation in hamsters with viral-induced hydrocephalus. Although the cerebellar lobules were not specifically mentioned they noted that "most of the cerebellum was displaced downwards as an elongated conical sleeve-like structure

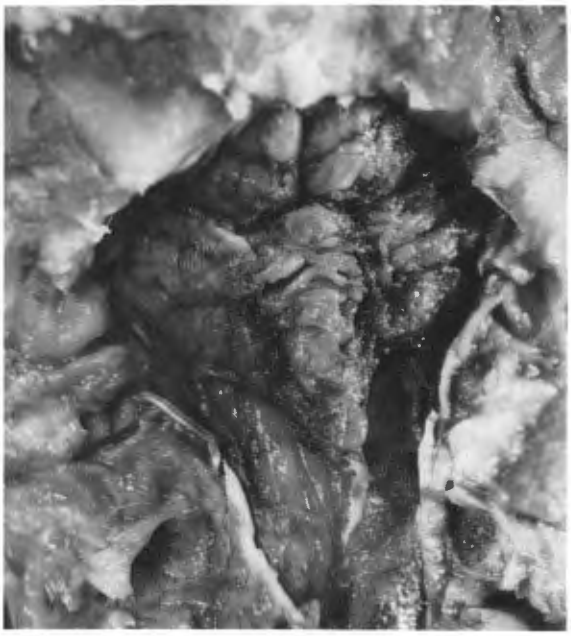


Fig. 3 A cerebellum from Group B showing the inferior semilunar lobules immediately below the posterior margin of the foramen magnum. The more caudal lobules are relatively compressed and lack differentiation.

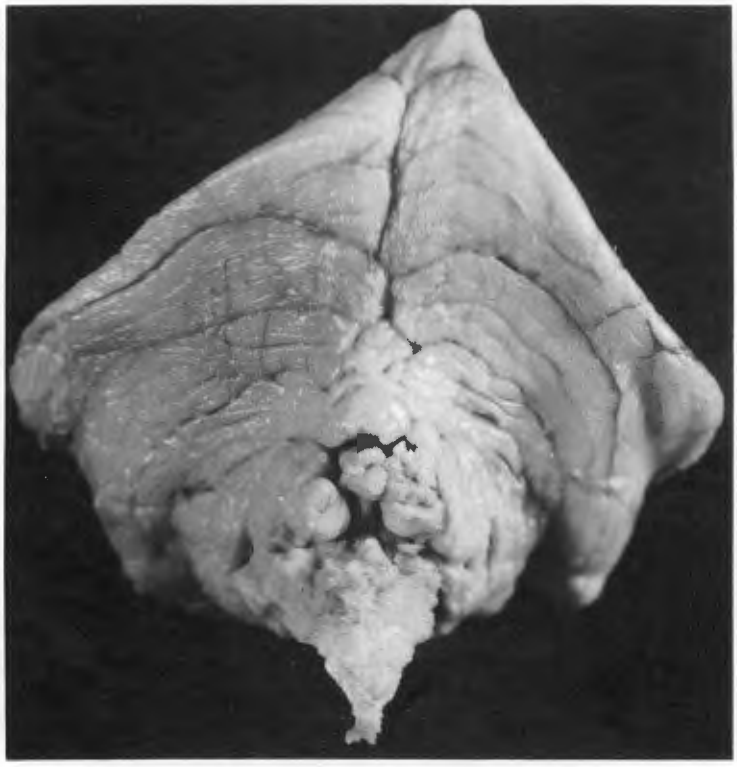


Fig. 4 The posterior aspect of the cerebellum is indented at the level of the biventral lobules which, together with the tonsils, pyramid, uvula, and nodule, form the dislocated cerebellar segment. The horizontal fissure is displaced about half-way down the posterior surface.

investing the posterior and lateral aspects of the pons, medulla and cervical cord, and extending far through the foramen magnum."

In the 10 cases without cerebellar tissue in the upper cervical canal, the cerebellum was invariably found to be abnormal. Such cases could be divided into 2 groups. The first belonged to the younger age group without shunt treatment. They showed compression of cerebellum resulting in a squeezing together of the hemispheres over the posterior surface so that the normal depression of the inferior vermis was obliterated (fig. 6) and, at the same time, the tonsils seemed to approximate the foramen magnum from above. There were 5 cases in this group. The other 5 cases were in older children where decompression treatment of the hydrocephalus had been established for a long time and where an additional finding was loss of tissue in the caudal aspect of the cerebellum, i.e., lobules had apparently been present and had become necrotic.

It was often impossible to identify the individual lobules below the foramen magnum without stripping off the pia-arachnoid and relating it to the lobular pattern of the posterior surface above the foramen magnum. It is likely that identification of individual lobules of the displaced segment of the cerebellum is not possible during limited surgical exploration.

Our results, as well as the results of others, show that the cerebellar defect of both the Chiari types 1 and 2 deformities occur in children with meningomyelocele although type 2 deformities are far more frequent. In half of the cases without herniation the cerebellum closely resembled that found in the type 1 deformity, but with the tonsils approximating but still

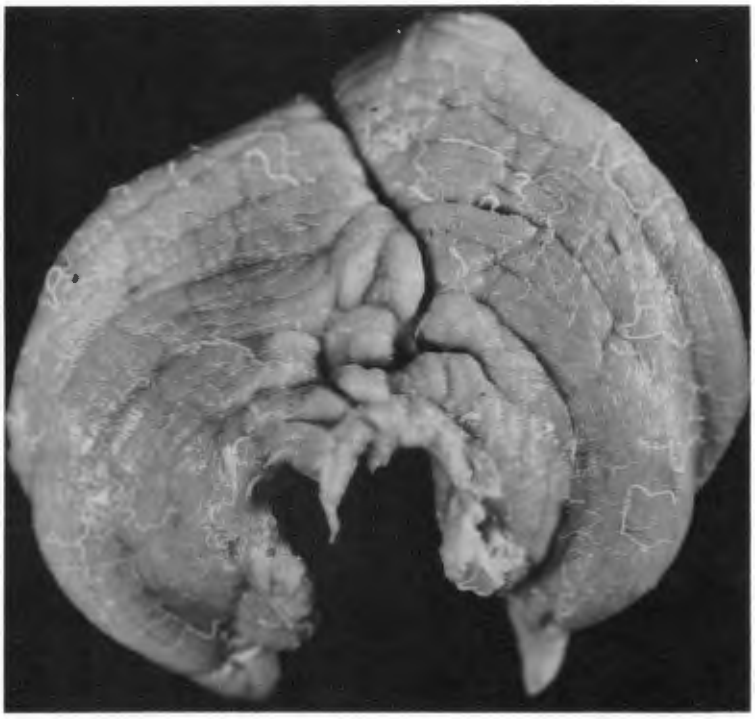


Fig. 5 The tonsils, pyramid, uvula, and nodule are inferior to the foraminal indentation. This is an example of the cerebellar deformity in Group D.

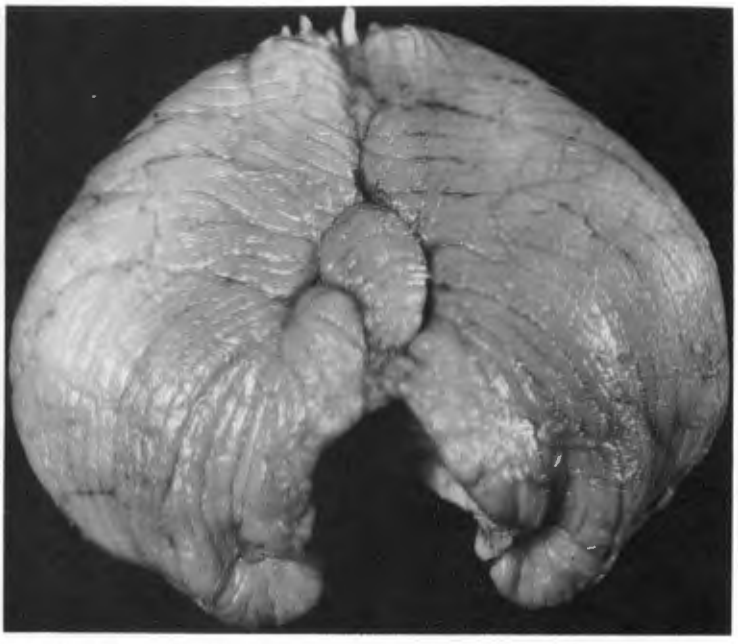


Fig. 6 Cerebellum from a child with meningomyelocele without cerebellar tissue in the upper cervical canal. The organ is poorly differentiated into hemispheres and the inferior vermis is obliterated. The pyramid is more superficial than normal.

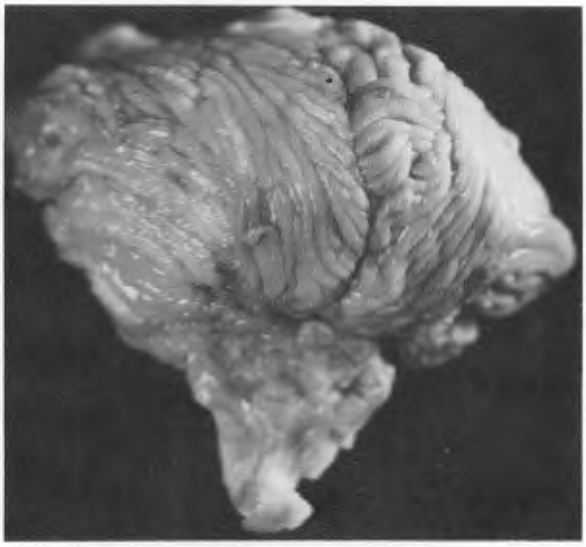


Fig. 7 A severe deformity with part of the superior surface dislocated into the foramen magnum. The tissue in the caudal part of the cerebellum is atrophied and cannot be differentiated into lobules.

above the foramen magnum. In cases showing the classical cerebellar defect of the type 2 deformity there was marked variation in the number of displaced lobules. We interpret this to mean that they are degrees of severity of the same basic defect of the cerebellum.

It is well known that the lobular arrangement of the caudal aspect of the fetal cerebellum changes with gestational age; the nodule forms the most caudal part at an early stage of development. According to Langelaan ('19) the flocculonodular lobe from which the nodule eventually develops is a well-developed structure at the beginning of the 4th month of intrauterine life, but it soon lags behind in development. This "regression" of the nodule seems to be augmented by the caudal movement of the posterior lobules secondary to increased growth in the inferior semilunar lobules so that the tonsils now assume the most caudal aspect of the fetal cerebellum. This transition seems to occur over a relatively short time and it is easy to imagine that a common insult acting at either end of this period could produce 2 different cerebellar deformities, compatible with the 2 types already described.

It therefore seems likely that the cerebellar deformities described have a common pathogenetic mechanism which is variable in terms of time of onset relative to cerebellar development and in its rapidity of action, or possibly both. Since Chiari's original description these hindbrain deformities have been traditionally classified as Chiari type 1 and the "Arnold-Chiari malformation" (Chiari type 2 deformity), but it would seem from the foregoing evidence that these terms have perhaps outlived their usefulness from a viewpoint of developmental pathology of the central nervous system. It would be more accurate and certainly more useful in future descriptions to record the precise lobular composition of the displaced segment of the cerebellum. In addition such graded alterations in the form of the cerebellum indicate a secondary rather than a primary developmental anomaly. It also supports Chiari's original impression that his type 2 deformity is but a severe form of his type 1 deformity.

LITERATURE CITED

Arnold, J. 1894 Myelocyste, Transposition von Gewebskeimen und Sympodia. Beitr. Path. Anat., *16:* 1-28.

Cameron, A. H. 1957 The Arnold Chiari and other neuro-anatomical malformations associated with spina bifida. J. Path. Bact., *73:* 195-211.

Chiari, H. 1891 Uber Veränderungen des Kleinhirns infolge von Hydrocephalie des Grosshirns. Deut. Med. Woch., *17:* 1172-1175.

——— 1896 Uber Veränderungen des Kleinhirns, des Pons und der Medulla Oblongata infolge von Kongenitaler Hydrocephalie des Grosshirns. Denkschrift. Akad. Wiss. Wien, *63:* 71-116.

Cleland, J. 1883 Contribution to the study of spina bifida, encephalocele and anencephalus. J. Anat. Physiol., *17:* 257-292.

Daniel, P. M., and S. G. Strich 1958 Some observations on the congenital deformity of the central nervous system known as the Arnold-Chiari malformation. J. Neuropath. Exp. Neur., *17:* 255-266.

Emery, J. L. 1967 Kinking of the medulla in children with acute cerebral oedema and hydrocephalus and its relationship to the dentate ligaments. J. Neurosurg. Psychiat., *30:* 267-275.

Emery, J. L., and R. G. Lendon 1973 The local cord lesion in neurospinal dysraphism (meningomyelocele). Path., *110:* 83-96.

Emery, J. L., and R. K. Levick 1966 The movement of the brain stem and vessels around the brain stem in children with hydrocephalus and the Arnold-Chiari deformity. Dev. Med. Child Neur., Suppl.) *11:* 49-60.

Emery, J. L., and N. MacKenzie 1973 Medullo-cervical dislocation deformity (Chiari II deformity) related to neurospinal dysraphism (meningomyelocele). Brain, *96:* 155-162.

Emery, J. L., and D. A. C. Reid 1962 Cerebral oedema and spastic hemiplegia following minor burns in young children. Br. J. Surg., *50:* 53-56.

Feigin, I. 1956 Arnold-Chiari malformation with associated malformation of the mid-brain. Neurology, *6:* 22-31.

Gardner, W. J., and R. J. Goodall 1950 The surgical treatment of Arnold-Chiari malformation in adults. An explanation of its mechanism and importance of encephalography in diagnosis. J. Neurosurg., *7:* 199-206.

Ingraham, F.D., and H. W. Scott 1943 Spina bifida and cranium bifidum. The Arnold-Chiari malformation: a study of 20 cases. New Eng. J. Med., *229:* 108-114.

Kryff, E., and R. Jeffs 1966 Skull abnormalities associated with the Arnold-Chiari malformation. Acta Radiol., *5:* 9-24.

Langelaan, J. W. 1919 On the development of the external form of the human cerebellum. Brain, *42:* 130-170.

Lichtenstein, B. W. 1942 Distant neuroanatomic complications of spina bifida (spinal dysraphism), etc. Arch. Neur. Psychiat., *47:* 195-214.

MacKenzie, N., and J. L. Emery 1971 Deformities of the cervical cord in children with neurospinal dysraphism. Dev. Med. Child Neur., (Suppl.), *25:* 58-67.

Margolis, G., and L. Kilham 1969 Experimental virus-induced hydrocephalus. Relation to pathogenesis of the Arnold-Chiari malformation. J. Neurosurg., *31:* 1-9.

Peach, B. 1964 Arnold-Chiari malformation with normal spine. Arch. Neur., *10:* 497-501.

——— 1965 Arnold-Chiari malformation. Anatomical features of 20 cases. Arch. Neur., *12:* 613-621.

Penfield, W., and D. F. Coburn 1938 Arnold-Chiari malformation and its operative treatment. Arch. Neur. Psychiat., *40:* 328-336.

Russell, D. S. 1949 Observations on the pathology of hydrocephalus. Br. Med. Res. Council, Special Report Series No. 265, London.

Russell, D. S., and C. Donald 1935 The mechanism of internal hydrocephalus in spina bifida. Brain, *58:* 203-215.

Schwalbe, E., and M. Gredig 1906 Uber Entwicklungsstörungen des Kleinhirns, Hirnstamms und Halsmarks bei Spina bifida. Beitr. Path. Anat., *40:* 132-194.

Variend, S 1974 The deformity of the lateral cerebellar lobes in children with meningomyelocele. Arch. Dis. Child., *49:* 495-496.

Variend, S., and J. L. Emery 1973 The weight of the cerebellum in children with meningomyelocele. Dev. Med. Child Neur., Suppl. *29,* 77-83.

The Weight of the Cerebellum in Children with Myelomeningocele

S. VARIEND, JOHN L. EMERY

Introduction

That the cerebellum is abnormal in children with myelomeningocele has been known since the original descriptions of the associated hind-brain anomaly by Cleland (1883), Chiari (1891, 1896), Arnold (1894) and Schwalbe and Gredig (1907). The last-named authors were the first to coin the term 'Arnold-Chiari' malformation. In 1891 Chiari described the anomalies of the hind-brain and divided them into four groups:—

Type 1—shows a variable displacement of the cerebellar tonsils into the upper cervical canal, without caudal dislocation of the medulla.

Type 2—shows a variable displacement of the inferior vermis of the cerebellum into the upper cervical canal, with a similar caudal displacement of the lower pons and medulla and an elongated fourth ventricle.

Type 3—shows a downward displacement of the medulla, with herniation of the cerebellum into a high cervical meningocele.

Type 4—shows hypoplasia of the cerebellum.

There is now an extensive literature on the subject. While some recent reports have effectively dispelled old theories such as traction of the cord (Barry *et al.* 1957, Emery and Naik 1968, Naik and Emery 1968), others have formulated new theories such as developmental arrest (Daniel and Strich 1958, Peach 1965). However, the question of morphogenesis remains unsettled.

The cerebellum has rarely been considered on its own in previous studies, and such an approach could well add information which has eluded a more general approach to the subject. This paper forms the first part of a study of the cerebellum in children with myelomeningocele and is concerned with the weight of the cerebellum and its relationship to the cerebral hemispheres.

Material and Methods

The material came from necropsies carried out by the Department of Pathology at the Sheffield Children's Hospital, and consisted of 60 cerebellums from apparently normal brains and 100 cerebellums from children with myelomeningocele. Of the latter, 19 had received decompression treatment for hydrocephalus with a Holter valve. The brains for the normal series came almost entirely from 'cot deaths' and were handled as described in a previous paper which reported the weights of cerebral hemispheres in children with myelomeningocele (Emery 1964).

The hind-brain structures were removed after fixation within the skull and were then handled in the same manner as the normal brains, care being taken not to damage the pons and fourth ventricle. The cerebellum was weighed after being cleanly divided at the cerebellar peduncle and along the superior medullary vellum.

Department of Pathology, The Children's Hospital, Western Bank, Sheffield S10 2TH.

Most of the children had been well nourished. The mean gestational age at birth of the children with myelomeningocele was 40 weeks; for the apparently normal children it was 37 weeks.

Detailed descriptions of other deformities in the spinal cords of the cases with myelomeningocele have already been reported (Emery and Levick 1966, MacKenzie and Emery 1971, Emery and Mackenzie 1973, Emery and Lendon 1973).

Results

The weights of the cerebellar hemispheres of 63 children with myelomeningocele who died before the age of one month are shown in Fig. 1, superimposed upon the total range of cerebellar weights of 15 apparently normal children of the same age. There is an obvious reduction in weight of the cerebellar hemispheres in the children with myelomeningocele as compared with the apparently normal controls.

The equivalent data for the children over one month of age (with an age-range up to six years) are shown in Fig. 2. This shows the mean line for the weights of the normal cerebellar hemispheres and also distinguishes between the children treated with a Holter valve and those who were not. It would appear that the diminution in the weight of the cerebellar hemispheres seen in the newborn period persists throughout the age-groups surveyed.

Fig. 3 shows the relationship between the weights of the cerebral hemispheres and the cerebellar hemispheres over the whole age-range. It is obvious that the ratio of cerebral : cerebellar hemisphere weights in the cases with myelomeningocele remains above the mean of the normal series. This appears to be a constant finding throughout the whole age-range studied, and to be unaffected by treatment in the older children.

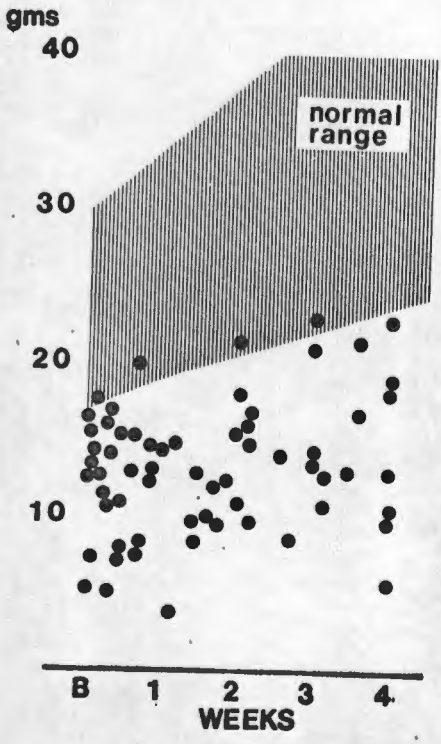


Fig. 1. The weights of the cerebellum in children with myelomeningocele dying within four weeks of birth, compared with the range of weights from overtly normal children.

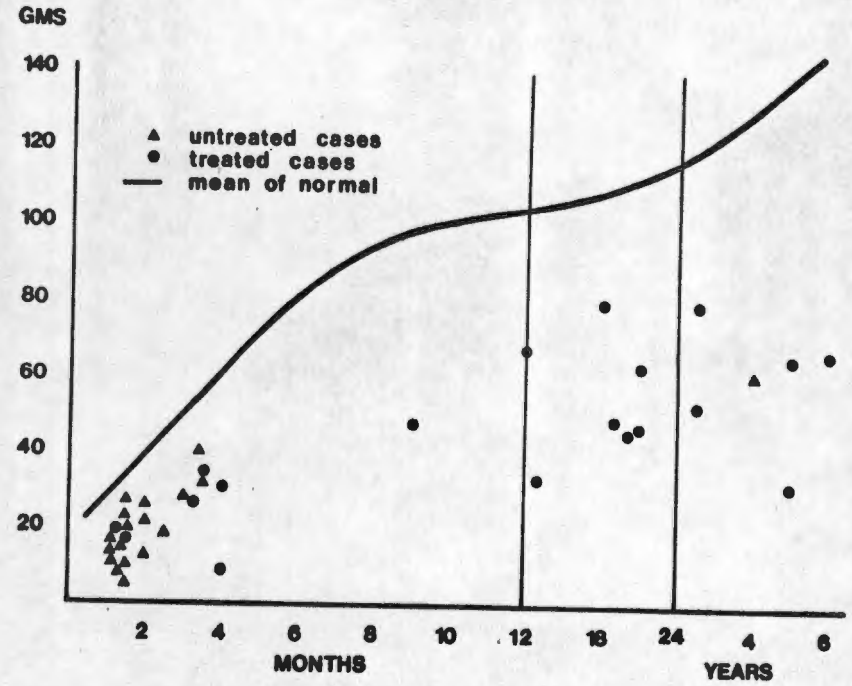


Fig. 2. The cerebellar weights of children with myelomeningocele dying after the age of one month compared with the normal mean.

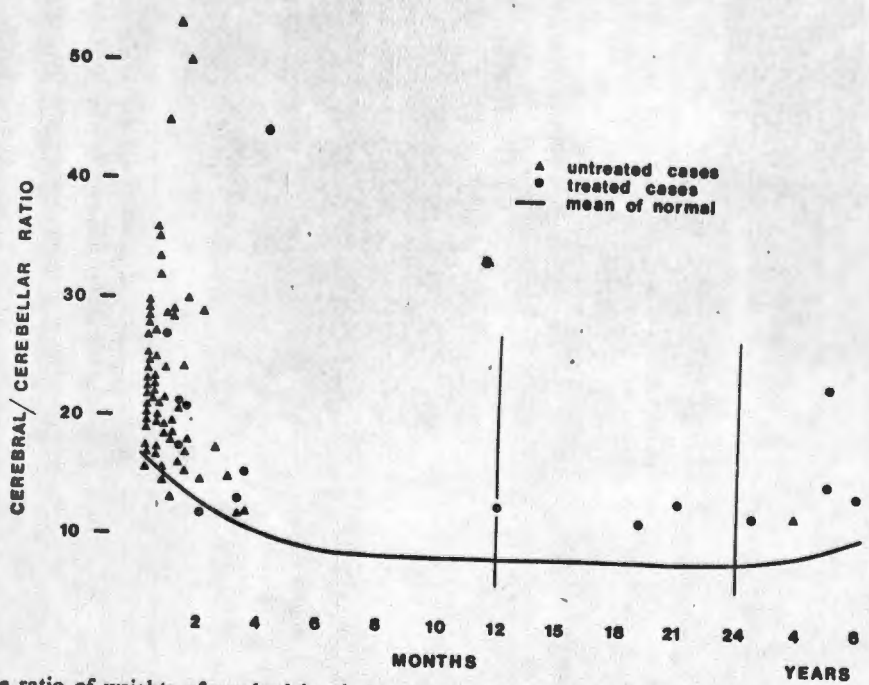


Fig. 3. The ratio of weights of cerebral hemispheres to cerebellum in children with myelomeningocele, compared with the normal mean.

Discussion

The disparity between the rates of growth of the cerebrum and the cerebellum is well known. The cerebellum grows more rapidly during the first two years after birth; the greater proportion of growth occurs during the first 12 months, at the end of which time it has reached almost two-thirds of its adult weight. After the end of the first year the growth is less rapid, and by the second year the weight of the cerebellum is about four-fifths the adult weight (Ellis 1920).

In contrast, the cerebrum increases in weight more slowly; by the second year the wet weight has increased about three-fold, compared with a seven-fold increase in the wet weight of the cerebellum (Winick *et al.* 1970). It is not so well appreciated that there is marked variation in the absolute cerebellar weights at different ages, 30g or more during the first three months after birth (Pfister, cited by Ellis 1920).

The weight of the cerebellum in children has been established by some other workers. The results of the study by Blinkov and Glezer (1968) are not very satisfactory, as they were derived mainly from hospital material at the end of the last century. Ellis (1920) calculated values for the weights of the cerebrum and cerebellum from a smooth curve, based on the results of three different authors and involving a large number of children.

We have calculated an average of the cerebellar weights for males and females which Ellis (1920) presented in his table. For this reason we have also calculated our values for cerebral and cerebellar weights from a smooth curve. The results of our normal series are compared with those of Ellis in Table I. The range of cerebellar weights in our series is somewhat higher than that of Ellis, which could reasonably be explained by the different populations studied. As an essentially identical procedure was used with our normal and abnormal brains, we have used our own material for local comparison rather than incorporating outside data.

The weights of the cerebellum of the deformed children in our series are uniformly diminished, not a single child having a cerebellar hemisphere weight reaching the mean of normal in the immediate postnatal period. This finding is markedly in contrast with that in the same children when the weights of cerebral hemispheres are compared with the normal range. It has been pointed out by Potter (1961), and confirmed by Emery (1964), that the hydrocephalic cerebral hemisphere weight at birth is higher than the mean weight in normal children of the same age. In untreated cases of hydrocephalus dying before the age of six

TABLE I

Cerebellar weights in present series compared with Ellis (1920)

	Ellis (1920)			*Variend and Emery (1973)*		
Age	*Cerebral weight (g)*	*Cerebellar weight (g)*	*Cerebral/ cerebellar weight ratio*	*Cerebral weight (g)*	*Cerebellar weight (g)*	*Cerebral/ cerebellar weight ratio*
Newborn	367	21	17·5	340	20	17·0
2 months	471	34	13·9	520	40	13·0
4 „	565	48	11·8	620	62	10·0
6 „	662	60	11·0	738	82	9·0
9 „	765	76	10·0	833	98	8·5
12 „	827	86	9·6	852	104	8·2
18 „	922	98	9·4	935	110	8·5
24 „	1000	106	9·4	1018	117	8·7
8–14 years	1231	129	9·6	1543 (6 yrs)	147	10·5

months, there appears to be a suppression of growth of the cerebral hemispheres, as determined by weight. In the untreated cases who survive for more than 18 months, the hemisphere weight approaches the normal range.

The weight of the cerebellum in the older children in our study is uniformly diminished in comparison with the normal range; even in children over the age of three years the weight does not approach the normal range. It would appear, therefore, that in children with myelomeningocele there is a consistently different weight pattern of the cerebellum compared with that of the cerebral hemispheres in the postnatal period. When the ratio of the weights of the cerebral hemispheres to the cerebellum is considered (see Fig. 3), it is seen that the greatest disparity lies in the immediate postnatal period, and that after about six months of age the ratio stabilises at a level just above the mean of normal. No difference was observed between the ratios of children who had been treated by Holter valve decompression and those who had not.

It is only possible to interpret these data in a very general sense, as many of the children in this study died from different causes—pulmonary or renal crises or shunt blockage. The reason for the diminution in weight of the cerebellum has not yet been elucidated. Russell and Donald (1935) and Schwalbe and Gredig (1907) have referred to the cerebellum as being hypoplastic, but whether this is due to necrosis of particular lobes that have herniated out of the posterior fossa of the skull, or to general growth arrest, or to vascular and ischaemic changes within the substance of the cerebellum will be the subject of further study.

SUMMARY

The cerebellums were removed and weighed from 100 children who had died with myelomeningocele and from 60 apparently normal control children who had died from other causes. 19 cases with myelomeningocele had received Holter valve decompression treatment for their hydrocephalus. The weight of the cerebellum in the children with myelomeningocele was uniformly diminished in the immediate postnatal period in comparison with the control group. This was in contrast with the weight of the cerebral hemispheres, which have been shown to be increased above the normal range at the time of birth.

Decompression treatment of hydrocephalus, even over a long period of time, had little effect in increasing the weight of the cerebellum to the normal range, which again differs from the findings for the cerebrum. The ratio of the weights of the cerebral and cerebellar hemispheres was above the normal ratio and this relationship is maintained despite prolonged treatment of the hydrocephalus.

RÉSUMÉ

Poids du cervelet chez des enfants présentant un myéloméningocèle

Les cervelets de 100 enfants morts avec un myéloméningocèle et de 60 enfants apparemment normaux morts pour une autre raison ont été prélevés et pesés. Parmi les enfants atteints de myéloméningocèle, 19 avaient bénéficié d'un traitement décompressif pour hydrocéphalie.

Le poids du cervelet chez les nourrissons avec myéloméningocèle a été trouvé invariablement plus bas que le poids moyen chez les enfants normaux de même âge. Ceci est en opposition avec les données concernant le cerveau, qui a été montré pesant davantage chez les enfants atteints de myéloméningocèle que chez les enfants normaux au moment de la naissance.

Le traitement décompressif de l'hydrocéphalie, même sur de très longues périodes, agit

peu pour accroitre le poids du cervelet chez les enfants avec myéloméningocèle jusqu'au poids normal, bien qu'il y ait des indications que le poids du cerveau chez ces enfants plus âgés tende à se situer dans la moyenne. Parmi les sujets atteints, le rapport des poids des hémisphères cérébraux et cérébelleux est au-dessus de la moyenne que l'enfant ait ou non reçu un traitement prolongé pour hydrocéphalie.

ZUSAMMENFASSUNG

Das Kleinhirngewicht bei Kindern mit Myelomeningocele

Die Kleinhirne von 100 Kindern, die mit Myelomeningocele gestorben waren, und von 60 Kindern, die an anderen Ursachen verstorben waren, wurden herausgenommen und gewogen. 19 der Kinder mit Myelomeningocele hatten eine druckentlastende Behandlung wegen Hydrocephalus erhalten.

Das Gewicht des Kleinhirns bei den Neugeborenen mit Myelomeningocele war konstant niedriger als das Durchschnittsgewicht bei gleichaltrigen normalen Kindern. Das steht im Gegensatz zu Untersuchungen über das Großhirn, die zeigten, daß das Gewicht bei Kindern mit Myelomeningocele höher liegt als bei normalen Kindern zum Zeitpunkt der Geburt. Druckentlastende Behandlung des Hydrocephalus sogar über längere Zeit ließ das Gewicht des Kleinhirns bei Kindern mit Myelomeningocele nur geringfügig bis innerhalb des Normalbereichs zunehmen, obwohl es dafür Beweise gibt, daß das Großhirngewicht bei diesen älteren Kindern wieder die Tendenz zeigt im Normbereich zu sein. Unter den betroffenen Patienten war der Großhirn/Kleinhirn-Gewichtsquotient übernormal, gleich ob das Kind eine längere Hydrocephalusbehandlung bekommen hatte oder nicht.

RESUMEN

El peso del cerebelo en niños con mielomeningocele

Se extrajo y pesó el cerebelo de 100 niños que habían fallecido con mielomeningocele y de 60 niños aparentemente normales que habían fallecido por otras causas. De los niños con mielomeningocele, 19 habían recibido un tratamiento descompresivo por hidrocefalia.

El peso del cerebelo en los niños recién nacidos con mielomeningocele era invariablemente más bajo que el peso medio de niños normales de la misma edad. Esto está en contraste con los hallazgos respecto al cerebro, que se ha visto que pesaba más en niños con mielomeningocelo que en niños normales en el momento del parto.

El tratamiento descompresivo de la hidrocefalia, incluso durante largos períodos, hizo poco para aumentar el peso del cerebelo en los niños con mielomeningocele hasta alcanzar el peso normal, aunque hay evidencia de que el peso del cerebro en estos niños mayores igualmente tiende a estar dentro del margen de lo normal. Entre los pacientes afectos, la relación entre el peso de los hemisferios cerebrales y cerebelosos estaba por encima de lo normal, tanto si el niño había recibido un tratamiento prolongado por hidrocefalia como si no.

REFERENCES

Arnold, J. (1894) 'Myelocyste, Transpositionen von Gewebskeimen und Sympodie.' *Beiträge für pathologische Anatomie*, **16**, 1.

Barry, A., Patten, B. M., Stewart, B. H. (1957) 'Possible factors in the development of the Arnold-Chiari malformation.' *Journal of Neurosurgery*, **14**, 285.

Blinkov, S. M., Glezer, I. I. (1968) *The Human Brain in Figures and Tables—A Quantitative Handbook*. New York: Basic Books. p. 152.

Chiari, H. (1891) 'Über Veränderungen des Kleinhirns infolge von Hydrocephalie des Grosshirns.' *Deutsche Medizinische Wochenschrift*, **17**, 1172.

— (1896) 'Über Veränderungen des Kleinhirns, des Pons und der Medulla Oblongata infolge von kongenitaler Hydrocephalie des Grosshirns.' *Denkschriften Akademie Wissenschaften, Wien*, **63**, 71.

Cleland, J. (1883) 'Contribution to the study of spina bifida, encephalocele and anencephalus.' *Journal of Anatomy and Physiology*, **17**, 257.
Daniel, P. M., Strich, S. G. (1958) 'Some observations on the congenital deformity of the central nervous system known as the Arnold-Chiari malformation.' *Journal of Neuropathology and Experimental Neurology*, **17**, 255.
Ellis, R. S. (1920) 'Norms for some structural changes in the human cerebellum from birth to old age.' *Journal of Comparative Neurology and Psychology*, **32**, 1.
Emery, J. L. (1964) 'Effects of continual decompression using Holter valve on weights of cerebral hemispheres in children with hydrocephalus and spina bifida cystica.' *Archives of Disease in Childhood*, **39**, 379.
— Levick, R. K. (1966) 'The movement of the brain stem and vessels around the brain stem in children with hydrocephalus and the Arnold-Chiari deformity.' *Developmental Medicine and Child Neurology*, Suppl. 11, 49.
— Lendon, R. G. (1973) 'The local cord lesion in neurospinal dysraphism (meningomyelocele).' *Journal of Pathology* (*in press*).
— MacKenzie, N. (1973) 'Medullo-cervical dislocation deformity (Chiari II deformity) related to neurospinal dysraphism (meningomyelocele).' *Brain*, **96**, 155.
— Naik, D. (1968) 'Spinal cord segment lengths in children with meningomyelocele and the "Cleland-Arnold-Chiari" deformity.' *British Journal of Radiology*, **41**, 287.
MacKenzie, N., Emery, J. L. (1971) 'Deformities of the cervical cord in children with neurospinal dysraphism.' *Developmental Medicine and Child Neurology*, Suppl. 25, 58.
Naik, D. R., Emery, J. L. (1968) 'The position of the spinal cord segments related to the vertebral bodies in children with meningomyelocele and hydrocephalus.' *Developmental Medicine and Child Neurology*, Suppl. 16, 62.
Peach, B. (1965) 'The Arnold-Chiari malformation.' *Archives of Neurology*, **12**, 527.
Potter, E. L. (1961) *Pathology of the Fetus and Infant*, *2nd edn.* Chicago: Year-Book Medical Publishers. p. 430.
Russell, D. S., Donald, C. (1935) 'The mechanism of internal hydrocephalus in spina bifida.' *Brain*, **58**, 203.
Schwalbe, E., Gredig, M. (1907) 'Uber Entwicklungsstörungen des Kleinhirns, Hirnstamms und Halsmarks bei Spina bifida.' *Beiträge für pathologische Anatomie*, **40**, 132.
Winick, M., Rosso, P., Waterlow, J. (1970) 'Cellular growth of cerebrum, cerebellum and brain stem in normal and marasmic children.' *Experimental Neurology*, **26**, 393.

Reprinted from Supplement No. 32 "Hydrocephalus and Spina Bifida" pp. 99–106

The Pathology of the Central Lobes of the Cerebellum in Children with Myelomeningocele

S. VARIEND JOHN L. EMERY

Introduction

Chiari (1895), in his description of the types of deformity of the cerebellum, drew the important distinction between the deformities seen in adults (distortion and dislocation of the tonsils), and those in infants associated with myelomeningoceles (distortion and herniation of the central lobes). The latter is related to the fact that the central lobes of the cerebellum develop before the lateral lobes and it is likely that the movement of the central lobes forms the key to the understanding of most of the cerebellar abnormalities associated with myelomeningocele.

We thought it worthwhile to make a detailed study of the changes that occur in the central lobes of the cerebellum, and this report concerns a detailed study of the lesions found in a series of 100 children with myelomeningocele.

Material and Method

The material comprised 100 cerebellums from children with myelomeningocele, being a random series coming to necropsy at the Children's Hospital, Sheffield. Detailed descriptions of other deformities of the spinal cord and of the medulla from many of these same cases have already been reported (Emery and Levick 1966, Mackenzie and Emery 1971, Emery and Lendon 1973), as have the weights of these cerebellums as compared with normals (Variend and Emery 1973). The ages of the children varied from birth to six years. 24 of the children had received decompression treatment for the hydrocephalus by means of a Holter valve for periods longer than two weeks. The causes of death varied from renal and pulmonary complications to ventriculitis and shunt blockage.

After fixation of the brain within the skull, the upper cervical canal was opened and the distance between the foramen magnum and the lowest part of the cerebellum was measured with calipers. The skull was opened from above and, after removal of the cerebral hemispheres at the level of the cerebral peduncles, the hind-brain structures were removed and the cerebellum was dissected free. The lobes were identified and mapped out in relation to the foramen magnum, and the cerebellum was separated from the pons. Each cerebellum was then bisected in the mid-sagittal plane. The midline lobes were photographed and identified and a gross assessment was made of compression, necrosis and loss of tissue in different lobes. A midline sagittal block was taken from the right half of each specimen for histology and microscopy. The midline photographs and histology of the midline sections were collated and a survey was made of the state of each of the six main lobes of the cerebellum, *i.e.* the central lobe, the culmen, the declive, the pyramid, the uvula and the nodule.

The lesions found were classified in the following way. The presence of haemorrhagic

The Department of Pathology, Children's Hospital, Sheffield S10 2TH.

necrosis and recent liquefaction of brain tissue with phagocytosis was termed 'acute necrosis' (both recent and old haemorrhages were included under this heading). Cases in which the brain tissue was not grossly disorganised but where there was loss of cellular elements and apparent atrophy of tissues, we termed 'long-standing necrosis'. We noted a variety of abnormal structural formations in tissues particularly related to the nodule, and in the central areas related to the inferior velum. These areas have been described by others as 'heterotopic folia' (Peach 1965) and 'internal microgyria' (Crome 1952). The essential features of these abnormalities seemed to be an abnormal arrangement of the tissues in their local growth, therefore we used the more conventional term of the developmental pathologist and classified them as dysplasias.

Calcification and old haemorrhage were usually confirmed by special staining techniques. An assessment was made of the proportion of Purkinje cells that had been lost; this was based on a scan of the Purkinje cell layer, on our knowledge of the normal variability in these parts, and on the values of the most normal part of the cerebellum under study. In most cerebellums there were small areas of relatively normal cerebellar cortex, if not in the central lobes then in sections from other parts of the cerebellum.

Results

The length of the cerebellar component in the upper cervical canal ranged from 0mm to 68mm. There were 11 children in whom the cerebellum showed no tissue below the foramen magnum. Six of these had received decompression treatment with a Holter valve, and they comprised 25 per cent of the shunt-treated group. The remaining five children comprised only 6 per cent of the untreated group.

When the weight of the cerebellum was related to the length of the dislocated segment, an inverse relationship was apparent (Fig. 1). There was a diminution in the length of the tail corresponding to children with larger cerebellums and also in association with increased survival time.

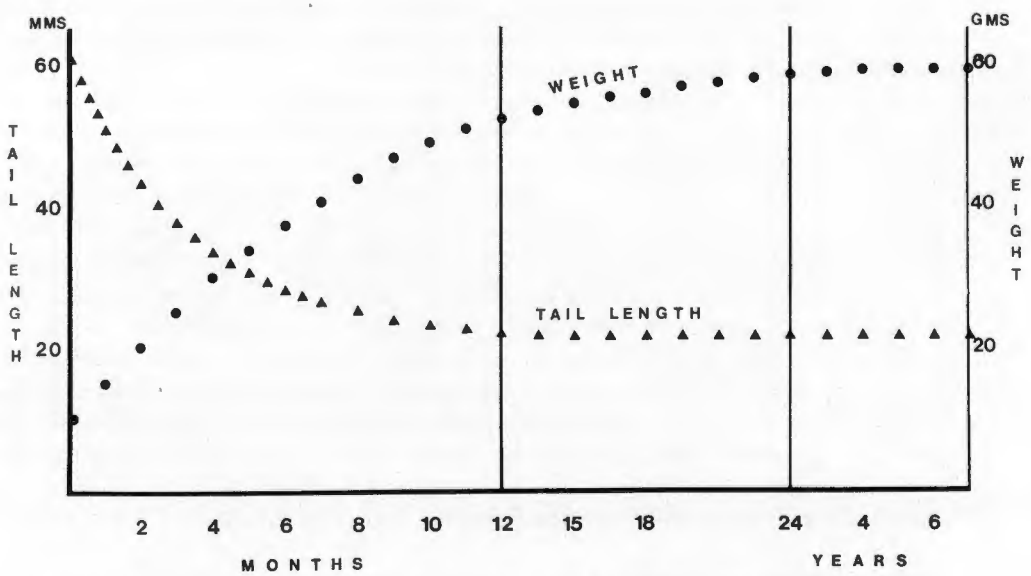


Fig. 1. Cerebellar 'tail' length, cerebellar weight and age in children with myelomeningocele.

Acute Necrosis

Of the 100 specimens, 33 showed histological and gross evidence of acute necrosis (Fig. 2), mainly confined to the upper central lobes. Acute necrosis was associated with two distinct clinical groups. The first group of 26 children were all under the age of one month, 14 being between the age of birth and one week, six between one and two weeks, and six between two weeks and one month. The second group were six older children with a recently introduced Holter valve. The interval between the introduction of the shunt and death varied from one day to one week. There was no overlap in age distribution between the two groups. The remaining child, who showed both acute and chronic necrosis, had been treated with a valve for many months; the course had been complicated by recurrent blockage and frequent revisions, one of which precipitated the terminal state.

Old Necrosis

Histological evidence of long-standing necrosis was found in all of the 100 specimens examined. 13 cases showed diffuse, chronic necrosis which affected all of the lobes. In general, the distribution of chronic necrosis was chiefly within the pyramid, uvula and nodule (Fig. 3). The principal feature of chronic necrosis was the loss of cellularity of the internal granular layer and Purkinje cell layer. These changes sometimes affected very local areas of the cortex and were more liable to affect the ridges of the folia than the deeper interstices. Individual folia were frequently affected, particularly in the pyramid, and probably corresponded to areas where the cerebellum had apparently been in direct contact with the posterior margin of the foramen magnum or the floor of the posterior fossa. These lesions were similar to those described by Cameron (1957). In a few cases the nodule seemed to have necrosed almost completely, there being merely small areas of ependyma and central nervous tissue, with ghost-like areas of depopulated cerebellar cortex. Small fragments of folia indicated the tissue origin.

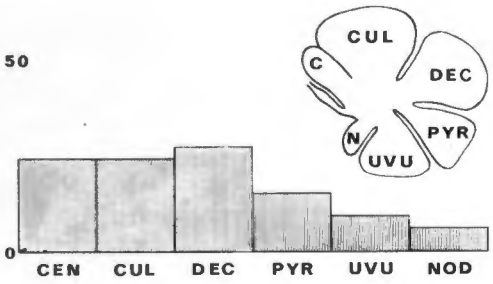
Purkinje Cell Loss

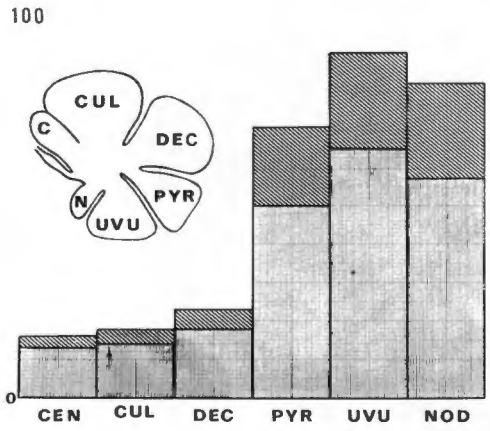
This was only considered to be significant when less than half the normal population of Purkinje cells appeared to be present; this occurred in some part of the section in 83 of the 100 cases studied.

The distribution of Purkinje cell loss is shown in Figure 4 and principally affected the

Fig. 2. (*below*) Distribution of acute necrosis in the central lobes of the cerebellum.

Fig. 3. (*right*) Distribution of chronic necrosis in the central lobes of the cerebellum.





same lobes as did chronic necrosis. However, Purkinje cell loss and chronic necrosis do not necessarily go hand in hand and there were a number of cerebellums in which there had been extensive Purkinje cell loss with little gross cortical atrophy.

Dysplasias

Dysplastic changes, the most difficult to define, occurred in 70 of the 100 cases (Fig. 5). About a quarter of the most grossly deformed cerebellums contained a central mass of dysplastic tissue lying just above the roof of the fourth ventricle and near the roots of the nodule and uvula. This area of dysplastic tissue usually appeared to be caudal or anterior to the central group of ganglion cells which were usually present in normal sections from the same area.

The most characteristic dysplastic lesions consisted of irregular masses of Purkinje cells and what appeared to be a mixture of internal granular cells and strands and foci of molecular layer tissue. These areas very rarely showed calcification or evidence of old haemorrhage and necrosis. We prefer to use the term 'dysplasia' rather than 'heterotopic folia', as this tissue is abnormal and there is no true folium formation.

Cystic Degeneration

Slit-like cavities occurred in eight midline sections. These were not lined with ependyma and occasionally contained groups of lipid-laden cells.

These cavities all occurred within the folia and showed branching into others. The appearance was of a degeneration of the centres of the white cores of the folia running into the hilum of the cerebellum, but not necessarily communicating with the fourth ventricle. Some of these cysts contained many compound granular cells but none were filled with blood. We did not examine serial sections to trace the ramifications of these lesions, but from our midline study we were not impressed by their linking with the fourth ventricle, nor with evidence of any associated dilatation of the fourth ventricle. The lining of the roof of the fourth ventricle in most of these children appeared to be very well organised with cuboid and even columnar ependyma. However, this did not apply to six children who showed gross dilatation of the fourth ventricle (this finding will be discussed as part of a separate study).

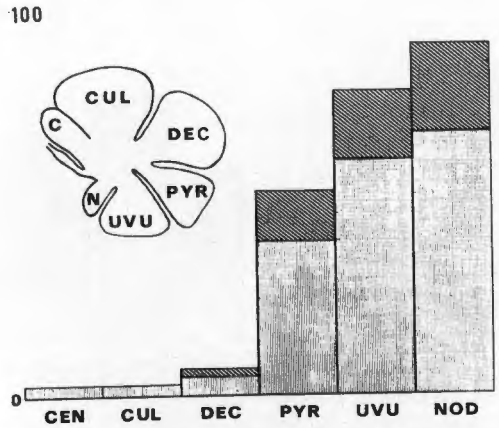


Fig. 4. Distribution of marked Purkinje-cell loss in the central lobes of the cerebellum.

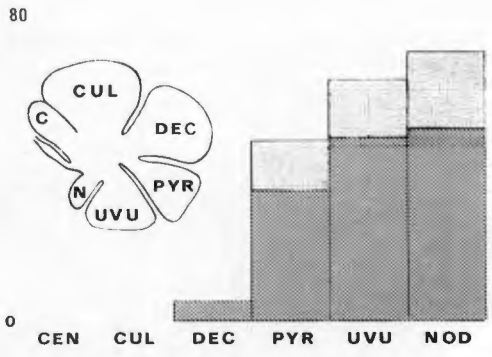


Fig. 5. Distribution of dysplastic change in the central lobes of the cerebellum.

Discussion

Our findings reveal a varying pattern of necrosis, dysplasia and acute degeneration. Most of the lesions we describe have already been noted by previous observers, but the purpose of this study of a large number of deformed cerebellums was to see if the lesions formed any distinct pattern which would help our understanding of the underlying condition.

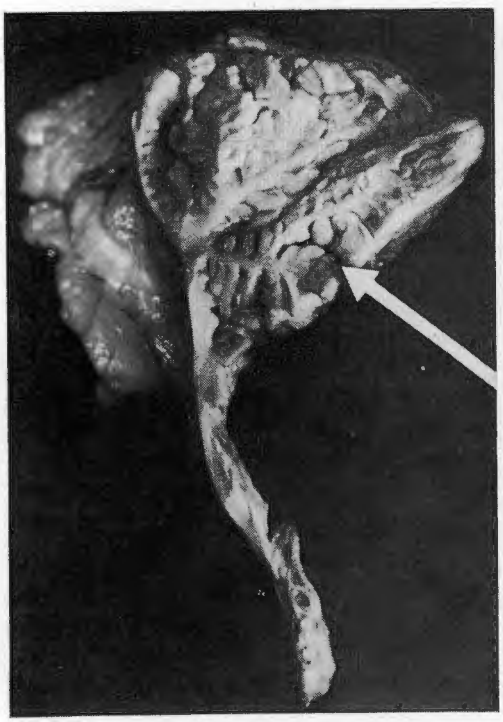
The most frequent abnormality was necrosis, chiefly involving the caudal lobes. As will be seen from Figure 3, the extent of the necrosis was directly related to the position of the lobe. Within the 100 organs examined, there was none with a remaining normal nodule, whereas in most cases the lingula and central lobes were probably within normal limits for the age of the child. This finding suggests that the deformities within the cerebellum were probably secondary and were not likely to be due to any primary general cerebellar condition. The areas of chronic necrosis, while affecting the caudal lobes, were not confined to the lobes that were dislocated at the time of death.

When we measured the extent of the cerebellar herniation into the neck (see Fig. 1) we found a diminution with age. Interpretation of these data is not easy, as we are dealing with a necropsy series and it could quite justifiably be argued that the longer-surviving children were those less deformed at birth. This is undoubtedly a factor, but we have further evidence within the skull which indicates that the growth of the cerebellum continues in children who have either undergone arrest or have been stabilised with Holter valves. The direction of growth alters from a caudal to a cranial direction: this can be seen clearly in the way in which the cerebellum in older children very frequently herniates upwards through the tentorium (Emery 1965). The occurrence of old focal necrosis in the pyramid suggests that at an earlier stage this part of the cerebellum was in very firm contact with the foramen magnum and that this had later been relieved. Also, in a number of children, we have direct evidence that there had been very extensive necrosis of the nodule and, in some instances, complete disappearance of this lobe, which seems to be independent of shunt treatment. This is illustrated in Figures 6 and 7.

We believe, therefore, that there is a reduction in the cerebellar dislocation following birth. Three factors are involved: (1) the severity of the condition related to mortality; (2) alteration in the direction of cerebellar growth; and (3) necrosis and atrophy of the herniated tissue.

Apart from simple necrosis, the next most frequent observation was areas of dysplasia, particularly affecting the tissues just deep to the surface of the fourth ventricle and near the roots of the nodule, pyramid and uvula. These lesions have been discussed by Lichtenstein (1942) and Cameron (1957), and our observations confirm the suggestion by Cameron that they are probably not primary developmental disorders but are due to interference with cortical development of the lobes of the cerebellum which are growing while being squashed into the vertebral canal. These areas of dysplasia are almost invariably associated with chronic necrosis of the overlying lobular folia.

As well as cortical atrophy and necrosis, there are areas in which the white matter of the folia have undergone degeneration, forming branchlike cavities within the white matter of the folia and, on occasion, forming fairly definite irregular cysts. In his study of 26 full cerebellums, Cameron (1957) found such lesions in 54 per cent of his cases. We found such lesions in 8 per cent of our single sagittal sections of the cerebellum. In no instance was this cystic change associated with normal overlying cerebellar cortex. Cameron considered that these cavities communicate with the fourth ventricle. Although we have not done serial sections to follow the extent of these lesions, our impression is that they are frequently widely



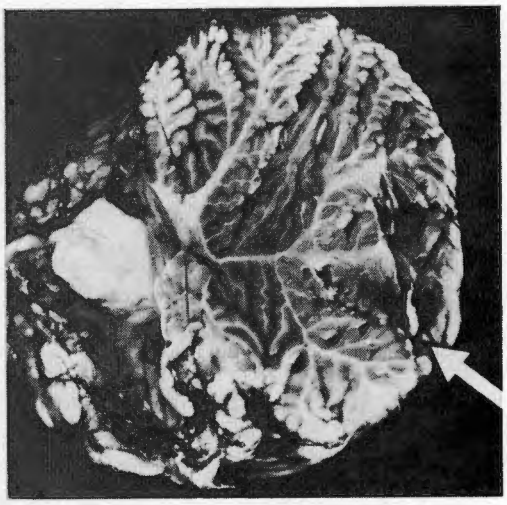


Fig. 7. Mid-sagittal view of cerebellum from a child with myelomeningocele, at age 18 months. Decompression treatment with Holter valve was performed at three months. Arrow shows the prepyramidal fissure. Although the pyramid appears to be comparatively normal, the nodule and uvula show marked atrophy and tissue loss.

Fig. 6. Mid-sagittal view of cerebellum from child with myelomeningocele, soon after birth. Arrow shows the prepyramidal fissure. The nodule and uvula are necrosed and elongated. The pyramid appears to be comparatively normal.

separated from a diminished fourth ventricular cavity and that they require further study. While frequently there is evidence of old haemorrhage near some of these cysts, their contents rarely suggest that they are caused by haemorrhage. They usually contain, if anything, small groups of compound granular cells only and are not lined by ependyma.

The pattern of acute necrosis in the cerebellum does not coincide with that of chronic necrosis. Acute necrosis was found in two groups of children, one consisting of children under the age of one month and the other consisting of children who had suffered alteration in pressure on the cerebellum following a very recent operation for decompression.

The drop in cellularity in the cerebellar cortex is the subject of a further study, but the more gross Purkinje-cell loss forms a pattern that is undoubtedly related to the chronic cortical necrosis. In addition, however, there is probably an over-all reduction in Purkinje cells related to the same factors—such as chronic hypoxia or congenital heart disease—which produce a similar loss in other children. The relatively low Purkinje cell loss in the most normal lobes of the cerebellum in our children suggests that the original number and distribution of these cells was probably genetically normal. The general counts of the cells in the most sheltered lobes of the cerebellum (the lingula, central lobe and culmen) are such that we would not normally expect them to be associated with any clinically observable cerebellar lesions.

The results of this study confirm our impression that the areas of necrosis and dysplasia found in these cerebellums are secondary and are due to intra-uterine pressure and dislocation, with necrosis of the most caudal lobes of the cerebellum. Further, in surviving children,

parts of the cerebellum which have not undergone necrosis appear to be capable of normal growth. Our other observations suggest that further damage to the cerebellum is liable to occur around the time of birth, and in association with periods of blocked shunt and acute decompression procedures.

SUMMARY

A study has been carried out of 100 cerebellums from children with myelomeningocele. Deformities were present in all to varying degrees. There was necrosis and atrophy of the most caudal lobes of the cerebellum, particularly the nodule, and there was evidence that the nodule could completely disappear in some cases.

Following birth and treatment of surviving children, the pressure on the caudal lobes diminishes and the surviving and residual parts of the cerebellum, *i.e.* the more cranial lobes, appear to develop in a normal way. Dysplastic areas in the cerebellum seem to be secondary to attempts at growth under abnormal pressures. Areas of acute necrosis are related to very recent alterations in position and pressure within the fourth ventricle, either related to birth or to recent bouts of intracranial hypertension or possibly hypotension.

The findings confirm the impression that the deformities usually described as Cleland or Arnold-Chiari deformity are due to secondary states and are not a primary condition.

RÉSUMÉ

Pathologie des lobes centraux du cervelet chez les enfants atteints de myéloméningocèles

Une étude a été faite de cent cervelets provenant d'enfants porteurs de myéloméningocèles. Des altérations étaient présentes dans tous les cas et à des degrés divers; ont été notées en particulier une nécrose et une atrophie de la plupart des lobes caudaus du cervelet, notamment le nodule; dans quelques cas, le nodule avait complètement disparu.

Chez les enfants qui survivent à la naissance et au traitement, la pression sur les lobes caudaux diminue et les portions subsistantes du cervelet, notamment les lobes les plus craniaux se développent normalement. Des zones dysplasiques dans le cervelet semblent secondaires aux effets de la croissance sous pression anormale. Les zones de nécrose aigue sont reliées à des modifications très récentes de position et de pression dans le quatrième ventricule, causées par la naissance ou par des accès récents d'hypertension ou d'hypotension intracranienne.

Ces découvertes confirment l'impression que les déformations décrites usuellement comme syndromes de Cleland ou d'Arnold-Chiari sont liées à des conditions secondaires et non primaires.

ZUSAMMENFASSUNG

Die Pathologie des Kleinhirnmittellappens bei Kindern mit Meningomyelocele

100 Kleinhirne von Kindern mit Meningomyelocele wurden untersucht. Veränderungen unterschiedlichen Ausmaßes waren in allen Fällen nachweisbar. Hinweise auf Nekrose und Atrophie fanden sich in den meisten Kleinhirnhinterlappen, insbesondere im Nodulus; bei einigen Fällen war der Nodulus vollständig verschwunden.

Bei Kindern, die Geburt und Behandlung überleben, verringert sich der Druck auf den Hinterlappen und die erhaltenen Kleinhirnteile, d.h. die mehr cranial gelegenen Lappen, scheinen sich normal zu entwickeln. Dysplastische Bezirke im Kleinhirn scheinen sekundär durch das Größenwachstum behindernden abnormen Druck zu entstehen. Bezirke akuter Nekrose sind bedingt durch Lage- und Druckveränderungen im Bereich des vierten

Ventrikels, verursacht entweder durch die Geburt oder durch kurz zuvor aufgetretenen erhöhten oder erniedrigten intracraniellen Druck.

Die Befunde bestätigen die Vorstellung, daß die Veränderungen, die gewöhnlich als Cleland oder Arnold-Chiari Mißbildung beschrieben werden, durch sekundäre Bedingungen entstehen und nicht als primäre Gegebenheit anzusehen sind.

RESUMEN

La patología de los lóbulos centrales del cerebelo en ninos con mielomeningocele

Se realizó un estudio con 100 cerebelos obtenidos de niños con mielomeningocele. Estaban presentes deformaciones en todos los grados variables. Había una evidencia de necrosis y atrofia de los lóbulos más caudales del cerebelo, particularmente el nódulo; en algunos casos el nódulo había desaparecido completamente.

En niños que sobreviven al parto y al tratamiento, la presión sobre los lóbulos caudales disminuye y las partes residuales supervivientes del cerebelo, esto es, los lóbulos más craneales, se desarrollan de un modo normal. Las áreas displásicas en el cerebelo parece son secundariasa a los intentos de crecer bajo presiones anormales. Areas de necrosis aguda están relacionadas con alteraciones muy recientes en posición y presión dentro del cuarto ventrículo, causadas bien por el parto o por recientes alteraciones de la hipertensión o hipotensión intracraneal.

Los hallazgos confirman la impresión de que las deformidades usualmente descritas como Cleland o Arnold-Chiari son debidas a estados secundarios y no a una alteración primaria.

REFERENCES

Chiari, H. (1895) 'Über die Veränderungen des Kleinhirns, des Pons und der Medulla oblongata in Folge von congenitaler Hydrocephalie des Grosshirns.' *Denkschriften der kaiserlichen Akademie der Wissenschaften, Mathematisch-Naturwissenschaftliche Klasse*, **63**, 71.

Cameron, A. H. (1957) 'The Arnold-Chiari and other neuro-anatomical malformations associated with spina bifida.' *Journal of Pathology and Bacteriology*, **73**, 195.

Crome, L. (1952) 'Microgyria.' *Journal of Pathology and Bacteriology*, **64**, 479.

Emery, J. L. (1965) 'Intracranial effects of long-standing decompression of the brain in children with hydrocephalus and meningomyelocele.' *Developmental Medicine and Child Neurology*, **7**, 302.

— Lendon, R. G. (1973) 'The local cord lesion in neurospinal dysraphism (Meningomyelocele).' *Journal of Pathology*, **110**, 83.

— Levick, R. K. (1966) 'The movement of the brain stem and vessels around the brain stem in children with hydrocephalus and the Arnold-Chiari deformity.' *Developmental Medicine and Child Neurology*, Suppl. 11, 49.

Lichtenstein, B. W. (1942) 'Distant neuro-anatomical complications of spina bifida (spinal dysraphism).' *Archives of Neurology and Psychiatry*, **47**, 195.

Mackenzie, N., Emery, J. L. (1971) 'Deformities of the cervical cord in children with neurospinal dysraphism.' *Developmental Medicine and Child Neurology*, **13**, Suppl. 25, 58.

Peach, B. (1965) 'Arnold-Chiari malformation; anatomic features of 20 cases.' *Archives of Neurology*, **12**, 613.

Variend, S., Emery, J. L. (1973) 'The weight of the cerebellum in children with myelomeningocele.' *Developmental Medicine and Child Neurology*, **15**, Suppl. 29, 77.