VOLUME 32

HANDBOOK OF CLINICAL NEUROLOGY

P.J. VINKEN and G.W. BRUYN

CONGENITAL MALFORMATIONS OF THE SPINE AND SPINAL CORD

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Foreword to volumes 30, 31 and 32

In these volumes the editors have endeavored to present a thorough and comprehensive treatise, encompassing all aspects of congenital malformations of the central nervous system and its encasing structures.

Human malformations and, in particular, those of the central nervous system, are no less perplexing today than they were twenty-five or fifty years ago. It is a disappointing fact that progress in the understanding of the etiology and pathogenesis of these malformations has not kept pace with the recent advances in clinical neurology. At a time when exciting discoveries in areas such as the metabolic etiology of disease, the immune response system, and latent viruses, justify the promise that success in elucidating the pathogenesis of a large number of neurological disorders is just around the corner, malformations of the nervous system still remain stubbornly resistant to the search for the basic defect, and hence, to their prevention and treatment. The clinician, especially the pediatric neurologist, who has to grapple with the malformation problem almost daily, is continually left with a sense of frustration and futility.

Some insight has been gained from experimental teratology which has been singularly successful in reproducing practically all malformations known to man by a variety of exogenous and endogenous agents. However, it is reasonable to predict that resolution of the malformation problem will come ultimately from molecular embryology, a field in which activity has been gaining momentum during the last few years. The recent probes into the molecular mechanism of the developmental clock which regulates cell interaction and migration during embryogenesis offers a glimmer of hope for understanding the nature of the basic defect in the malformation process.

In the meantime, progress in clinical teratology has been and is being made, though painfully slowly and with faltering steps. The genetic etiology of some malformations and the chromosomal basis of others have been recognized. For these there is hope of prevention through genetic counseling. Very occasionally, an infectious agent or a chemical is identified as a teratogen in man, but not before it has spread misery and tragedy to scores of victims and their families. Such occurrences alert us to exercise greater caution in the administration of prenatal care, and to intensify our search for new teratogens.

In the area of diagnosis and treatment success has been a little more heartening. Malformations of the nervous system are particular beneficiaries of the recently developed prenatal diagnostic techniques of alpha fetoprotein level determination and

sonography. Progress in radiologic examination and computerized tomography has opened new vistas in establishing the correct diagnosis of previously vague and ill-defined malformations and malformation syndromes. And the daring skill of the neurosurgeon has achieved, in selected cases, stunning corrective and cosmetic results. Unfortunately, these admittedly spectacular advances still affect only a small proportion of cases.

It is altogether fitting, therefore, that three of the forty-odd projected volumes of the Handbook of Clinical Neurology be devoted to congenital malformations of the central nervous system.

In our effort to design a scholarly work, one that would cover all aspects of malformations of interest to the clinician, we thought it wise to proceed from a general survey of the field to a detailed discussion of each specific malformation. Thus, a series of five introductory chapters set the stage by reviewing concepts, definitions and classification, normal developmental anatomy and histology of the central nervous system, errors in differentiation which result in malformations, etiology, and natural history of central nervous system malformations. An additional chapter of introductory nature, on human chromosomes and their aberrations, precedes the chapters on specific malformations produced by, or associated with, chromosomal defects.

Practically all types of central nervous system malformations are found as a frequent or occasional component of malformation or disease syndromes, not primarily of the nervous system. In recent years, an enormous number of such syndromes has been described in the world literature Most of these are reports of single observations; others have not yet been recognized as distinct nosological entities. Only well-established and accepted syndromes are included here. They are presented and discussed in separate chapters: syndromes with infectious pathogenesis, bone defects, growth deficiency, metabolic disturbance and chromosomal abnormalities. In these chapters, special emphasis has been placed on the associated nervous system malformations and neurological findings.

In a work of the scope and length of the Handbook of Clinical Neurology, it is inevitable that there is some overlap and even duplication of subject matter. A little duplication is desirable and in some cases the editors have, frankly, encouraged it. It provides a new and often welcome approach, a fresh point of view. Previous volumes of this series, for example, have been wholly devoted to the phakomatoses, tumors of the brain and spinal cord, and arteriovenous malformations. But it would be well-nigh fraudulent to claim comprehensiveness in the present volumes without including chapters on these malformations simply because they have been covered in detail in other Handbook volumes. Besides, the emphasis here is on those malformations thought to be of congenital origin. It would not do to send the interested clinician who has acquired the present volumes, scrambling to other volumes of the series in order to locate and study these malformations.

Almost four years have elapsed between the initial design of these volumes and their publication. The task has been a difficult one and the course arduous, at times dishearteningly so, for editors and contributors alike, and we are grateful to the contributors whose individual and collective efforts have come fully up to our expectations.

We owe an apology to the readers of this volume for the placement of the chapter on spina bifida at the end of the volume instead of at its proper place, between the chapters on rachischisis, and anterior and lateral meningoceles. As was already mentioned in the Foreword to Volumes 30 and 31, not all contributors who became involved in these volumes made it to the end. Indeed, in the case of the spina bifida chapter, not one but two invited authors in succession failed to meet their deadlines. With the rest of the chapters already in first proof, the volume came perilously close to being published without the spina bifida chapter, which would have been deplorable in a comprehensive treatise of malformations of the spine and spinal cord. Fortunately, the situation was rescued by G. Brocklehurst, S. Campbell and D. Little who through gallant efforts were able to produce a chapter in time to be included in the final printing, albeit out of place. We offer them our special thanks.

We also wish to acknowledge the invaluable help of Jenny Kruseman, Brenda Vollers and Kris Lucas, and the editorial staff, throughout the planning and preparation of these volumes.

P.J.V.
G.W.B.
N.C.M.

Acknowledgement

Several illustrations and diagrams in this volume have been obtained from other publications. Some of the original figures have been slightly modified. In all cases reference is made to the original publications in the figure caption. The full sources can be found in the reference lists at the end of each chapter. The permission for the reproduction of this material is gratefully acknowledged.

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CHAPTER 1

Bone malformations of the craniocervical region

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Definitions and short historical survey

The rounded convexity of the vault of the skull lies opposite to a concave depression centered in the region of the sella turcica (Fig. 1). The phylo- and ontogenetic significance of this bend in the base has been under investigation by anatomists and anthropologists since the middle of the last century (Virchow 1857a, b; Welcker 1866; Schaeffer 1893; Weidenreich 1924; Dabelow 1929/31; Diepen 1948; Hofer 1954; Simon 1954; Biegert 1957; and others). A diminution of this bend, i.e. flattening of the base of the skull, was called 'platybasia' by Virchow (1857a), although it had been recognised since 1790 (Ackermann). Considered from another view, namely looking upwards from the caudal direction, such an alteration will appear as an impression of the base of the skull (Fig. 2). As this deformity of the base of the skull is particularly frequent in cretins, it was initially considered to be the cause of cretinism.

Most anatomists of the last century thought that the deformation had a mechanical cause, hence the name applied to it – 'Impressio baseos cranii' (Berg and Retzius 1855, cited by Virchow 1876), or basilar impression (Virchow 1876). Virchow, and more particularly Grawitz (1880), suggested that the condition was largely the result of a developmental abnormality of the bone.

Once used, the term 'impression' has been retained, although strictly it can only be justified in instances of true impression, i.e. inward displacement of the base of the skull, as may occur if the bone is pathologically softened, e.g. in Paget disease (Marie and Léri 1919; Bull 1946/7; and others) and in destructive diseases and trauma (Schmidt and Fischer 1964).

Schüller (1911) was the first to demonstrate basilar impression radiologically in living patients. Further radiological investigations have confirmed the view of Grawitz that platybasia and basilar impression are often the result of under- or maldevelopment of the craniovertebral transition region. Chamberlain mentioned both symptoms in his work 'Basilar impression (platybasia)' published in 1938/39; however, justified criticism was soon made of his use of both terms synonymously (Cohen 1942; Moreton 1943; and others).

Platybasia and/or basilar impression are often the first abnormalities apparent in X-rays of the skull that draw attention to the occurrence of developmental bone defects in the craniovertebral transition zone.

The developmental abnormality consists of underdevelopment of three parts of the occipital

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bone – its basilar and lateral part and the occipital condyles. Stunting of the latter reduces the distance between the atlas and the occiput, which may lead to ankylosis of the atlanto-occipital joint and ultimately to total assimilation of the atlas into the occipital bone. Colombo (1577), a pupil of Vesalius, gave the first account of assimilation of the atlas into the skull. A range of malformations is frequently associated with anomalies of the atlas and axis, some of which may be quite atypical, and with fissures or defects and bone projections from the spinal column in the craniovertebral transition zone. The latter anomalies were grouped by von Torklus and Gehle (1970) under the heading 'suboccipital dysplasia'.

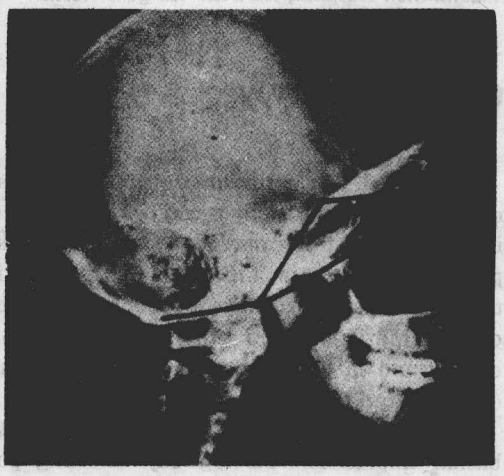

Fig. 1. Lateral radiograph of the normal skull. The basal – foramen magnum – basal angles have been outlined (127° and 150° respectively).

Feasibility and limitations of radiological diagnosis with reference to published monographs

The external appearance of a patient is often suggestive of an anomaly of the craniovertebral transition region, but this can be proven only by radiological examination of the affected parts of the skeleton.

Monographs on the topic have been published by Brocher (1955), Schmidt and Fischer (1960a–c), Dieckmann (1966), Klaus (1969), von Torklus and Gehle (1970) and more recently by Wackenheim (1974).

Fig. 2. Lateral view of the skull in platybasia and basilar impression. The basal angle is flattened and the foramen magnum – basal angle is negative (157° and 187° respectively).

It is very unusual for skeletal abnormalities to cause mechanical lesions of the neural tissues. Often the bone abnormalities present in patients with neurological symptoms, are taken as sufficient explanation for the clinical disorders, whereas the clinical findings are really due to malformations of the nervous tissue itself.

Direct radiological proof of this is possible only to a limited extent. Pneumencephalography, initiated in 1941 by Lindgren, permits demonstration of the ventricles, the cisterns and the superficial surface of the brain. Spillane et al. (1957) reported deviations from the normal vascular pattern in angiograms of patients with bone abnormalities. Driesen (1960) published the first results of a series of angiograms in such cases. Until recently, however, the most that angiography could do was to show abnormalities in the major vascular pathways (Klaus 1969).

New viewpoints have arisen recently through study of the effects of vascular occlusion. In the following account most attention has been devoted to skeletal findings, but it has also been considered necessary to discuss diagnosis by contrast medium radiological technique, and to refer particularly to angiography, which is dealt with in another section.

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Radiological features

H. SCHMIDT

Before bone abnormalities in this region can be discussed it is necessary to describe the normal osseous development of this region and to consider the radiological demonstration of normal relationships in the skull-neck transition region.

NORMAL SKELETAL DEVELOPMENT IN THE CRANIO VERTEBRAL TRANSITION ZONE

Those parts of the occipital bone that develop from the primitive cartilage belong embryologically to the vertebral column and are not part of the skull.

The following account of prenatal development has been taken from the observations of Töndury (1958) and that of postnatal development from the work of von Torklus and Gehle (1970). The human embryo initially has 40 to 42 somites. Of these, three or four become absorbed in formation of the tail and five are involved in formation of the occiput. The occipital plate and the two uppermost vertebrae which acquire the function of a rotary joint, differ in their development from all the other vertebrae. These peculiarities are the basis for regarding the craniovertebral transition region as a unique area and for considering its malformations separately.

In general the vertebral anlage in the occipitovertebral region behaves as do all other vertebrae: the caudal half of the first sclerotome of each protovertebra blends with the cranial half of the neighbouring protovertebra (Remak 1850).

Mesenchymal development

The notochord traverses the vertebrae and intervertebral discs and is responsible for inducing the normal separation of vertebrae from one another by the intervertebral discs. Its course alters cranial to the atlas. 'The blastemata of the anlage of the occiput and the atlas begin laterally as small cellular bands between the myotomes, corresponding to the neural arches, and they enlarge medially from the associated nerves to the precursors of the lateral masses of the atlas or to the occipital condyles. These are joined together by the hypochordal cell bands which are separated in the midline by loose mesenchyme. The dorsal notochord runs dorsally from the hypochordal cell bands. At first the notochord lies on the hypochordal mass, until, in embryos of 10 mm crown-rump length, mesenchyme begins to push between it and the hypochordal peg. In embryos of 16 mm crown-rump length a dense layer of parenchymatous tissue forms the anlage of the base of the skull. This produces the conditions necessary for formation of the ligamentum apicis dentis' (translation of quotation from Töndury 1958, pages 101/102). The anlage of each vertebral body pushes out dorsally both neural processes, which extend to the level of the spinal ganglia in embryos of 10–11 mm crown-rump length; unlike the vertebral bodies they consist of very dense mesenchyme. They end freely in the mesenchyme which then thickens to form the membrana reuniens. In 50 mm long embryos both ends join in the middorsal line.

Cartilaginous development

Cartilage development in the vertebral column generally commences in embryos of 12 mm crown-rump length (approximately six weeks old). In the upper cervical spine it extends from the dorsal part of the lateral mass. The nuclei of chondrification lie segmentally in the blastema on both sides. The occipital plate becomes chondrified from two centres in the occipital condyles. The notochord remains dorsal in the occipital plate, extends through the cartilaginous base of the skull diagonally towards the front and then lies ventral to the plate. The anlage of the anterior arch of the atlas appears as a hypochordal mesenchymal thickening. Ludwig (1953, 1957) reported that the body of the atlas was not laid down. The dens of the axis develops from paired cartilaginous dental processes, which fuse after a short period but are separated from the body of the axis by a mass of embryonic tissue that resembles an intervertebral disc. Kladetzky (1955, 1956)

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supported a contrary view, which had been held up to that time, namely that the nucleus of the tip of the dens corresponds to the body of the atlas. Töndury (1958) wrote 'The dens of the axis cannot develop from the body of the atlas which does not exist', without mentioning the work of Kladetzky. In the body of the axis a uniform cartilage nucleus develops as in other vertebral bodies. Töndury considered that the dental processes were associated laterally with the body of the axis. As stated above, they are separated in the middle by a septum rich in cells. Superficially this is associated with the perichondrium and deeply with dense blastema which resembles an intervertebral disc. The notochord thrusts forwards from the body of the axis to penetrate this tissue in the same way as the anlage of the intervertebral discs. At the end of the period of cartilage formation the last remnants of blastema separating the vertebral body from the dens disappear. The homogeneous cartilagenous anlage which is formed, resembles the bone that is ultimately formed. Deep in the zone between the dens and the body of the axis there is a rudimentary segment of notochord which, as the anlage of an intervertebral disc, lacks a sheath. In contrast to animals, e.g. the mouse, not every segment in man has a true intervertebral disc; the first recognisable one lies between C2 and C3.

In its later cartilaginous stage, the part of the notochord that emerges from the dens is surrounded by a cell-rich sheath that arises from longitudinal fibres. A suspensory ligament is formed which securely anchors the dens to the skull. At the same time the anterior arch of the atlas becomes chondrified. The posterior part of the arch undergoes chondrification in all vertebrae of embryos between 12–15 mm crown-rump length. The process begins bilaterally in the root of each arch, extends dorsally and ends finally in the spinal processes. As far as the authors know, similar investigations of the development of the cartilaginous parts of the occipital squame have not been made.

Bone development

Bone development in the vertebral column begins in embryos of 50–70 mm crown-rump length (in approximately the third embryonic month) with the appearance of unpaired nuclei of calcified cartilage in the vertebral body and central, symmetrical nuclei in the vertebral arches.

According to Töndury (1958) ossification in the vertebral bodies begins with ingrowth of blood vessels which dissolve the cartilage from the centre outwards (relatively, a large part of the spongiosa and little of the corticalis). A perichondral bone process develops initially in the vertebral arch which helps to maintain its form; afterwards, blood vessels invade causing bone destruction (a relatively large amount of corticalis and little spongiosa). Ossification of the vertebral bodies begins in the lower thoracic spine and extends both cranially and caudally. Ossification of the vertebral arches starts at the top and ends at the bottom. In foetuses of 120 mm length (about the fourth or fifth month of embryonic life) all these ossification centres have normally been laid down. Töndury considered that the body and dens of the axis ossify from one ossification centre. The nucleus in the body contains a single primary narrow space, bone and cartilagenous trabeculae and a characteristic zone of cellular proliferation. In the dens the nucleus consists at first of a focus of calcified cartilage which extends from the dorsal notochord and is often divided into two unequal parts. Kemény and Köteles (1962) observed a nucleus both on the right and the left of the basal part of the dens in the sixth foetal month. At the time of birth the nuclei would have fused. Von Torklus and Gehle (1970) also observed that two ossification centres developed at the base of the dens which had merged by the time of parturition. Ossification extends cranially in two processes. The cartilaginous 'dental processes' described by Ludwig (1953, 1957) and Töndury (1958) were recognised in the ossification stage, too, by von Torklus and Gehle. Ossification of the posterior vertebral arch of the axis corresponds to that in the arches of other vertebrae. It begins in a similar way in the atlas, in which it extends from the lateral mass. Ossification of the anterior arch of the atlas starts later, e.g. in the newborn. Tompsett and Donaldson (1951) and Geipel (1955) found no bone there on radiological examination. Geipel (1955) described how normal ossification of the anterior arches of the atlas

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might occur in three different ways: (1) formation of a central unpaired ossification centre in the anterior tubercle; (2) formation of two or more paramedian nuclei in the anterior arch; and (3) in rare cases in which nuclear precursors were missing, ossification began from the lateral mass.

Usually the centres of ossification develop by the end of the sixth year (Camp and Cilley 1931). The human foetus has a nucleus in the basal part of the occipital bone, another in the squamous occipital bone and a further nucleus in the lateral part of the occipital bone. In the newborn, there are also broad cartilage masses between the bones. Ganguly and Singh Roy (1964, 1965a and b) reported that the neural arch of the anlage of the last occipital vertebra, the so-called 'proatlas', divided bilaterally into a posterior and an anterior part of the arch. The anterior one extended into the basi-occipital region and formed both condyles, the posterior one fused with the ring of the atlas and took part in the formation of the upper facet of the joint of the atlas. This accounts for the division of the joint surfaces of the occipital condyles which may be observed in adults.

After birth, further ossification centres may arise in cartilaginous parts of the vertebral arch. In the arch of the axis ossification extends towards the perichondrium and eventually finishes dorsally between the second and third year. The arch fuses with the body of the axis on both sides by the seventh year.

The cartilaginous band between the dens and the body of the axis does not lie at the site of the medial border of the joint surface of the axis (von Torklus and Gehle 1970). In childhood, the dens is deeply sunken into the body of the axis. Von Torklus and Gehle mentioned a 'dens socket' in the body of the axis, which was involved in formation of the medial part of the lateral joint surface of the axis.

In about 25% of children (Cattel and Filtzer 1965) there is a separate nucleus at the tip of the dens. It is called the ossiculum terminale Bergmann. Von Hayek (1927) considered that it developed from the centre of the proatlas. According to von Torklus and Gehle (1970), this ossification centre does not develop in the second year but may be seen quite often in the first months of life. Initially, it is round in shape and lies a relatively long way from the bony odontoid process and during growth the ossification centre appears in the lateral view to develop into a dome-shape. The cartilage band appears V-shaped in the sagittal view and has usually been bridged by the tenth to twelfth year of life.

The synchondrosis beneath the dens breaks down during the first years of life. Cattel and Filtzer (1965) reported that it was visible in all 3-year old children, but in only 50% of 3- to 4-year olds. In older children even a radiologically apparent area of reduced density as a representative of the joint is rare.

Two small synchondroses develop bilaterally between the bone nuclei of the occipital bone, one anterior and one posterior. The anatomical assertion that the posterior cartilage joint closes earlier (in the second year according to Zaaijer, 1884) than the anterior, has not been confirmed by radiological observations. Grob (1938) found that both cartilage joints had closed in 98% of 9-year olds and in 13% of 10-year olds.

The spheno-occipital synchondrosis does not close until the sixteenth to twentieth year (Welcker, 1862; see Figs. 8 and 9).

It is noteworthy that the sutura mendosa is the seam between the upper and lower layers of the occipital squama. It is usually closed at birth and only very rarely does it persist. Between the fourteenth and sixteenth year of life five secondary centres appear (Wackenheim 1974): one in the spinal process, one in each transverse process and one each in the upper and lower surface of each vertebra (apo- and epiphyses) which may remain visible until the twenty–fifth year.

ABNORMAL DEVELOPMENT

Atlas

Töndury (1958) regarded fissures in the posterior vertebral arches to be the result of disturbed development of the vertebral column in the early mesenchymal phase, when interruptions in the continuity of the vertebral arches become apparent. Chondrification and ossification occur from two nuclei separated by the cleft in the arch. Corresponding malformations include incomplete closure of the arch, absence of the arch or absence of the lateral mass of the atlas.

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