part of the skull onto the upper part of the spine. The lordosis following the shortening and distortion of the vertebræ markedly influences the position of the head, the occiput being bent backward and the face thrown upward. This, in conjunction with the flattened cranial vault, deficient brows, and the consequent seemingly excessive protrusion of the eyes, gives to these malformations the peculiar appearance described as "toad-headed."

*Cephalocele.*—Associated with partial defects of the skull, but antedating the bony deficiencies, protrusions of the cranial contents may occur as various forms of cerebral hernia. The fallacy of regarding cephalocele as secondary to and dependent upon the defect in the brain case is suggested when we recall the time (end of the third month) at which ossification begins—a date manifestly too late for the production of changes so profoundly affecting the brain. The tumor escaping through the limited area of defective skull may consist of brain substance, only of its membranes, or of both. When composed of brain substance, the hernia is termed *encephalocele; hydrencephalocele*, or *hydrocephalus*, implies an accumulation of fluid within the ventricles and a more or less extensive prolapse of the dilated brain. Should, however, the accumulation of fluid take place after the development of the skull has well progressed, the condition may result in the general enlargement of the cranium, with the attendant alteration in the brain, seen in congenital hydrocephalus. The excessive production of the intraventricular fluid, which may reach a litre in quantity, takes place from the choroidal plexus, the lateral and third ventricles especially undergoing marked dilatation, while the surrounding nervous substance usually suffers greatly. The cranial vault shares in the expansion and becomes excessively thin, the fontanels being abnormally large and the sutures wide and ununited. When the hernia contains only the distended arachnoid and pia the condition is known as *meningocele*, or *hydromeningocele*. In case the brain substance is at the same time involved, as frequently it is, *meningo-encephalocele* is the appropriate designation for such deformity.

The most frequent seats for cerebral herniæ are the occipital region immediately above the foramen magnum and the vicinity of the root of the nose. The seats of the herniæ are indicated in the forms variously described as naso-frontal, naso-ethmoidal, naso-orbital, or, exceptionally when at the base or side of the skull, as spheno-pharyngeal, spheno-orbital, spheno-maxillary or lateral.

*Iniencephalus.*—In rare instances the cranial defect includes a combination of hydrencephalus and encephalocele with fissure of the adjoining cervical vertebræ. The distended occipital tumor overhangs the spine, the encephalocele being received in the vertebral cleft and the integument of the head, passing directly into that of the back.

*Microcephalus and Micrencephalus.*—These conditions, distinguished by abnormal smallness of the cranium and the enclosed brain, represent defective development of the nervous mass, the arrested growth of the latter probably preceding, not following, that of the skeleton. In contrast to the etymological comprehensiveness of the term, as including all forms of diminished head, microcephalus, as at present understood, implies the associated presence of a brain which, with the exception of its abnormally small size, may not be materially deformed. Further, that the diminished brain case is part of a body of usual stature, thus excluding the microcephalus seen in dwarfs (*nanocephalus*).

The decrease in the microcephalic skull affects especially the cranium, the facial portion often suffering but little arrest in its development. Assuming the average cranial capacity as 1,500 and 1,300 c.c. and the average horizontal circumference as 52 and 50 cm., for the adult male and female skull respectively, in extreme cases of microcephalus the cranial capacity may be diminished to little more than one-fourth of the normal, and the circumference may reach only two-thirds of the normal measurement. The unusual closeness, although not necessarily disappearance, of the sutures and the absence of the fontanels are among the characteristic features of the young microcephalic skull, the cranial vault, both in its sagittal and frontal curvature, being decidedly diminished. In consequence of the slight involvement of the face the narrowing of the cranium becomes conspicuous and confers upon the microcephalus a simian type, since the skull seemingly possesses a median crest. An additional peculiarity is also seen in the forward bend of the outer surface of the occipital bone, the external protuberance apparently being displaced upward. The partial or complete obliteration of the cranial sutures, upon which much emphasis was formerly laid, is far from constant, since synostosis in young microcephalic skulls is unusual, such crania even in later life occasionally exhibiting persistent sutures. Union of the sagittal suture, however, is not infrequent; since arrested growth of the brain occurs early, the elongation of the skull usually associated with such synostosis is not observed.

The *micrencephalus* associated with the diminished cranial capacity presents wide varations of brain weight (from 200 to 800 gm.), the loss being chiefly due to that suffered by the cerebral hemispheres, although usually the cerebellum is also under the normal weight. While in micrencephalus of low degrees the fissures and convolutions are practically normal, in the higher forms the frontal, parietal, and occipital lobes may be greatly distorted and disturbed. Often along with simplification of the gyri unusual prominence and partial exposure of the central lobe, or island of Reil, are highly characteristic in the more marked grades of micrencephalus.

*Malformations of the brain*, depending upon arrested development, affect chiefly the cerebral hemispheres, since these represent the more highly specialized portions of the encephalon, although the cerebellum and the brain stem are at times also involved. The defects of the cerebrum include irregularities, simplification, and suppression of the convolutions, imperfect development of the olfactory lobes, corpus callosum, basal nuclei, and other parts derived from the subdivisions of the primary anterior cerebral vesicle. The lateral and third ventricles sometimes become the seat of abnormal accumulations of cerebro-spinal fluid, followed by distention and more or less unfavorable change in the surrounding parts. To such congenital defects, when not sufficiently grave immediately to endanger life, although always productive of impaired intellect, the term *porencephalus* has been applied as distinctive from hydromicrencephalus, in which the defective features are more exaggerated. The former condition may be associated with extensive involvement of the adjacent frontal and parietal lobes, the affected convolutions and fissures presenting a characteristic radial disposition. In consequence of the impairment of the cortical motor areas contractions and atrophy of the limbs of the opposite side are frequently observed.

*Cyclocephalus.*—A conspicuous group of defects involving the great brain, eyes, and nose is derived from arrested development of the primary anterior cerebral vesicle. It will be recalled that the latter soon subdivides into forebrain (prosencephalon) and interbrain (thalamencephalon), from which are subsequently developed the cerebral hemispheres, including the lateral and third ventricles and the parts surrounding these spaces. The early outgrowth of the eye sacs from the posterior segment of the primary cerebral vesicle is closely connected with the changes which the latter undergoes. Arrest of development of the primary brain sac, when profound, may prevent the secondary longitudinal subdivision of the forebrain into the two cerebral hemispheres, the latter in extreme cases being represented by a single sac which may occupy a large part of the cranial space and be filled with fluid. When less aggravated and of low degree, the defective development may find expression only in particular parts, as the olfactory region, the anterior convolutions, the corpus callosum, the optic thalamus, etc. Those derived from the middle and posterior primary cerebral vesicles, as the





corpora quadrigemina and the parts surrounding the fourth ventricle, are usually little disturbed.

The failure of the cerebral hemispheres to develop, hence apparently to fuse, exerts a profound influence on the relation of the optic vesicles, since instead of being widely separated as in the normal condition, they may become closely approximated or blended and lead to the formation of a single visual organ, this condition constituting *synophthalmus* or *cyclopia*.

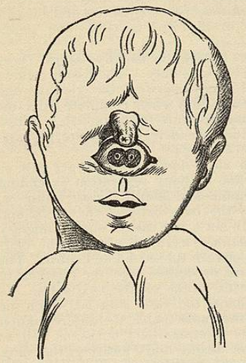

FIG. 4678.—Synophthalmus. (Heyman.)

Since the fronto-nasal process, which takes an important part in the formation of the external nose, shares in the general defective development of the forebrain, malformations of the nose are usually associated with synophthalmus. The typical cyclopian monster is distinguished by a single eye within a single orbit, occupying the middle of the face. A true nose is wanting, but about the orbit protrudes a fleshy proboscis provided at its end with a single or double opening. Depending upon the extent of developmental arrest, transitional forms of all degrees exist. Beginning with the slightest, in which an unusually narrow face, closely set eyes, and a rudimentary, although normally situated nose are the chief features, the relations of the eyes become progressively more intimate until, in marked instances, they lie within the fused orbits side by side, the rudimentary nose having been replaced by a proboscis above the orbital opening. The two eyes may be represented by a single ball of unusual size, in which double or partially blended corneæ, pupils, lenses, and optic nerves are present. When synophthalmus of high degree exists, the fusion of the two optic organs and nerves may be complete.

Since the normal union of the fronto-labial and maxillary processes (which plays an important rôle in the formation of the face and upper oral boundaries) may be hindered by the same influences that produce cyclencephalus, it is not unusual to find clefts of the lip and palate associated with the characteristic deformities of a well-marked cyclops. Likewise disturbed relations in the position of the visceral arches may result in coincident deformity of the external ear, the fusion of which constitutes *synotus* or *cyclotus*. In extreme cases, in addition to disappearance of the nose (*arhinencephalus*) as well as proboscis, the oral aperture may also become closed (*cyclostomus*) by fusion of the displaced visceral bars. When only feeble development is conjoined with fusion of the optic vesicles, the resulting organ may be so imperfect that a distinct eye is absent (*anophthalmus*), or at best represented by an extremely rudimentary organ occupying a slight central depression.

Coincident with cyclencephalus of high degree, defects involving the parts adjacent to the orbital, nasal, and oral cavities are not infrequent. Such malformations may include imperfections or absence of the ethmoid bone and nasal septum and cleavage of the palate and upper lips; less commonly the inferior boundary of the oral opening may be deficient.

*Malformations of the Eye.*—In addition to the foregoing conspicuous changes (cyclopia) in the position and development of the visual organs associated with the grave general arrest affecting the development of the anterior brain vesicles, the eye may be the seat of local defects, the more important of which may conveniently be briefly noted in this place.

Retention of fœtal structures and conditions which usually disappear before birth account for some of the slighter anomalies, including persistence of the pupillary membrane in the form of vascular fringes attached to the free edge of the iris; persistence of the remains of the hyaloid artery, as a fibrous cord stretching from the optic papilla toward the posterior surface of the lens; coloboma of the iris and of the choroid, as well as cysts connected with the eyeball and containing portions of its contents, are referable to imperfect closure of the fœtal choroidal fissure.

When the developmental arrest has been more general, the entire organ remains undersized (*microphthalmus*) and retains many features of its fœtal condition, as shown by the unusually large lens, which may occupy the greater part of the eyeball, the persistence of the vascular primary vitreous tissue and remains of the hyaloid artery. The retina is often imperfect and the effects of an unclosed choroidal fissure are seen in coloboma of the iris and choroid. The small eyeball is enclosed by a relatively thick sclerotic coat and diminutive, illy defined and often untransparent cornea. Microphthalmus may be unilateral or bilateral and associated with impaired development of the skull and brain.

*Anophthalmus*, or total absence of the eyeball, represents the extreme condition of an arrested development which fails to produce even a rudimentary organ within the small and imperfect orbit. This condition may exist on one or both sides.

The eyelids also share in the defective development, and may enclose a palpebral fissure of abnormal narrowness (*ankyloblepharon*), often seen in conjunction with microphthalmus. The fissure may be wanting (*cryptophthalmus*), owing to fusion of the lids, or the latter may be congenitally adherent to the eyeball (*symblepharon*). *Epicanthus* is distinguished by the presence of a cutaneous fold, occupying the inner canthus to a variable extent, attributable to the persistence of the plica semilunaris to a degree corresponding to the nictitating membrane of lower forms.

MALFORMATIONS OF THE FACE AND NECK.—Since these malformations result largely from arrested or defective union of the visceral arches with one another and with the surrounding parts, a brief outline of the normal development will be a useful preface to the description of the defects in question.

The face and neck are primarily formed by the fusion of a paired series of lateral bars, the *visceral arches*, with one another and the unpaired median *frontal process*, the downward prolongation of the region of the forebrain. The visceral arches in man and mammals for a time are separated by *external* and *internal furrows*, the representatives of the slit-like apertures, or *branchial clefts*, of the lower forms (fishes). The median ends of the first pair of visceral arches are subdivided into a short upper or *maxillary*, and a longer lower or *mandibular process*, between which and the frontal process the primary oral cavity is included. With the appearance of the nasal pits the frontal process differentiates into the median *naso-labial* and the *external nasal process*, lying respectively between and outside the olfactory depressions. The lateral angle of the naso-labial process thickens and becomes the *internal nasal* or *globular process*, which on each side

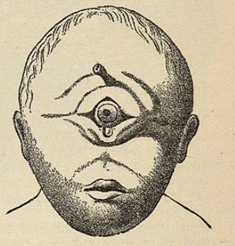

FIG. 4679.—Synophthalmus Cyclopia. (Jourdan.)

bounds the olfactory pit. The further differentiation of the fronto-nasal and inner nasal processes gives rise to the nasal septum and inner boundaries of the nasal apertures and the *nasal groove*, the latter marking the line of fusion between the maxillary and internal nasal processes. The external nasal processes contribute the cartilages and the lateral boundaries of the front of the nasal fossæ. These processes, in conjunction with the adjacent maxillary divisions of the fourth visceral arch, also bound the *lachrymal groove* leading from the eye to the nasal furrow. Fusion of the adjacent portions of the fronto-nasal process with the maxillary bars gives rise to the cheeks and superior oral boundary, the latter differentiating into the upper lip and the superior and intermaxillary alveolar borders. The widely open recess which for a time constitutes the primary oral cavity becomes divided into a respiratory and an alimentary part by the formation of a septum formed by the union of the palatal plates differentiated from the maxillary processes. The palatal shelf thus formed unites with the nasal septum to compensate the closure of the nasal fossæ. The external visceral furrows, with the exception of the first which persists as the external auditory canal, are obliterated by the approximation and fusion of the arches. The internal furrows, or *pharyngeal pouches*, likewise disappear; the first, however, is converted into the Eustachian tube, and secondarily is associated with the tympanic cavity. The entoblastic lining of the third and fourth pouches gives rise to the epithelial anlages of the thymus and thyroid bodies respectively. The inner ends of the second arches contribute a V-shaped area, from which the posterior third of the tongue is formed, the anterior two-thirds of the organ being derived from an unpaired elevation, or tuberculum impar, which arises in front of the junction of the second arches.

*Facial Clefts.*—From the foregoing it is evident that such defects may arise as the result of *primary* arrest of

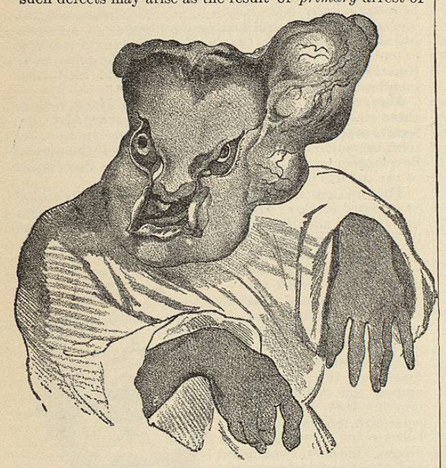

FIG. 4680.—Facial Clefts. (Ross.)

development and union of the embryonal processes, or that they may follow *secondary* disturbances affecting parts already partially formed.

*Aprosopus* is the most pronounced degree of such primary malformations, and implies an early and complete arrest of development of the parts normally concerned in forming the face. The latter in this condition is practically absent and replaced by a widely open, irregular oral recess.

*Clefts of the Lip, Jaw, and Palate.*—Usually the primary defective development is less general and limited to faulty union between the processes concerned in forming the upper and lateral parts of the face. The clefts follow the lines of primary union, and may involve (1) the upper lip alone (*cheiloschisis*), (2) the lip and maxilla (*cheilo-gnathoschisis*), (3) the lip, maxilla, and palate (*cheilo-gnatho-uranoschisis*).

*Simple cleft lip*, or *harelip*, is usually lateral (very rarely median) and on one side only. The fissure follows the line of the nasal groove between the globular and maxillary processes, extending when complete from the inner border of the nasal aperture to the mouth. Subsequent union may reduce the defect to a mere prenatal scar.

The *labio-maxillary clefts* involve the upper jaw as well as the lip, the line of bony separation extending either between the canine and lateral incisor tooth, or, as is most frequently the case, between the lateral and the central incisor. In not a few cases a supernumerary incisor tooth, or sometimes teeth, is present, the cleft then usually passing between the second and third. The defect may be unilateral or double, and the relations to the teeth symmetrical or unlike on the two sides. As emphasized by Marchand, the early stage at which the faulty union is established anticipates the differentiation of the maxilla and the intermaxillary bones, as well as the appearance of the dental buds locating the milk teeth. These facts, together with the possible variations in the relation of the teeth germs to the bony segments later blended to form the upper jaw, detract from the assumed importance of these malformations as evidence in determining the mooted existence of double intermaxillary bones on each side. Symmetrical cleavage involving only the lip and jaw, the intermaxillæ standing out as an isolated process between the lateral fissures, are rare, the labio-maxillary clefts being usually combined with some form of palatal fissure.

Such defects, involving the palate as well as the lip and superior maxillary bone, include two groups, the *median* and the *lateral*. The former, in which a wide median cleft of the lip and jaw is continuous with an extensive central deficiency of the palate, is usually associated with malformation of the fore end of the brain-case, as seen in cyclencephalus, the facial defect being an expression of the same profound developmental arrest that is responsible for the cerebral deformity.

The second and more usual type is distinguished by the lateral fissure, which is very frequently continued into a cleft palate. When one-sided, the imperfect union between the nasal and maxillary processes very often affects that between the corresponding palatal plate, the fellow of the opposite side and the vomer, and results in the cleft palate. With lip-jaw clefts of the two sides, the defect of the palate may appear as a conspicuous median hiatus, in consequence of very imperfect formation of the plates, or the attempt at closure may result in leaving a slit on either side of the septum. The latter may be intact and attached to the intermaxillæ, which then sometimes present a snout-like protrusion.

Not rarely only part of the lines of juncture remain permanently ununited, as seen in cases in which slight indentations or linear scars on the lips, partially cleft palate, or split would alone persist as evidences of the imperfect closure. The observations of Friccius, covering 550 cases of harelip, showed the defect to be almost twice as frequent in males (62.5 per cent.) as in females (37.5 per cent.). It occurred on the left side in 52 per cent.; on the right in 21 per cent.; on both in 27 per cent. It was uncomplicated in 35.2 per cent., and complicated by alveolar or palatine cleft in 64.8 per cent. Hereditary influence was indicated in 11.5 per cent.

Occasionally the defective union involves the entire path of junction between the maxillary process and the internal and external nasal processes, the result being a cleft extending from the mouth, through the lip and superior maxillary bone, alongside of the nose, to the inner canthus of the eye. Such defect is known as primary *oblique facial cleft* (*cheilo-gnatho-prosoposchisis*), and is to be distinguished from similar, but less regular, secondary deformities sometimes arising from mechanical influences exerted by abnormal relations of the amnion. These latter defects may vary greatly in position, form, and extent, since they are accidental and do not represent suspension of normal lines of development, as do the primary clefts.





*Nasal clefts*, median or lateral, occur as rare malformations. The median involve the tip of the nose and depend upon the persistence of the original tubular form of nares separated by a deep groove. The lateral clefts occur in consequence of insufficient fusion of the external nasal with the fronto-labial processes. Lehmann-Nitsche [91] and Lexer [92] report interesting cases.

The mouth may also be the seat of malformations caused by defective union of the embryonal processes constituting its primary boundaries. Where these fail properly to fuse to form the usual lateral limits, the oral opening may remain as a widely open cleft (*macrostomus*), extending laterally almost or quite as far as the ear, on one or both sides. When less marked the defect is sometimes known as *cheek-cleft*. Abnormal fusion, on the contrary, may partially obliterate the oral opening (*microstomus*), this condition being sometimes associated with labio-maxillary clefts. Complete fusion with resulting closure (*astomus* or *atresia oris*) may also occur.

Malformations due to faulty development and union of the mandibular processes of the first visceral arch also occur, but are much less frequent than the foregoing facial clefts, owing to the greater number of processes concerned in the formation of the upper lip, nose, and upper segment of face, and hence the greater opportunity for incomplete fusion.

Defects of the *lower lip*, in the form of median cleft or fistulæ, are rare, since fusion of the mandibular processes takes place unless development be profoundly disturbed.

*Micrognathus* implies defective formation and growth of the embryonal bars, resulting in a rudimentary and under-sized condition of the lower jaw. Pronounced arrest of these processes may be shown in *agnathus*, in which the mandible may be seemingly totally wanting. According to Winckel and to Kuse,[93] however, rudiments of the inferior maxillary bone are always to be found by critical examination. In consequence of the disappearance of the mandible the external ears are shifted downward and inward until their approximation may become blending (*synotus*). Usually defective development of the ears and, not infrequently, also of the maxillary processes are associated with the malformations of the jaw. The mouth may be imperfectly represented and the lower part of the face appear as if cut off and occupied by a widely open pharyngeal recess.

Partial or complete duplication of the lower jaw (*dignathus*) is an expression of more or less extensive redundant differentiation of the mandibular processes. The doubling may involve only one side, or be limited to the alveolar processes, the accessory segment bearing supernumerary teeth. When partial the additional part projects from the mandible, or, when complete duplication occurs, may be fixed above or below the normal bone.

Cleft *tongue* may also exist as a rare malformation.

The external visceral furrows are the seat of abnormalities due to aberrations in the closure of these depressions between the adjacent arches. Variations in the development of the first furrow and its bordering arches give rise to malformations of the external ear.

Since the auricle is formed by the fusion and differentiation of six tubercles surrounding the outer end of the first furrow, defective development or imperfect union of these parts frequently produces malformations involving the pinna, including the auricular appendages which originate from displaced tubercles. Malformations of the auricle may be associated with closure or absence of the external auditory meatus due to partial or complete abnormal fusion of the first and second arches, with the consequent occlusion or disappearance of the external auditory canal. As already incidentally noted, malformations of the ears are sometimes associated with defective development of the face.

*Congenital cervical fistulæ* are the results of imperfect closure of the visceral furrows, coupled often with secondary rupture of the ecto-entoblastic epithelial septa, which in mammals separate the external furrows from the internal pharyngeal pouches. The most usual situation of the fistulæ is immediately above the sterno-clavicular articulation; less commonly along the anterior border of the sterno-mastoid muscle. Although it is difficult to determine the exact genetic relations of the fistulæ to the original furrows on account of the changes and displacement which occur during the evolution of the neck, it may be assumed, according to Kostanecki and Mielecki,[94] that the majority of these fistulæ are derived from the second furrow, between the second and third arches. Originally the fistula is only a short pocket separated from the corresponding pharyngeal pouch by the delicate occluding membrane formed by the opposed ectoblast and entoblast lining the outer and inner diverticula. This independence being retained, the fistula is only a short and narrow passage, directed upward and inward, soon ending blindly and without communication with the pharynx. When, as is not infrequently seen, fluids escape from the fistula on swallowing, we must assume that secondary rupture of the delicate epithelial septum has taken place, thereby establishing communication between the pharynx and the exterior.

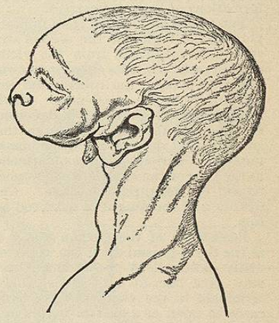

FIG. 4681.—Agnathus. (Guardan.)

*Median cervical fistulæ* constitute a group modified by the position of their external opening, which is central instead of lateral. As pointed out by Kostanecki, the outer opening of the fistulous passage corresponds to the remains of the precervical sinus of His; the latter is a median depression, resulting from the drawing inward of the blended lower visceral arches, which later becomes closed in by the union of the second arches with the thoracic wall. When complete, the fistulæ in question usually pass upward and inward, but end on the lateral wall of the pharynx in the same positions as do the lateral fistulæ. The median location of their outer end, therefore, must be regarded as secondary and supplementary in consequence of the primary visceral furrow being carried away from the surface and into the sinus, the remains of the latter persisting as the outlet of the original cleft. At times the remains of the precervical sinus alone appears as a median fistula, in which case a short passage is traceable downward instead of up.

*Branchial Cysts.*—The exceptional opportunities offered by the series of visceral arches and clefts for partial closure and the persistence of an isolated portion of the various furrows and pouches results in frequent production of various forms of cysts and tumors. The most common of these are simple cysts, which differ in character with their origin. If from the external furrows, they are lined with modified integument and are dermoid in type; if from the pharyngeal pouches, their lining approaches the columnar type and their contents are serous. As emphasized when considering true dermoids, the distinction between the productions of transplanted integumentary constituents and true fœtal inclusions, although

often difficult, depends upon the presence of derivatives of all three germ layers. Since consideration of the various forms of branchial cysts and tumors does not fall within the province of this article, the reader is referred to the article on *Branchial Cysts* in Vol. II.

Defective or aberrant development of the pharyngeal pouches and the bordering arches may give rise to malformations of their derivatives.

The *tongue* may suffer from impaired development involving the region of the second arches, since its posterior third originates from the vicinity of their fused median ends, while its anterior two-thirds arises from the unpaired anlage, the tuberculum impar, which grows forward from the basal area. Faulty development of the anterior anlage results in deficiency or absence of the front part of the organ, although the base may be present. Glossal defects are often associated with micrognathus. Various degrees of attachment of the tongue to the floor of the mouth depend upon imperfect differentiation of its anterior anlage. Cleavage and partial doubling of the tongue is observed as a rarer malformation.

Persistence of the median anlage of the thyroid body as the thyro-glossal duct, the upper end of which is normally indicated by the foramen cæcum on the tongue, may give rise to a fistulous canal which descends to terminate in the vicinity of the hyoid bone, or in some cases to open as a median fistula in the neck. Isolated portions of the retained duct may become the seats of cysts.

Pharyngeal diverticula are occasionally observed, being due to local persistence of the inner visceral furrows.

Variations in the development of the *thyroid body* are also connected with the visceral arches, since the lateral anlages of this organ are derived as epithelial outgrowths from the fourth pharyngeal pouch and the median anlage as a similar outgrowth from the ventral wall of the pharynx in the vicinity of the second arches. Accessory thyroids occur in connection with both the lateral and the median lobe, those arising from the persisting remains of the embryonal condition of the latter appear at various levels, including a sublingual and a hyoid group. Disturbed development involving the thymus anlage of the third visceral cleft may lead to the formation of dermoid cysts which are subsequently carried into the anterior mediastinum.

When the closure of the precervical sinus remains very imperfect, the deficiency may lead to the rare malformation known as *cervical fissure*. Coupled with thinning and distention of the floor of the depression, the heart may project through the opening, thereby producing the rare suprathoracic type of *ectopia cordis*. The lungs and thymus have been observed to accompany the displaced heart.

Malformations of the Thorax and Abdomen Depending upon Imperfect Closure of the Ventral Body Wall.—The underlying process in the differentiation of the thoraco-abdominal cavity and the contained alimentary canal from the flat and widely extended germ layers is the ventral folding of the splanchnopleura and the somatopleura. By the approximation and union of the first folds is formed the digestive tube; by those of the second the ventral or anterior body wall, the intervening space being the primary pleuro-peritoneal cavity. In each case closure proceeds from all directions, cephalic, caudal, and lateral, the point of latest closure being the umbilicus, through which for a time the gut-tube communicates with the yolk-sac by means of the vitelline duct. Defective union of these ventral somatopleuric folds, the *membrana reuniens anterior*, results in a more or less extensive median cleft, which may be limited to a small portion of the thorax or abdomen, or involve the entire anterior body wall, reaching from the neck to the pelvis.

The most frequent seat of imperfect closure is at the umbilicus, this region in consequence of closure being here longest delayed, being inherently vulnerable. The simplest expression of such imperfection is *congenital umbilical hernia*, portions of the intestines and sometimes omentum protruding through a ring of unusual size. When the defective closure is more extensive and the abdominal contents are confined by a membranous wall composed of the peritoneum and the amnion covering the umbilical cord, the viscera may push before them the occluding membrane, which becomes converted into the hernial sac, lined by peritoneum and occupied by the displaced organs. This condition constitutes *omphalocele* or *funicular hernia*. The umbilical cord, being invaded by the hernial sac and contents, apparently springs from the sac near its apex or toward the side, the entire length of the cord frequently being greatly reduced. A large part of the abdominal organs may find its way into the hernial sac, which may contain, in addition to a variable length of intestine, a portion of the liver, the stomach, and the spleen.

When the defective union is still more extensive, the resulting fissure may involve the larger part or the whole of the ventral body wall. When limited to the abdomen, the condition is known as *gastroschisis completa;* when including also the chest wall, as *thoracogastroschisis*. In the former case the abdominal fissure is bounded by the ununited somatopleuric folds, which are directly continuous into the amnion. The latter, in conjunction with the peritoneum or alone, may constitute a considerable or even a huge sac, containing the greater part of the abdominal organs (*ectopia viscerum*). The ununited umbilical vessels may course in the wall of the sac without being collected into a distinct cord, the placenta in such cases being often fused with the sac. Spinal curvature, skoliosis, or lordosis is frequently associated with eventration. The thoracic involvement depends upon the extent of the sac; in exaggerated cases almost complete axial rotation with approximation of the upper and lower segments of the trunk may be present. The pelvis and the lower extremities may also share in the defective development, at times the limbs suffering complete backward luxation and extreme atrophy.

At times the defective closure of the abdominal wall is associated with fissure of the intestinal tube, usually in the vicinity of the beginning of the large intestine (cæcum or adjacent colon). The cleft gut is attached to the belly wall behind the opening through which the wall of the intestine may protrude (*ectrophia intestini.*)

Fissure of the chest wall (*thoracoschisis*) may be coextensive with the anterior wall of the thorax, or it may be limited to the partial cleavage of the sternum alone. Since the latter is primarily formed by the blending of two curved vertical cartilaginous bars, arrest of union results in complete or partial fissure of the sternum. In the former case the isolated halves bear the costal cartilages and ribs; in the latter, the defective union may be limited and indicated by an opening in the gladiolus, or, more frequently, by fissure of the ensiform process. Rarely the defective development affects only one of the primary bars, this condition resulting in total absence of one-half of the sternum and the associated costal cartilages. When the defective union is extensive, owing to early arrest of development, the pericardium is uncovered or even wanting, and the heart displaced (*ectopia cordis*). According to the position of the protrusion, suprathoracic, thoracic, and subthoracic varieties of the ectopia are recognized, the second form, in which the heart escapes through the cleft sternum, being the most usual. The displacement of the heart into the abdominal cavity seen in the subthoracic ectopia is sometimes due to a defective diaphragm. When entirely exposed, as sometimes happens, life is prolonged only for a few hours after birth. Usually, however, the organ is more protected, and if the defect be small and the protrusion slight the malformation may be masked by the integumentary covering. Malformations of the heart itself, or of the great vessels, are not uncommon in marked ectopia. Concerning the cause of the arrested development in-





volving the general thoracic wall, little is known, although it is certain that amniotic and other abnormal adhesions play an important part in bringing about displacement of the heart and in preventing union.

*Subumbilical clefts* result from faulty union of the anterior body wall invading the region below the navel, which may be the seat of fissures of varying extent, not only of the immediate abdominal parietes, but also of the associated organs, as the bladder and the external genitals. When the bladder is only slightly involved, the defect may be limited to a small *vesical fissure*, or, when the arrest of development is more extensive, the anterior wall of the organ may be entirely wanting and the exposed mucous membrane covering the postero-inferior wall of the bladder, with the openings of the ureters, be seen lying within the opening, constituting the condition known as *vesical ectrophy* or *ectopia vesicæ*. At times displacement and complete turning inside out (*inversio vesicæ*) may accompany the cleavage as a secondary consequence of traction induced by unusual relations of the allantois and amnion. The pelvis, urethra, and penis are also seats of clefts associated with faulty union of the lower body wall.

Of the various *causes* to which extensive cleavage of the abdominal wall has been attributed, the most potent primary factor, as emphasized by Marchand, is to be sought in the early abnormal attachment between the ventrally placed vitelline sac and the chorion. This union interferes with the normal differentiation of the somatopleuric folds, which form the ventral body wall, from the amnion, the latter in a measure replacing the usual anterior parietes. In conjunction with these abnormalities a possible unusual dorsal union between the chorion and the amnion may hinder the expansion of the latter, with the result of inducing an early over-extension (lordosis) of the embryo, which further favors non-approximation of the component halves of the ventral body-wall and eventration. Early amniotic adhesions undoubtedly play an important rôle in subjecting the anterior parietes to abnormal tension and pull, in consequence of which arrest of development, delayed union, and displacement of organs may follow.

Malformations of the Diaphragm.—Since the partition subdividing the primitive body cavity into the pleuro-pericardial and peritoneal compartments is completed by fusion of segments which for a time are separate, arrested development or delayed union results in abnormal clefts. The formation of an antero-lateral fold —the *septum transversum*—early effects an incomplete isolation of the pleuro-pericardial cavities from the peritoneal space, and foreshadows the appearance of the primitive diaphragm. The latter is differentiated from the cephalic part of the septum, the caudal portion being intimately concerned with the development of the liver. The completion of the diaphragm is delayed for some time, an opening on either side of the primitive gut tube maintaining communication between the peritoneal and the pleural cavity. Finally, when the developing lungs have reached the young liver, the partition is completed by the forward growth of dorso-lateral folds, which fuse with the previously existing anterior segment. From the foregoing sketch it is evident that varying degrees of developmental arrest and delayed union may produce corresponding grades of imperfection in the septum. These include total absence or rudimentary condition of the diaphragm due to failure or insufficiency of development of the component primary folds. More frequently the defects result from the imperfect union of the anterior and posterior segments, and are therefore less extensive. The communications, larger or smaller in size, between the peritoneal and pleural cavities preserve the primary continuity of the serous membrane lining the abdominal and pulmonary spaces, the peritoneum passing directly into the pleura. In general, these defects occupy the posterior half of the diaphragm and are often in the vicinity of the œsophagus, the congenital orifices being much more frequent on the left than on the right. Other defects lie in the anterior part and correspond to the area of weakness between the sternal and adjoining costal portions.

The most conspicuous result of these imperfections is the displacement of organs as *diaphragmatic herniæ*. These may include a portion of the right lobe of the liver on the right, and the stomach, left liver lobe, spleen, and a variable part of the intestine on the left (E. Schwalbe [95]). Usually the dislocated viscera lie entirely free within the pleural cavity; exceptionally they are

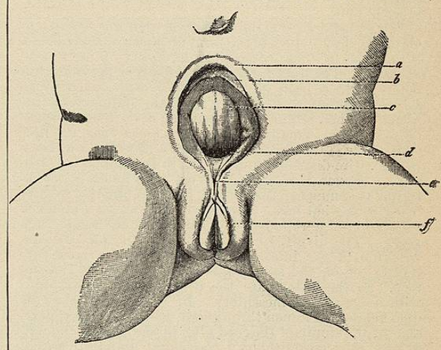


Fig. 4682.—Abdominal Fissure with Open Bladder. *a*, Skin; *b*, peritoneum; *c*, bladder; *d*, cavity of bladder; *e*, urethral groove; *f*, nymphæ. (Ziegler.)

enclosed within a hernial sac derived from the serous membrane. The influence of the intruding viscera upon the lungs and heart may be unfavorable, and these thoracic organs, particularly the lungs, in consequence often exhibit the effects of impeded development. The defective development of the diaphragm is frequently associated with other malformations, such as cleft sternum anteriorly, or imperfectly closed spinal canal dorsally. In certain cases of subthoracic *ectopia cordis* the heart escapes from the chest through the imperfections in the diaphragm, which are often associated with defective closure of the belly wall.

Malformations of the Digestive Tract.—*Mouth.*—Malformations of the boundaries of the oral cavity—the lips, cheeks, and palate—together with those of the jaws, usually depend upon arrested development and defective union of the embryonal processes which surround the primitive oral recess. These defects have been already considered under Facial Clefts (page 700).

The *tongue* likewise has been already considered in connection with imperfect development of the visceral arches (page 702), with the formation of which its origin is related.

The *pharynx* is the seat of fistulæ, cysts, and diverticula resulting from aberrant development of the primary pharyngeal pouches, in connection with which they have been noted (page 702). The slight dorsal recess which usually marks the transition of the pharynx into the œsophagus may be the starting-point of a considerable pouch extending between the spine and the gullet.

The *œsophagus* very rarely is entirely wanting or replaced by a fibrous cord; more usually the gullet is defective only in certain segments. Thus it may end blindly a short distance below the pharynx, or, on the other hand, its lumen may terminate above the stomach, the œsophagus being continued by a cord of fibrous tissue attached to the pharynx above. The atresia may be accompanied with more or less extensive dilatation, not infrequently associated with an abnormal opening into the lower part of the trachea (Hoffmann [96]). A divided condition of a portion of the œsophagus has also been observed.

The *stomach* is only rarely the seat of congenital mal-