the subject having been left-handed. The superior longitudinal sinus joined the left lateral sinus. The apex of the heart lay about four inches to the right of the mid line and a right aortic arch passed back to the right of the vertebral column and continued downward in that relation to the spine. A left innominate artery, right common carotid and subclavian sprang from the aortic arch. The left lung consisted of three lobes, the right of two, and the bronchi were transposed, the right passing beneath the aortic arch. The liver lay on the left, the stomach protruding to the right, while the spleen enjoyed its usual but reversed relations on the right. The duodenum, pancreas, cæcum, sigmoid flexure, and rectum were all transposed. The left kidney was lower than the right and the right testicle lower than the left.

The explanation of the production of situs transversus shares the uncertainty of our knowledge concerning the cause of the asymmetry which normally affects the heart and great blood-vessels and other organs. The early primitive heart, as is well known, after fusion of the two isolated primary heart tubes, for a short period occupies a median position as a straight canal which receives the vitelline veins at its caudal end and gives off the truncus arteriosus from its cephalic extremity. Very soon, however, marked flexion toward the right takes place and inaugurates the conspicuous asymmetry which henceforth distinguishes the heart and later involves the large arterial trunks.

In seeking an explanation of the constant flexion of the growing heart tube toward the right, the facts presented by the development of the chick are very suggestive. The earliest deflection of the heart takes place while the embryo lies extended upon the vitelline sac and before the torsion of the head toward the left has occurred; the primary cause of the cardiac expansion toward the right, therefore, cannot be referred to the twisting of the head and the application of its left side to the yolk sac. On the contrary, it is probable that the tendency of the rapidly increasing head to seek support for its broad lateral surface on the left side rather than the right is influenced by the development of the heart. The preponderance of the left vitelline, or omphalo-mesenteric vein, which normally is larger than the right in consequence of the greater development of the corresponding half of the vasculosa, has been regarded by Dareste and by Martinotti as the primary factor in causing the deflection of the heart tube in the opposite direction. Indeed, no one can carefully study the relations and evident impression of the left vitelline vein to the early heart in the chick embryo without recognizing the direct influence of this vessel in producing the right-sided expansion of the heart loop. The subsequent suppression of the right vitelline vein still further aids the early influences of the larger left vessel. It is not improbable that similar influences affect the development of the mammalian heart, although the inequality of the vitelline vessels, as shown by van Beneden in the rabbit, is conspicuous in the secondary changes which lead to the preponderance of the left vitelline artery.

The commonly accepted view that deflection of the primary heart toward the left is the initial morphological factor in producing transposition of the viscera finds support in the observations of Kölliker, Dareste, and others, as well as in the experiments of Fol and Warynski. These investigators likewise show that the reversed position of the early heart is associated with reversed torsion of the cephalic segment, so that the embryo rests with the right side of its head upon the yolk. While we may accept, therefore, unusual size and persistence of the right vitelline vein, associated with a corresponding diminution and suppression of the left, as the immediate cause of a reversed torsion of the heart tube and the subsequent situs inversus, we are compelled to recognize further influences to account for the fact that the abdominal viscera may be transposed, although the thoracic organs retain their normal position.

In seeking an explanation of such conditions, an examination of the causes leading to the normal asymmetry of the abdominal viscera will furnish suggestive facts. Kölliker, and especially His, have shown that the changes affecting the umbilical and the vitelline veins have much to do in determining the relations of the liver and the stomach. In the early embryo, the vitelline veins return the blood from the vascular area and, as a common trunk, open into the primary auricular extremity of the heart. After the establishment of the allantoic circulation, the two umbilical veins course in the lateral belly walls, passing beneath the diaphragm and over the primary liver anlage, to empty into the *sinus reuniens*, a transversely placed venous channel, which receives all the principal venous trunks—the vitelline, the umbilical, and the ducts of Cuvier. After a time the connection of the umbilical veins with the sinus reuniens is broken when the formation of a vascular network within the rapidly growing liver takes place. The right umbilical vein, always less well developed than the left, subsequently largely undergoes atrophy, while the left umbilical vein increases and becomes the channel for the blood returned from the now rapidly augmenting placental circulation. The vitelline veins, which ascend at first in front of the intestinal canal and, higher up, lie on either side of the duodenum and the stomach, form transverse communications which thus enclose the duodenum within two vascular rings. The latter undergo partial atrophy in such manner that the right half of the lower and the left half of the upper annulus disappear, the remaining parts forming the upper part of the portal vein. The primary relations of the persistent portions of the venous rings to the primitive gut tube are preserved in the spiral course of the portal vein around the duodenum; the stomach lies to the left of the portal vein.

Since, in general, the usual situation of the liver and stomach are influenced by the persistence of the left venous trunks, the effect of the exceptional retention of these stems on the right side offers an intelligent explanation of the conditions producing transposition of these organs, the relation between a transposed stomach and a reversed portal vein being particularly intimate. Lochte[26] has emphasized, and we believe rightly, the responsibility of the omphalo-mesenteric and the umbilical veins in the production of transposition of the abdominal viscera, in this manner accounting for the reversed position of these organs when associated with normally disposed thoracic contents.

While the heart tube is extremely sensitive to influences inducing transposition, the impression of the vitelline veins on this organ is exerted only so long as these vessels have a direct communication through the sinus reuniens with the primitive heart. After these veins suffer interruption by breaking up into capillary networks within the primary liver, their influence no longer directly affects the heart, but, in conjunction with that of the umbilical veins, is expended upon the abdominal organs, which may be regarded, in a measure, as having an independent development. Since the modifications of the veins occur relatively late, and after the definite relations of the heart are established, the transposition of the abdominal organs may take place subsequently to the normal development of the heart and other thoracic viscera. Regarding the primary cause, which results in the persistence of the right venous trunks of the embryonic area, nothing is known. The very common, but not invariable (Koller[27]) transposition of the viscera observed in the right member of monomphalic double monsters is referable, according to Lochte, to the reversed relations which the right fœtus bears to the umbilical vein.

Duplicities.

The conspicuous malformations embraced in this group have attracted the study and the speculation of the most competent observers from the days of the Greek philosophers to the present, and even to-day, notwithstanding the advances in our knowledge of the primary phases of development, no problem of teratology calls forth more

divergent opinions than the production of double monsters.

The salient peculiarities of these malformations readily suggested an origin by union, Aristotle holding that double monsters in viviparous animals were due to fusion of two yolks. Such views held sway for many centuries as the generally accepted doctrine, until the bitter discussions of ovists and animalculists, regarding the relative importance of the ovum and the spermatozoa, were extended to the production of duplicities by the rival schools. Lemery, in 1724, first advanced the opinion that double monsters resulted from the union of two embryos within the uterus—a theory, however, that met many opponents, among whom were Haller and Wolff. The objections of the latter were based upon his insight into the normal processes of development which his observations had taught him were incompatible with the assumption of a fusion of embryos already well advanced in their formation. Wolff pictured the possibility of a double monster arising within an originally single anlage* as the result of divergent growth due to "surplus vegetation."

During the first half of the nineteenth century the writings of the foremost authorities, among whom were I. F. Meckel, Johann Müller, Geoffroy St. Hilaire, Gurlt, Otto, Bischoff, and others, indicate an abandonment of the older conception of fusion as the union of two ova or of well-advanced embryos and the acceptance of the doctrine of fusion in a modified sense, it being recognized that the union must take place at a very early stage. Meckel, however, dissented from the generally accepted explanation of double monsters, as the result of the union of embryonic areas primarily distinct, and held, on the contrary, that such malformations might be produced by the excessive growth of the component halves of a single embryo due to unusual formative energy. Meckel thus appears to have first suggested the theory of fission, which subsequently had, and still has, many enthusiastic supporters.

The later writers who have busied themselves with the discussion of the production of double monsters constitute two schools: the one regarding the duplicity as the result of the union of two primary anlages in a single ovum; the other, as the result of a cleavage of a single anlage. Among the supporters of the first view may be mentioned Panum, Foerster, Dareste, Rauber, Gerlach, Marchand, Ziegler, and others, while the "fission" theory has been defended by Dönitz, Dittmer, Oellacher, Ahlfeld, and not a few later followers.

In considering the merits of these opposed views concerning the production of double monsters, it may be accepted as a fundamental principle that the initial changes leading to duplicity occur during the very earliest stages of development, an assumption of either fusion or cleavage of advanced embryos being untenable. The present conception of *fusion* recognizes the presence of two originally distinct anlages within a single ovum; these may remain separate and develop independently, leading to the formation of twins, or they may come in contact during growth and undergo more or less extensive union, thereby producing some variety of double monster. The fact that in such unions fusion occurs always between parts which are identical in character, as skull with skull, or liver with liver, although not necessarily at points identical in situation, has been advanced as an argument of weight against the acceptance of the fusion theory. It must be remembered, however, that equally remarkable exhibitions of selective affinity (*Loi d'affinité de soi pour soi* of St. Hilaire) are displayed during the normal processes of development, in the approximation and fusion which the somatopleura, splanchnopleura, and other originally separate parts undergo in the evolution of the body walls, the gut tube and organs developed from symmetrical halves.

* The writer adopts the convenient German word, "Anlage," as indicating the primary formative area of an organ, or of the embryo, as more satisfactory than any of the numerous English synonyms that have been suggested.

The explanation of the union of similar parts in double monsters is to be found in the extremely early age at which junction is effected and the inherent attraction of the subsequently produced differentiating tissues for their own kind, muscle seeking muscle, connective tissue joining connective tissue, and epithelium fusing with epithelium. The experiments of Born,[28] in which he succeeded in grafting portions of one amphibian larva upon another, afford many suggestive facts bearing upon the malformations under consideration. Examination of the artificially produced composite larvæ showed that in consequence of the tissue affinity, like organs became united by the fusion of their specific components; thus, the spinal cord of the anterior segment of one larva joined the like structure of the posterior part of a second; the sectioned immature digestive tubes united into a common canal, the Wolffian ducts sought each other, while among the simpler fusions were liver with liver, cartilage with cartilage, cutis with cutis, and epidermis with epidermis. Gemmill[29] confirms the law of union of homologous structures and points out that the primitive embryonic axis, the notochord, is tardier in uniting than either the neural or the digestive tube. It is to be noted that such direct unions are possible only in the early formative condition of the tissues; when once matured, union is effected only by means of comparatively elaborate reparative processes.

The *fission theory*, as presented by its most enthusiastic supporter, Ahlfeld, regards the duplicity as the result of cleavage of a single anlage during the very earliest stages of development, before the formation of the primitive streak. The earlier the cleavage, the more complete the division of the anlage, or, conversely, the longer deferred, the more incomplete the fission. The cleavage force is probably expended earliest and most forcibly upon the cephalic pole of the anlage, from which it follows that partial division of the upper half of the body is so commonly encountered. According to Ahlfeld, the immediate agency in producing the cleavage is to be sought in the mechanical resistance offered by the zona pellucida in consequence of an abnormal increase of the formative material. Since the greatest force exerted by the zona pellucida will be expended on the most prominent part of the embryonal mass, later the cephalic portion of the embryo, the early and profound cleavage affects this segment. Ahlfeld's conception of the results of cleavage so induced includes an associated secondary rotation and divergence of the separated segments of the anlage in proportion to the extent of the fission. If the cleavage be complete and the pressure of the zona pellucida be exerted equally on all portions, the segments will separate but remain parallel; if the cleavage be incomplete, and, therefore, the anlage be still undivided throughout part of its extent, the separated portions will bend in opposite directions, or diverge, thus producing anterior or posterior duplicity. In case the cleavage is complete, with the exception of a limited undivided portion at either cephalic or caudal pole, the segments may diverge and rotate until their axes form a straight line, as in the conspicuous examples of craniopagus, where head is attached to head and the body axes coincide.

The ingenious theory advanced by Ahlfeld, as sketched above, in support of the fission doctrine does not stand the test of embryological criticism, since, as pointed out by Gerlach and emphasized by Marchand, the assumption, that the early embryonic anlage, constituting a part of the delicate and yielding blastodermic vesicle, can be influenced by the attenuated zona pellucida to the extent of inducing a mechanical cleavage, is not in accord with the facts of development.

Although neither the theoretical views of Ahlfeld concerning the production of double monsters, nor the universal application of fission in explaining all forms of duplicity accorded by this author, can be accepted without challenge, yet it must be admitted that certain types of anterior incomplete duplicity are accounted for more satisfactorily by an assumption of cleavage of the anterior end of a primarily single anlage than by fusion.

Were two separate anlages to unite to an extent necessary to produce an anterior doubling of the form shown in Fig. 4655, it is difficult to admit that the anterior ends of the primary embryonic areas would fail to become likewise blended during the development of the prominent cephalic segments. We are compelled, therefore, to seek an explanation of anterior incomplete duplication in some process resulting in the doubling of the early head end to a greater or less degree.

Gerlach, who presents in his admirable monograph [30] a critical analysis of the various theories regarding the production of double monsters, suggests a modification of the usual conception of fission which has much to recommend it. According to the later views of this author,[31] incomplete anterior duplication results not in consequence of a fission of the anterior end of the anlage, but is the result of "bifurcation" accompanying the development of the cephalic end of the young embryo along diverging axes. Bifurcation in this sense fundamentally differs from fission, since the former is the product of active formative processes, the latter the passive result of mechanical forces. Whether the duplication and divergence of the axes are the direct result of mechanical influences, as held by Klaussner,[32] or whether bifurcation occurs independently of such forces, as assumed by Marchand,[33] it is certain that the impression inducing the division affects the anlage at an early stage, and that the degree of duplication is directly proportionate to the time at which the influence was exerted—the earlier its action the more profound the impression and the more extensive the anterior duplication. Examples of comparatively late impressions are seen in the slight duplicity involving limited parts of the head.

The suggestive facts contributed by the results of the interesting investigations in experimental embryology by O. Hertwig, Roux, O. Schultze, Driesch, Wilson, Morgan, and others, are of importance in adding to our understanding of the fundamental principles of both normal and abnormal development. These investigations have shown that in the segmenting ova of amphibian and lower forms the first cleavage virtually establishes a differentiation into right and left body halves, since under normal conditions from each of the two segmentation cells, or blastomeres, a half embryo arises. Under modified conditions, however, each blastomere is capable of producing an entire perfect, although undersized, embryo. The conditions necessary to secure the latter result seem to be such that bring about a readjustment of the egg materials contained within the blastomere to correspond, in a sense, in arrangement and equilibrium to the entire ovum. Morgan [34] discovered that according to the position of the blastomere half-embryos, or whole dwarf embryos, could be produced at will. If, after destruction of one blastomere of the two-celled stage, the other be retained in its normal position, a half-embryo resulted; if, on the other hand, the blastomere be inverted, either a half-embryo or a whole dwarf was produced. These observations are in accord with the discoveries of O. Schultze,[35] who found that by fixing a frog's ova in an inverted position for about twenty hours he obtained, with remarkable regularity, double malformations instead of the usual simple embryos. It is of interest to note that the experiment was successful only when the eggs were inverted as soon as the first cleavage had been completed; double monsters were never produced when the misplacement was effected before or after this stage. The resulting malformations presented various arrangements in the relation of their axes; sometimes one blastomere developed into a complete dwarf, while the other produced only the anterior segment. In some cases the dwarf embryos were united along their ventral surfaces, or back to back; in others a common trunk terminated in two distinct diverging heads; exceptionally, the cephalic segments were directed in opposite directions.

These experiments point to the important conclusion that each of the two primary blastomeres contains the materials necessary to produce an entire body, although under usual conditions of development each contributes but half. O. Hertwig [36] has recently expressed his belief that duplicity is associated with the occurrence of double gastrulation, such variation resulting in the production of the double malformations conspicuously seen in the lower vertebrates. He also regards the duplicities among the amniota as referable to a modification of the same process.

Etiology.—The complete or partial symmetrical duplicity, whether produced immediately by fusion or cleavage, is evidently the result of primary disturbances or unusual conditions affecting the primitive germ mass. The determination of the initial causes which bring about double malformations has been, and still is, one of the most difficult and vexed of teratological problems toward the solution of which little more than speculation can be offered with our present imperfect knowledge.

A. The assumption of inherent peculiarities within the unfertilized ovum, while perhaps of much importance for the current theories concerning the causes leading to the production of double monsters, is speculative and incapable of direct demonstration by the means at the disposal of the biologist.

Suggestive facts, pointing to the possibility that at times the peculiarities of the ovum may be responsible for the production of double monsters, are afforded by the observations of Rauber and of Born. These experimenters showed that the eggs of certain individual fishes were conspicuous by reason of the frequency and repeated occurrence of double malformations arising from their development. It cannot be assumed, however, that the existence of such predisposition can be discovered in any recognizable morphological peculiarity in the ova.

The presence of more than one nucleus, or germinal vesicle, within the ovum has long been regarded as a condition favoring the production of double malformations. The observations of Féré [37] on the hen's eggs show that while in certain cases the development of such ova leads to the formation of two distinct embryos, in others fusion of the early embryonal areas takes place and duplicity results. Wetzel [38] describes interesting examples of multiple areas originating in snake eggs, and regards the evidence convincing in establishing such origin for certain types of duplicity. In addition to the many instances encountered in the eggs of birds and of the lower forms, a number of observers, Franque, Stöckel, Rabl, and Schumacher and Schwarz, have noted human ova containing more than a single nucleus. The last-named authors [39] regard such eggs as capable of giving rise to duplicities. Blanc [40] agrees with Dareste in holding that all double forms originate from ova with two nuclei. O. Schultze,[41] while less radical, regards the presence of two nuclei as one of three possible sources of double malformations.

The most serious obstacle in accepting such origin of duplicities is the difficulty of explaining satisfactorily the fertilization of the double ova. According to our present conceptions relating to the higher animals, fertilization implies the addition to the egg of a definite number of paternal chromosomes and a centrosome through the entrance of the spermatic filament and the formation of the sperm-nucleus. Since the quota supplied by a single spermatozoon is sufficient to unite with only a single egg-nucleus, it follows that no provision is made for the fertilization of the second germ. The assumption, frequently accepted, that fecundation in these cases is accomplished by the entrance of more than a single spermatic element—polyspermia—seems very doubtful when applied to the human species, since it is probable that this never takes place so long as the ovum is healthy and capable of developing. Sobotta,[42] one of the most recent writers who has reviewed the merits of the double-nuclei theory, rejects the latter as insufficient to account for double monsters. Broman,[43] in meeting these objections to the foregoing theory, holds that certain double-tailed forms of spermatozoa (more fully described under the next heading) are capable of fertilizing the two nuclei, since by this means two centrosomes,

as well as a double quota of paternal chromosomes, are introduced into the egg.

B. Peculiarities of the male sexual cell, when assumed as inherent predisposing influences, are as much a matter of speculation in relation to the production of double monsters as are similar causes attributed to the ovum. The aberrant forms of spermatozoa, described by many observers and regarded by some [44] as physiological, have been considered as directly connected with the production of duplicity, being looked upon as homologous with the ova with two germinal vesicles. Retzius,[45] however, inclines to the view that doubling of the tail results from separation of the two filaments, which, probably, normally constitute the axial filament. Broman has exhaustively studied these atypical forms and divides them into:

(*a*) Spermatozoa presenting deviations in size—giant and dwarf cells.

(*b*) Spermatozoa with a single head, but with two or more tails.

(*c*) Spermatozoa with two or more heads with one or more tails.

(*d*) Spermatozoa deviating from the normal in the form.

Of these, the variations included within groups (*a*) and (*b*) are those accredited as being most closely related to the production of double monsters as assumed by Ballowitz [46] and Broman. The latter excludes the influence of the double-headed forms since their morphological peculiarities impede progress to such extent that the handicap precludes victory in the race toward the ovum with the normal competitors. The double-tailed spermatozoa, on the other hand, possess an advantage both in their more efficient propelling apparatus and in the double centrosomes which the filaments convey. Broman regards the double-tailed forms as important factors in producing duplicities, not only since they may possibly lead to fertilization of ova with double nuclei, but also since, according to this author, they may supply the impulse resulting in the later subdivision of the segmentation mass into two germ centres.

Abnormal segmentation, as an assumed distinct cause of duplicity, is closely related to the foregoing group, since polyspermia is regarded as a potent factor leading to such variation. The considerations weighing against the latter assumption, as applied to the higher animals, are, as already noted, the improbability that more than one spermatozoon gains entrance to a normal ovum and the probable inability of an ovum so invaded to undergo development, since the lessened resistance implies diminished vitality.

Although abnormalities of segmentation *per se* cannot be regarded as playing an essential rôle in producing double malformations, the nearly related condition, in which more than a single formation centre is established, must be regarded as the most important immediate forestep of duplicity.

The difference between the results of the development of the separated first or second pair of segmentation cells and of the subdivided germ mass originating from the normal cleavage of the ovum must be distinguished. The first conditions would probably give rise to two entirely distinct individuals; under the second would follow the production of two closely related germinal areas capable of undergoing fusion.

The most important influences leading to double monsters are, therefore, those that are expended upon the segmented ovum during its early differentiation and result in the establishment of two centres from which development proceeds. Windle [47] regards such condition as dependent upon superfluity of germ-plasm attributable to faulty extrusion of the polar bodies following the entrance of double-headed or atypical spermatozoa [48] or of polyspermia. The latter is also accepted by Duval [49] as the chief cause of the redundant development. Laguesse and Buê,[50] incidental to the description of an early anterior duplicity of only 19 mm. length (probably the smallest human double monster ever recorded), follow Duval in assigning to polyspermia an important rôle.

Although little more than speculation, the most plausible view concerning the origin of the two formative centres, in the light of the more recent experimental studies upon segmentation, attributes the division of the blastula to influences which impress the ovum before their effects are manifested in the appearance of the two germs. That these influences may at times be external is suggested by the experiments of Schultze, Wetzel, Wilson, Loeb, and others with the eggs of the lower forms under modifying conditions. Regarding, however, the development of the higher animals, the assumption of influences dependent upon internal causes seems more plausible. That such may be paternal, as well as maternal, is supported by direct observation. The period at which the deviation from the normal development first becomes definite probably varies, in some instances closely following the early stages of segmentation, in others not until the blastodermic vesicle has been formed.

In connection with the production of true parasitic duplicities, distinguished by great primary inequality of the two anlages, the possible importance of a polar body as the origin of the parasite has been suggested. In our present knowledge, the polar bodies must be regarded as ova of greatly reduced size, but capable of being fertilized (Sobotta [51]). The development of such cells into an imperfect blastula, and later parasite, has been assumed by Marchand [52] as a plausible explanation of the origin of the lesser embryo. These true parasitic duplicities must be distinguished from those in which the disparity between the germs is due to differences in growth and nutrition of what originally were equal anlages.

Classification of Duplicities.—Any adequate grouping of double forms must take into account the developmental as well as the morphological characteristics of the malformations, hence the classifications proposed by different teratologists from time to time have exhibited, more or less markedly, the impress of their views regarding the production of these abnormalities. Although the influence of the teachings of St. Hilaire, and especially of Foerster, is evident in the classifications suggested by later writers, the extent to which the theory of fission or of fusion is accepted as sufficient for the explanation of duplicities largely determines the classification adopted. That proposed by Ahlfeld represents a fission-grouping of the most pronounced type, while the elaborate classification advanced by Taruffi is based upon the opposite assumption of fusion.

In view of the probability, now admitted by many, that although some forms of duplicity are attributable to fission, in many others fusion occurs, a classification is desirable which shall take into account the possible variations in the mode of production. This necessity was recognized by Cleland, who, although accepting fission as the primary process, included in his grouping secondary unions. The division of duplicities adopted by Marchand, which includes the best features of the classifications of St. Hilaire and of Foerster, presents a happy compromise in accordance with recent opinion; this classification, therefore, forms the basis for the grouping here followed.

Duplicities fall into two chief divisions: those in which the two primary germ masses, or anlages, are originally *symmetrical*, and those in which, from the beginning, marked discrepancy exists; the latter are, therefore, *asymmetrical*.

Symmetrical Duplicities.—These may be either *complete* or *incomplete*, the former group including the double forms in which the bodies of the two embryos are entirely distinct, as in twins developed from a single ovum, the latter group embracing the double forms which present more or less extensive union, as exhibited in the various types of double monsters.

Twins developed from a single ovum are distinguished from those originating from different eggs by the possession of a common chorion, although an amnion and an umbilical vesicle are usually formed for each; such twins are said to be *monochorionic*. They are further distinguished by remarkable similarity in their physical, as

well as mental, characteristics, being always of the same sex, complexion, and feature. In recognition of these close resemblances, and of their assumed origin by complete fission of the original anlage, Ahlfeld applied the name, "homologous twins" to these duplicities. The only suggestion of union presented by such fœtuses is the single placenta which serves as the common source of nutrition. The conditions of nutrition and the rate of growth of one-egg twins may be so similar in both individuals that their development is *equal*. In exceptional cases the one may exactly correspond with the other in length and weight, as shown by the careful observations of Schatz.[53] More commonly, however, the development of such twins is *unequal*, as evidenced in the more or less marked discrepancy in their size and weight. If the difference is slight, the less favored individual suffers only to an unimportant degree and after birth is fully able to maintain an independent existence. If, on the other hand, the nutrition of one fœtus becomes seriously impaired, its death may occur and its body be subjected to pressure by the increasing bulk of the more fortunate companion. When such conditions arise during the earlier months of pregnancy, the dead product of conception is pushed against the wall of the enveloping sac and later the uterus, and subjected to gradual compression, which results in flattening and distortion to such extent that it is known as *fœtus papyraceus*.

The intimate relations between the placental circulations of monochorionic twins include not only a common placental area containing anastomoses of the capillaries of the chorionic villi, but also, with few exceptions, a superficial anastomosis between the smaller twigs of the umbilical vessels.

The most constant and important of these direct communications between the circulatory systems of the twins is that formed by the capillaries within certain villi to which the blood is supplied by vessels from one fœtus and carried away by those from the other. These areas of *capillary transfusion* usually occur along the blending line of the two placentæ and are designated by Schatz as the *third placental circulation*. This author concludes from his careful observations that the most common type of placental anastomosis is where, in addition to the constant communication existing within certain villi, a single, seldom double, *arterial* anastomosis is formed between the superficial vessels. The next most frequent type is distinguished by a single, rarely double, superficial anastomosis of both the *arteries* and the *veins*. The additional possible relations of the superficial vessels, *venous* union and *absence* of anastomosis, are comparatively rare.

In consequence of the communications within the villi common to both circulations, it follows that in some villi the blood supplied by one fœtus, A, passes into the vessels of the other, B, and, conversely, blood contributed by B enters the circulation of A. The transfusion is, therefore, opposed. Although an accurate balance of these contrary blood streams is supposable, in fact a greater or less discrepancy exists with few exceptions. In many cases this difference is compensated by the superficial anastomosis, but in others this means does not suffice, and the adjustment of the dynamic asymmetry must be attempted by functional changes within the fœtuses. The necessity thus established may be productive of only inconsequent alterations; on the other hand, when associated with obstruction of the blood current within the umbilical vein of one twin, it may result in profound and even disastrous change.

Unequal Monochorionic Twins.—Since equal growth of one-egg twins implies an equal apportionment of the placental area, any condition that materially disturbs the nutritive balance tends to affect adversely the less favored fœtus. Among the early sequelæ of such disturbances are the impaired, or even arrested, growth of the heart and the appearance of symptoms resulting from the stasis induced by obstruction of the blood stream within the weaker fœtus, expressed by the hepatic congestion and subsequent atrophy, œdema, and ascites.

When impairment of the circulation of the weaker fœtus occurs at an early period, the heart may suffer to such extent that not only is its development arrested, but atrophy and even disappearance of the organ may follow, thereby contributing to the malformation known as *acardius*. The loss by the affected fœtus of its capability of maintaining an independent nutrition is compensated, to a greater or less degree, by the stronger twin, which, by means of inosculations established between its placental vessels and those of the impaired fœtus, assumes the nutrition of its weaker mate. By virtue of such arrangement the blood current within the latter suffers reversal, usually a single umbilical artery conveying the blood to and a corresponding vein from the body of

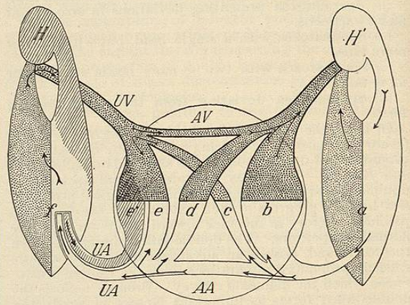

Fig. 4646.—Diagram Showing Relations of Blood Stream of Autosite and Parasite in Acardius. Circle indicates fused placental areas. Blood passes from autosite (*a*) by umbilical arteries to placenta (*b*); in addition to returning to heart of autosite (*H'*), part enters circulation of parasite by villous (*c*) and by arterial anastomoses (*AA*), following the paths indicated by arrows. The reversed current passes by umbilical artery into arteries of parasite, finding its way into the venous stems in consequence of obstruction and obliteration of heart (*H*) and associated large vessels, and returns to placenta by umbilical vein and thence by venous anastomoses (*AV*) into circulation of autosite. Unshaded areas represent arterial paths; light stipple, venous circulation of fœtus; dark stipple, venous paths; lined areas, obliterated tracts. (After Schatz.)

the dependent fœtus. Under such conditions of unequal development one twin becomes in a sense a parasite, since the continuance of its life may be entirely dependent upon the circulation of the other.

The period at which the fœtus becomes thus dependent exerts a profound influence upon the general development which it attains. Occurring early, before the organs and definite form of the fœtus are well established, the formation of such parts may be rudimentary or entirely suppressed. In consequence of the inadequacy of the donated circulation, which at best is only an imperfect substitution, it is usual to find acardius associated with conspicuous deficiencies of other parts of the body. The head particularly is imperfectly formed, often bearing little resemblance to the normal part. When partially developed, the condition is known as *paracephalus*, in which the brain is very rudimentary or entirely wanting, the eyes are imperfect or absent, and the face is malformed. Total absence of the head constitutes *acephalus*. These deformities of the head are usually associated with malformations of the trunk and limbs, the former being abnormally small, contracted, or misshapen, the latter defective or partially suppressed. The upper extremities are particularly prone to suffer, not infrequently being entirely wanting, although the lower limbs, by reason of their more favorable relations to the nutritive vessels, may be fairly well developed. In rare cases even these suffer, so that only a rudimentary single inferior extremity is present.

The internal organs, especially those closely related to the vascular system, are profoundly affected. Thus, in addition to lack of development of the heart, the liver is

usually wanting, and, further, the lungs are more or less rudimentary. Defective development of the digestive tube, the kidneys, and other abdominal organs often coexists.

When the arrest of development is of the highest degree, the body of the dependent twin becomes reduced to a misshapen mass presenting slight resemblance to the human form. Such monsters, which may be little else than irregular nodules invested with œdematous skin and attached by an umbilical cord, constitute the form termed *amorphus*.

Acardiac Monsters.—Reference has been made to the occurrence of acardiac monsters in consequence of impairment of the placental circulation of one of monochorionic twins. It will be desirable, therefore, to consider more fully the group of malformations in which partial or complete absence of the heart is often a conspicuous, but by no means essential, feature. The distinguishing characteristics of a true acardius include not only the impaired development of the heart, but also a circulation dependent upon a stronger fœtus and a *reversal of the blood current*.

The views regarding the production of acardius held during the middle and immediately succeeding decades of the last century by many teratologists, including H. Meckel, Dareste, and Panum, assumed primary defect or death of the heart as the essential factor in bringing about this condition, the cardiac imperfections, in the first place, being caused or accompanied by primary defects of the entire embryo.

Claudius, however, opposed this opinion and maintained that in placental anastomoses lay the chief factor, since, according to this author, the arteries of the two fœtuses united and thus brought the two blood streams into direct opposition. Assuming that the heart of one twin acted less vigorously than that of its mate, Claudius held that the blood current propelled by the stronger heart overcame the circulation of the weaker and reversal of the blood stream within the latter followed. In consequence of this change in the direction of the blood current, Claudius assumed that the heart of the weaker fœtus becomes embarrassed and impaired, and is brought to a standstill, followed by atrophy and final disappearance. Absence of heart was regarded, therefore, by this author as a constant condition of all forms of acardius.

The particular service of Claudius was to emphasize the important fact, originally observed by Hempel, of the reversal of the blood stream and to contradict the assumption of an inherent defect of the heart as necessary for the production of acardius. The effects attributed by Claudius to the arterial anastomoses and the supposed struggle for supremacy between the blood currents are less happy, since, as pointed out by Schatz, the assumed opposition does not exist, for instead of being driven against the stream propelled by the heart along the umbilical arteries, the blood entering the circulation of one fœtus from that of the other must pass in the direction of least resistance. This being toward the placenta, and not toward the heart, the transferred blood will join that already journeying along the umbilical arteries to the placenta, and within the latter pass into the returning veins, and so on to the heart to the nutrition of which it will contribute instead of impair. Ahlfeld has championed the views advanced by Claudius and attempted by new assumptions to strengthen their defective arguments. Thus, this author regards the capillaries of the placental villi as the seat of the reversal of the blood stream, and suggests that from the beginning the acardius may be regarded as an "allantoic parasite" in consequence of the tardiness with which it forms its placental attachments. According to Ahlfeld, during this late development, the allantois of the weaker fœtus grows into that of the stronger, in the course of which process anastomoses become established between the two circulations; as a result, that of the less vigorous twin is overpowered by the blood stream propelled by the stronger heart.

Although recognizing, as all now must, that the explanation advanced by Ahlfeld is incompatible with our present knowledge concerning the formation of the early attachment of the human embryo to the serosa by means of the belly stalk and the absence of a free allantoic vesicle, Marchand inclines toward a modified acceptance of somewhat similar views. This authority assumes a primary inequality of the two embryonic anlages with a corresponding discrepancy in the development of the mesoderm, belly stalk, amnion, and umbilical vesicle of the two embryos. In consequence of this unequal growth, asymmetry results by which the smaller fœtus becomes united by its belly stalk to that of the larger in such manner that they represent a form analogous to double monsters with posterior union and diverging axes. The anastomoses between the blood-vessels of the dissimilar placental areas furnishes the path through which the circulation of the weaker fœtus is overpowered and replaced by the extension of blood stream of the stronger. The defect of the above theory lies in its inapplicability to the explanation of the important group of hemiacardii in which the changes may appear so late in intra-uterine life that the heart and other organs closely associated with the development of the circulation are affected to only a relatively slight degree.

It is to the careful investigations of Schatz that we are indebted for a comprehensive view of the acardii and the related forms of malformation. The conclusions of this author form the basis of the opinions here expressed. Before entering upon a consideration of their production, it will be of advantage clearly to appreciate the groups into which these malformations fall. They are: *holoacardius*, in which the circulation is derived *entirely* from the stronger twin, irrespective of the presence of a more or less perfect heart in the affected fœtus; *hemiacardius*, in which only a part of the fœtus is supplied by the stronger heart, the remainder being nourished from the circulation of the affected fœtus. It is sufficient for the production of a hemiacardius that the reversed blood current is limited to one umbilical artery and only a lower extremity is supplied by donated blood. On the other hand, the entire body of the hemiacardius, with the exception of a small part, may be nourished by the reversed blood stream. Schatz recognizes an additional group of analogous malformations, *pseudoacardii*, in which reversal of the circulation never occurs and placental anastomoses are wanting. *Microcardius* and *macrocardius* are conditions of under- and over-weight of the heart depending upon the variations of nutrition associated with modifications of the placental circulation of monochorionic twins.

Reversal of the circulation, therefore, is the one condition constant in all forms of true acardius, complete or partial alike. Absence of the heart is not, since in hemiacardius developed at a late period this organ may be present and even functionating; conversely, single, unassociated embryos sometimes possess hearts no more perfectly developed than those of recognized acardii.

The periods at which acardii may originate are:

1. *Before the heart has developed.* The heart is formed, as well known, by the fusion of two heart-tubes which are developed independently of the vessels of the vascular area, the latter vessels subsequently growing toward the embryonic axis and joining the primitive heart. When, for any reason, the development of this organ is arrested and the vascular areas of the two embryos lie in close relation, the vitelline circulation of the impaired embryo may form anastomoses with that of the normal twin so that the latter assumes, as far as possible, the nourishment of both embryos. Under such conditions, the embryo, which if unaided would necessarily die, continues its development and becomes a parasitic acardius.

2. *After the heart has developed*, but before the establishment of the allantoic or placental circulation. In case heart-death occurs, either primary or secondary, at a time when the vitelline circulation is still formative, anastomoses may still occur in sufficient number to provide succor for the imperilled embryo, which under such conditions may become a parasitic acardius. Since the