EXTROVERSION OF THE BLADDER, COMPLICATED BY THE PRESENCE OF INTESTINAL OPENINGS ON THE SURFACE OF THE EXTROVERTED AREA.

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NUMEROUS methods of classification have been suggested for cases of extroversion of the bladder and its kindred anomalies. The case recorded in this paper falls into the third group of Keith's (1) classification, which is characterised by "ectopia vesicæ combined with fistulous condition of the intestine." A large number of similar cases have been recorded, and Wood Jones (2) has recently described the gross anatomy in detail. On this account the following description is purposely brief.

The child was born at the seventh month and lived for three days. At the time of birth a competent and reliable nurse failed to notice anything unusual about the placenta or membranes, and no membranous bag was attached to the margins of the extroverted area, such as is suggested by Wood Jones (2).

Gross Anatomy.—The umbilical cord was normal in appearance, and lay entirely cephalad to the extroverted area. It was median in position, and was situated 8 cm. from the xiphi-sternal junction and 7·5 cm. from the tip of the coccyx. Only the right umbilical artery was present.

The extroverted area showed, as usual in these cases, a median and right and left lateral subdivisions. The small intestine opened in the middle line (fig. 1), 3 cm. caudad to the umbilicus, and about 2·5 cm. more caudally there was a button-like elevation which could be readily invaginated to form a short blind diverticulum (fig. 2). At the caudad edge of this diverticulum there was a slit-like opening leading into the large intestine, which did not open in the perineum, although a distinct proctodœal depression was present.

On the right lateral subdivision there were two openings (fig. 1), which communicated with the right ureter and vagina respectively; no similar openings were found on the left lateral area.

At the caudal end of the extroverted area, in the middle line, there was a small tag-like elevation which resembled a small clitoris.

The stomach and liver were normal, but rotation of the intestines round the axis of the superior mesenteric artery, which normally is present in a

9·4 mm. embryo, had either been incomplete or had not taken place. This was evidenced by the fact that the superior mesenteric artery lay behind the third part of the duodenum, whereas in the ordinary course of development the gut is carried behind the vessel during the process of rotation. The small intestine measured 30 inches from the pylorus to the point where it opened on the surface. The large intestine passed backwards and downwards into the pelvis for 3 cm., and ended blindly. It was supplied upon its posterior surface by the inferior mesenteric artery.

No paired appendices were found in connexion with the large intestine,

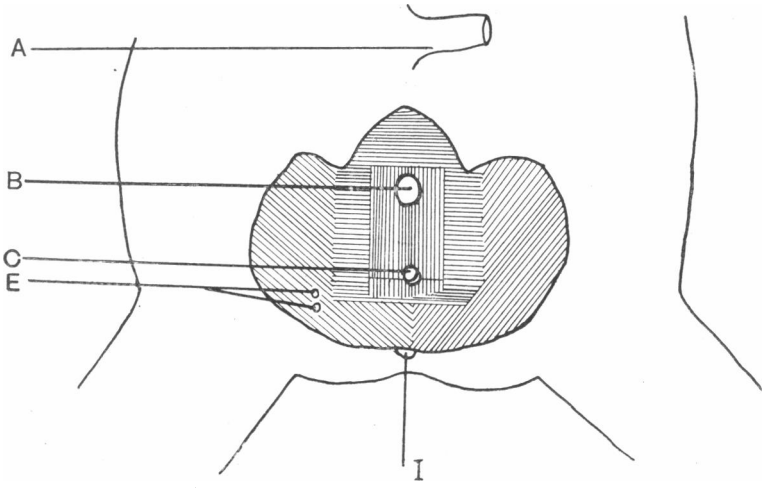

FIG. 1.—Diagrammatic representation of surface view of the case of extroversion described in the text.

A, umbilical cord; B, orifice of small intestine; C, small blind diverticulum, with orifice of large intestine at its left lower margin; E, orifices of right ureter and vagina; I, clitoris. *Note.*—Areas shaded obliquely were covered by mucous membrane of bladder: areas shaded vertically were covered by intestinal mucous membrane: areas shaded horizontally showed transitional appearances.

although these have been described as being constantly present in these cases.

The right kidney lay in the pelvis, but the left kidney was normal in position. The left ureter was enormously distended, and ended blindly in the wall of the left vagina.

The genital organs were female in character. The uteri were quite separate, and the vaginæ were only connected by an impervious fibromuscular bridge at their lower ends. So far as could be discovered, the left vagina did not open on the surface.

Spina bifida, a feature which has been described as constant in these cases, was not present.

Microscopic Appearances.—The histology of extroversion of the bladder and its allied conditions is by no means complete. Shattock (3), von Enderlen (4), and Keith (1) have all contributed to the subject, but their work deals mainly with the uncomplicated variety of extroversion of the bladder. In the case recorded in the present paper, most of the extroverted area was subjected to microscopical examination, and the results are given in some detail.

(*a*) The umbilical cord, close to the body, was perfectly normal, except

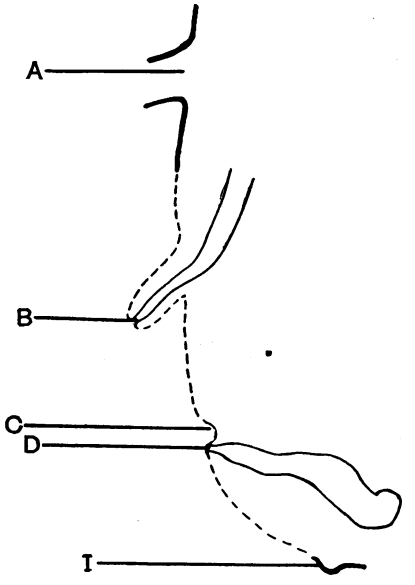

FIG. 2.—Median sagittal section through the caudad part of the anterior abdominal wall of the fœtus described in the text. (Diagrammatic.)

A, umbilical cord; B, orifice of small intestine, prolapsed; C, small blind diverticulum; D, orifice of large intestine; I, clitoris. *Note.*—The extroverted area is represented by a dotted line.

that it contained only one umbilical artery. It was surrounded by a layer of flattened epithelial cells, which constituted a complete amniotic covering. No trace of the urachus was observed, and no remains of the exocœlom were found.

(*b*) Small intestine, caudal end. Typical villi covered the surface, and the submucous and muscular coats were well developed. Very little lymphoid tissue was present in the submucosa, and it was difficult to determine, by the microscopical appearances alone, whether the part examined was jejunum or ileum. The length of the gut from the pylorus to the surface

opening was 30 inches, and, as the child was born at the seventh month, it is practically certain that the caudal portion represented the ileum.

(*c*) The area cephalad to the opening of the small intestine, but caudad to the umbilicus (fig. 1), was covered, at its cephalad end, by stratified epithelium. True skin papillæ were found in places (fig. 3), but not throughout the area. The underlying substance consisted almost entirely of connective-tissue fibres. Where the papillæ were absent, the appearance of the surface epithelium and the underlying tissue supported the view that it represented skin in a slightly modified form.

Sections from the most caudad part of the area, *i.e.* close to the orifice

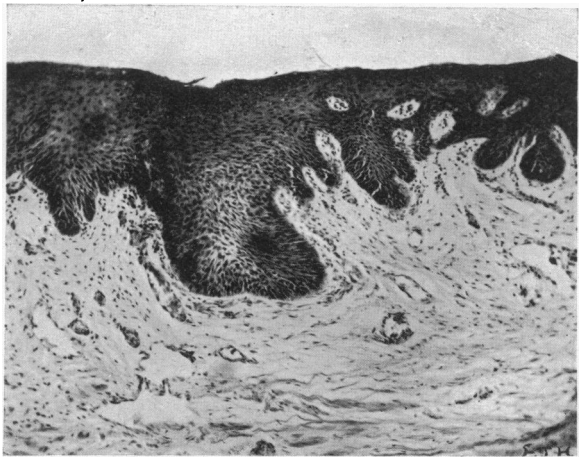

FIG. 3.—Transverse section through area immediately caudad to umbilicus, showing several true skin papillæ.

of the small intestine, showed the typical appearance of mucous membrane of small intestine.

The intermediate part of the area, which should have shown the transition between the two types, was not sectioned at the same time, and, unfortunately, was not in such a good state of preservation when cut at a later date. It was not possible to be certain whether it showed a direct transition from intestinal mucous membrane to skin, or whether there existed an intermediate portion which represented mucous membrane of bladder. The appearances found were suggestive of the latter condition, but, until some further histological evidence is forthcoming, the exact nature of the transition must remain doubtful.

(*d*) The area in the middle line between the two intestinal orifices was cut sagittally. In its cephalad part, the mucous membrane had been par-

tially rubbed off, but it showed the bases of intestinal villi, and the glands of small intestine, lined by secreting cells. In its caudal part, the surface epithelium was well preserved. Typical villi covered the surface (fig. 4), and the number of mucus-secreting cells increased in number towards the caudad end of the area. The general appearance of the glands and the interglandular substance suggested a gradual transition from the mucous membrane of small to that of large intestine.

(*e*) The central area, to each side of the middle line (fig. 1), showed the same appearance as (*d*).

(*f*) The small diverticulum at the surface opening of the large intestine

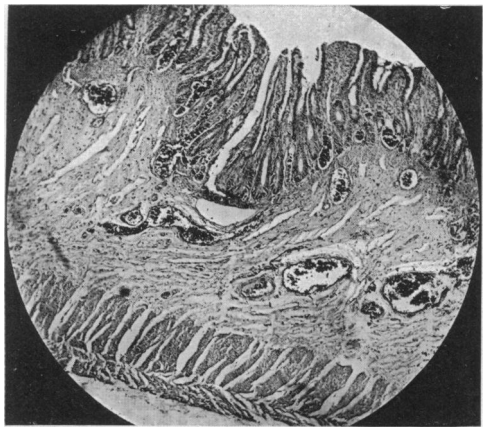

FIG. 4.—Sagittal section through area in median plane between the orifices of the small and large intestine, showing the typical muscular coat and typical villi of the small intestine.

(C, fig. 2) was lined by mucous membrane which, in its caudad part, presented all the characteristics of the mucous coat of the large intestine. In its cephalad part this area was identical with the caudad part of (*d*). No lymphoid tissue was found in the submucosa.

(*g*) Large intestine. The surface was covered by columnar epithelium, which dipped in to line simple tubular glands. The cells were practically all mucus-secreting. The general appearance was identical with that found in the large intestine of a normal fœtus.

(*h*) The lateral area was much denuded of its surface layer, which, however, was intact in places. It consisted of stratified epithelium of the type usually found in the urinary bladder. The submucous tissue contained many plain muscle and white connective-tissue fibres. All the blood-vessels

were greatly engorged, and extravasated blood was found amongst the submucous tissue.

(*i*) The central area, caudad to the opening of the large intestine (fig. 5), was covered by stratified epithelium similar to that found in (*h*), but in a state of better preservation. Embedded in the submucous tissue there was a tube, the walls of which were lined by squamous epithelium. It is possible that this represented the terminal part of the left vagina, but, as the area was not cut serially, it was not determined whether it opened on the surface or with what it was connected above.

(*k*) Sections of the clitoris, uteri, and vaginæ were examined, and the identity of these structures was confirmed.

FIG. 5.—Section through area caudad to orifice of large intestine, showing surface covered by transitional stratified epithelium of the type found in the bladder wall.

Historical.—The recorded cases of extroversion of the bladder and its kindred anomalies are extremely numerous. In 1865, Förster (5) collected a number of cases of epispadias, of pure extroversion of the bladder, and of cases similar to the one described in this paper. He referred to the last group as examples of "Kloakbildung," but the term is used not in its morphological sense, but to express the fact that the urogenital ducts and alimentary canal open on the same surface. He believed the condition to be due to an arrest of development at an early period. "In diesen Fällen ist also der Enddarm, nachdem die Allantois aus ihm hervorgewachsen, allmählig wieder geschwunden und der Mitteldarm ist offen geblieben, verharrt also bleibend auf der Entwickelungsstufe der dritten oder vierten Woche des embryonalen Lebens."

Wood (6), in 1865, described eight cases of pure extroversion of the bladder, and suggested the following explanation: "An important observation has been made in these cases, that, at the time of birth, the hypogastric surface of the fœtus, from the umbilicus to the genital organs, is usually found to be adherent to the placenta or its membranes, the adhesions becoming separated by the process of parturition at the parts in which the cicatrised appearance is afterwards found. Such an adhesion explains very fully how the anterior or superficial portions only of the structures implicated are afterwards found to be deficient." With regard to the complicated variety, his view is that "these are evidently cases in which the arrest of development has taken place at an earlier period, while the fœtus still presents a cloacal formation." Later observations have failed to confirm the presence of adhesions between the extroverted area and the placenta, and, indeed, it is difficult to imagine how such adhesions could be so limited as to produce exactly similar results in each case.

In 1877, Champneys (7) reviewed the literature, and gave a brief account of the theories as to causation which had been brought forward up to that time. He groups them under the following headings: "A, Mechanical; B, Pathological; C, Developmental, or combinations of them." He criticises the views of Breschet (8), Duncan (9), and Mörgelin (10), who all held to the "Berstungstheorie" or mechanical explanation; Velpeau (11) and Phillips (12), who believed the condition to be due to destruction of the bladder and abdominal walls by ulceration; Meckel (13), Wood (6), and others, who all supported the "Hemmungsbildungtheorie." Champneys sums up as follows: "There can be little doubt that the theory which attributes the deformity to arrest of development is the correct one, because the other theories do not bear inspection, some of them being even unimaginable; because of the frequency of accompanying proofs of arrested development; and, lastly, because of the known development of the allantois." With regard to the last point, Champneys believed that the allantois arose as a bilateral structure, and that the two parts ultimately fused to form the bladder and the urogenital sinus. He supposed that failure of the ventral walls of the two allantoic diverticula to unite produced extroversion of the bladder, and that, when both dorsal and ventral walls failed to unite, the condition of extroversion of the cloaca was brought about. It is now known that the allantois does not arise as a paired structure in the human embryo, and, in any case, the explanation fails to account satisfactorily for the accompanying fissure of the abdominal wall.

In 1880, Ahlfeld (14) collected a number of cases and expressed the view that the intestinal openings on the extroverted area represent a patent vitello-intestinal duct. "Der Umstand, dass in einigen Fällen (Meckel,

Reil's Archiv., Bd. 9, S. 449, und Rose, *Monatsschrift für Gebürtskunde*, Bd. 26, S. 244) bestimmt angegeben wird, ein vas omphalo-mesaraicum sei vom widernatürlichen After in der Blasenwand zum Mesenterium gelaufen, beweist dass an dieser Stelle der Ductus eingemündet hat und dort abgerissen sein muss. . . . Ich halte das Zwischenstück von Darmschleimhaut nur für eine probabirte Partie bei ziemlich weiter Dottergangspalte."

In 1881, Doran (15) recorded a similar case of extroversion, and concluded that "failure of union of the visceral plates in the abdominal region, arrested development of the intra-abdominal part of the allantois, and persistence of a primitive condition of the alimentary tube in the region of the omphalo-mesenteric duct will account for the protrusion of the viscera, the condition of the bladder, and the opening of the intestine by an aperture far above its blind extremity and above the imperfect vesical elements." Doran assumed that the intestinal orifice was the patent omphalo-mesenteric duct, but the vague nature of his explanation gives no reason for its presence below the umbilicus. This case presents certain peculiarities which are not found in other examples of the condition, including what Keith (1) assumes to be persistence of the post-anal gut. Unfortunately no account is given of the histology of the region, and, without that, the identification of a tube, opening in the neighbourhood of the groin, as post-anal gut cannot be taken as certain.

Shattock (16), in 1887, writing on pure extroversion of the bladder, suggested that "the primitive cloacal invagination of the surface which normally lays open the lower end of the rectum and the lower end of the urogenital sinus, does in these cases, by an undue extension forwards and upwards, lay open the anterior wall of the urogenital sinus and the anterior wall of the bladder." In support of his view he evidenced the fact that epispadias invariably accompanies pure extroversion of the bladder.

In 1894, the same author (3) recorded the microscopic appearances of the mucous membrane in another similar case. He states that the investing epithelium shows a regular series of deep ingrowths; "it is not a papillary production or one due to outgrowths, for the free surface is in the intervals smooth for what are, microscopically, considerable distances." The general appearance is like "an adenoma arising in the intestinal mucosa, except that no antecedent gland tissue is concerned in its production." In considering these statements the reader must bear in mind that the preparation was obtained from an adult, aged 38, who had worn a urinal for 34 years, and who was the subject of suppurative inflammation of the right kidney.

In 1895, Bryce (17) published a case of complicated extroversion in a fœtus, which was the subject of retroflexion of the trunk, ectopia viscerum,

and spina bifida. He criticised Ahlfeld's view that the intestinal openings, represent a patent vitello-intestinal duct, and, in the light of His' description of the development of the bladder, came to the conclusion that "cases of anus vesicalis must, therefore, be explained by imperfection in the formation of the septum," which normally divides the cloaca into a ventral, urinary, and a dorsal, alimentary, segment. In this case the ileum and a blind dilated sac—which seems to represent the large intestine—opened by a common orifice on the surface of the extroverted bladder. Bryce suggests that this sac "represents not the whole intestine behind the yolk stalk, but the much-dilated 'bursa pelvis'" (the name given by His to the cloaca interna). He believes that the primary cause of the whole series of abnormalities present in this case lies in the retroflexion of the trunk, and suggests that the persistence of a very short allantoic stalk has interfered with the growth in the pelvic region and resulted in the abnormalities found. No reason is given for the rupture of the bladder or cloaca, and though the shortness or absence of the umbilical cord might account for this particular case, it cannot account for the similar conditions found in cases like the one recorded in the present paper, where the umbilical cord is normal.

It is interesting to compare Bryce's case with the one recorded by Emrys-Roberts and Paterson (18) in 1906. The condition of the fœtus was very similar, with two important exceptions. No red mucous-membrane covered area was exposed on the surface; the ileum was normal and became continuous, with a short dilated tube which opened at its lower end into an internal cloaca. This case is quoted by Keith (1) as an example of "Extroversion of the Bladder with a Meckel's Diverticulum opening on the Surface," but the reason for identifying what is almost certainly an orifice in the large intestine as the opening of a patent Meckel's diverticulum is by no means clear. Emrys-Roberts and Paterson follow Fleischman's (19) description of the development of the bladder. In consequence, they conclude that the allantois was absent in their case and that "most if not the whole series of malformations appear to have been primarily caused by the failure in development of the hinder portion of the alimentary canal." No indication is given of the nature or of the cause of the arrest of development, but it is suggested that "the period at which arrest of development has occurred appears to be after the formation of the cloaca, but before the separation of rectal and genito-urinary passages."

In 1896, Sequeira (20) recorded a case in which a funnel-shaped orifice in the middle line communicated with the ileum and the large intestine. This he regards as a patent vitello-intestinal duct. With reference to the

causation, he supports the views of Shattock, which have been mentioned above. "If, as in the present case, the vitelline duct opens at the umbilicus, it would, of necessity, be involved in this forward extension of the proctodœum."

In 1900, von Steinbüchel (21) recorded a case of extroversion in which two small openings, placed one on each side of the middle line, communicated with what he believed to be a Meckel's diverticulum. The large intestine was very rudimentary, and, according to the writer, was represented only by the cæcum. He believes that pure extroversion of the bladder is the first step, and that, at the same time, the large intestine fails to develop. Thereafter "der Ductus omphalo-mesaraicus . . . drängt sich zwischen die beiden noch getrennten anlage der Harnblase . . . und verlöthet sich mit jeder der beiden Blasenanlagen. Durch den Druck des Meconiums, der im Ductus immer bedeutender wird, da ja der Dickdarm nicht ausgebildet ist und sich an das unterste Ilium nur ein kleiner, blind endigender Darmtheil (Cæcum) anschliesst, erfolgt schliesslich in die vielleicht mittlerweile schon vereinigten Blasenhälften der Durchbruck, so dass wir symmetrisch von der Mittellinie zwei Oeffnungen, die in das Darmrohr führen sehen." The chain of events is so complicated that it is improbable that this is the correct explanation. It is curious to find that, after rejecting the Berstungstheorie with regard to extroversion of the bladder, von Steinbüchel resorts to that theory in order to explain the presence of a communication with the alimentary canal.

In 1901, Berry Hart (22) discussed the question of pure extroversion of the bladder, and came to the conclusion that its causation might be ascribed to an abnormally extensive rupture of the cloacal membrane. With regard to those cases in which the alimentary canal opens on the surface of an extroverted bladder, he was hardly prepared to accept von Steinbüchel's explanation, but he offered no other solution.

In 1904, Enderlen (4) examined the mucous membrane of the extroverted bladder in two new-born children. He found "das Uebergangsepithel der Blase mehr oder weniger gut erhalten." In adults, who were the subject of this malformation, his results were different, "Plattenepithel in verschiedener Form wechselt mit verschieden gestaltetem und funktionierendem Zylinderepithel ab." This he regarded as a metaplasia, although Keith (1) puts a somewhat different interpretation on the facts.

In 1908, Keith (1) classified the malformations of the hind-end of the embryo. He included all cases in which intestinal openings are present on the surface of an extroverted bladder in one group, to which he referred as "Ectopia Vesicæ with a Meckel's Diverticulum opening on the exposed vesical surface." In giving a brief account of the characteristic features

of the condition, he says that the intestinal orifice may vary in position. "It may be situated almost in the perineum, near the posterior angle of the exposed mucous area." How the orifice of a Meckel's diverticulum comes to open at a point so far distant from the umbilicus is not explained. Further, he states that "the depression into which the ileum and cæcum open . . . is usually lined by a villous mucous membrane," but he does not mention the grounds on which this observation is based. He is of opinion that the condition is due to an arrest of development occurring at about the period shown in the Graf Spee embryo "Gle," and suggests that the allantois fails to become differentiated. As a result "the hind-end of the embryo, with the primitive streak, rests directly on the yolk-sac, instead of being separated from it by the allantois and the cloaca, as in the Graf Spee embryo. The primitive streak thus comes to rest directly over that part of the yolk-sac where the unseparated rudiment of the cloaca is situated. If an opening were to occur in the primitive streak, the yolk-sac and endodermal cloaca would open on the hypogastric region of the embryo, and give rise to the condition seen where ectopia vesicæ is combined with a fistula opening into the intestine." Later he says, "It is plain . . . that ectopia vesicæ is due to a non-fusion of the lips of the hypogastric stretch of the primitive streak." Keith believes that the active agent is chorionic inflammation during the third week of embryonic life, "when the chorionic circulation is being established, and that is just when the lips of the primitive streak are in a state of fusion, a fusion which is to secure the anterior closure of the bladder and lower belly wall." In referring to Enderlen's work he omitted to mention that in the only cases of new-born children which Enderlen examined the mucous membrane was typical bladder epithelium. Keith cut sections of the junctional area between the "part supposed to be yolk-sac or its stalk" and the bladder. The former he found "lined by a double layer of columnar epithelium, while that supposed to be vesical mucous membrane was covered by a stratified epithelium similar to that which covers the lips of the mouth." He also cut sections from the mucous membrane in a case of pure extroversion of the bladder, and found that "unfortunately all the epithelium had been lost, but it showed villous processes with depressions between their bases, recalling the structure of the small intestine, and quite unlike the mucous membrane of the normal fœtal bladder."

In 1910, Wood Jones (2) advanced a theory which is diametrically opposed to the views of Keith. He believes that "abnormal distension of the allantois and urinary tract" is the causative factor, and, consequently may be taken as a supporter of the "Berstungstheorie." Two stages are necessary for the production of the deformity. In the first instance the

allantois becomes greatly distended and "encroaches on" the yolk-sac. It is not quite clear what the author wishes to be understood by the term "encroach." In his hypothetical figure he shows that after the "encroachment" the yolk-sac and allantois are thrown into a common sac, which receives the openings of the caudal end of the fore-gut and the cephalic end of the hind-gut. In the second instance this common sac ruptures on to the surface. Wood Jones calls attention to the position of the umbilical arteries relative to the extroverted area, and suggests that a study of this point should decide whether it is the yolk-sac or the allantois which ruptures. "The information to be gathered concerning the actual disposition of the membranes and vessels at the time of birth seems to be very slight, but such accounts as are available agree that a sort of skirt of membranes is attached—on the one hand around the margins of the exposed red area, and on the other to the placenta." The author concludes with the statement that "the typical human body-stalk placentation is lost, and a highly developed allantoic placentation has taken its place." No account is given of the histology of any of the parts described.

As Champneys has pointed out, the explanation of this condition must be given in the light of the currently accepted views on the development of the hind-end of the embryo. It is now generally believed that the allantois takes little or no part in the formation of the bladder, which is derived entirely from the endodermal cloaca. This view was first put forward by Keibel (24), and has recently been fully substantiated by Pohlmann (23). Both these authorities agree that the endodermal cloaca does not normally open on the surface. According to Pohlmann, the primitive streak consists of all three germ layers, and that, after the formation of the tail-fold, the mesoderm disappears, leaving the ectoderm in apposition with the endoderm as the cloacal membrane. The subdivision of the cloaca into ventral, urinary, and dorsal, intestinals egments involves the subdivision of the cloacal membrane into urogenital and anal parts, which break down, independently of each other, at a later period. Normally, the subdivision of the cloaca is effected by the tailward growth of a frontal mesodermal septum.

It may be as well to point out at this stage that the term cloaca is used to indicate that part of the primitive gut which lies caudal to the point of origin of the allantois after the formation of the tail-fold, and that, in the early stages, the terms cloaca and hind-gut are synonymous. As growth proceeds, the extent of the cloaca relative to the extent of the gut rapidly becomes smaller, so that the segment of gut derived from the subdivision of the cloaca is very much shorter than would have been the case if the subdivision occurred at an earlier stage.

Rupture of the urogenital and anal segments of the cloacal membrane is a perfectly normal occurrence at a certain period of development, and this fact, as pointed out by Berry Hart, at once suggests a clue to the causation of cases of epispadias and extroversion of the bladder. In hypospadias the urogenital membrane breaks down at the normal time and to a normal extent. If, however, the membrane ruptures cephalad to the genital tubercle instead of caudal to it, the condition of epispadias is produced; and if the rupture is excessive—the membrane is probably more extensive in these cases—pure extroversion of the bladder plus epispadias is the result. Both the conditions of epispadias and pure extroversion can therefore be accounted for on the ground of rupture of the urogenital membrane at an abnormal site but at the normal time.

It may be as well to indicate the reasons for rejecting the theories which have hitherto been advanced before attempting to offer a somewhat different explanation. For a criticism of the earlier theories the reader is referred to a paper by Champneys (7), whose own theory is rendered untenable by our present knowledge of the development of the allantois. Ahlfeld (14) and Bryce (17) both believe that abnormal shortness of the umbilical cord is the active agent, but the former holds that it is the vitello-intestinal duct which opens on the surface, whereas the latter inclines to the view that it is the cloaca only. This view, however, can only apply to those cases in which the umbilical cord is absent or unusually short, and cannot be regarded as explanatory of all the recorded cases.

Emrys-Roberts and Paterson (18) do not put forward any theory with regard to the causation of the condition, but they agree with Bryce in believing that the arrest of development occurs before the separation of the bladder and gut segments of the cloaca.

Sequeira's (20) explanation is very similar to that brought forward by Keith (1). He applies Shattock's explanation of pure extroversion of the bladder to the more complicated condition, but he omits to explain how the rupture of the cloacal membrane can pass forwards to involve the vitello-intestinal duct in the presence of the allantois. Further, it is almost certain that he believes the condition to arise after the bladder has been completely shut off from the gut, and the extension, at that period, of a rupture of the bladder to the yolk-sac or its duct would necessarily involve the opening up of the cœlom.

Von Steinbüchel (21), as already pointed out, postulates a number of anomalies, all occurring in the same embryo, together with a pathological process. The statement that the hind-gut fails to develop after its separation from the bladder is untenable, since by the time that the separation has occurred there is a relatively large segment of gut caudad to the vitello-

intestinal duct. Von Steinbüchel's view appears to be much too complex to be capable of explaining every case of this anomaly.

Keith (1) adopts a somewhat different explanation. In the first place, he postulates the absence or non-differentiation of the allantois, a hypothesis which is rendered necessary by his interpretation of the intestinal orifices as the surface opening of the vitello-intestinal duct. He suggests that during the third week of embryonic life, " when the lips of the primitive streak are in a state of fusion," chorionic inflammation so alters the condition of growth that " non-fusion " follows. The statement that the fusion of the lips of the primitive streak " is to secure the anterior closure of the bladder and lower belly wall " is rather misleading, as it suggests that the ventral wall of the bladder is at first absent. Pohlmann (23) has shown that the cloacal membrane is formed by the disappearance of the mesoderm from the region of the primitive streak, *i.e.* that normally there is a decrease in substance in this area and not an increase, as the word " fusion " would lead one to suppose. It is not clear in what sense Keith employs the word " cloaca," but from the quotations given on p. 99 it would appear that the primitive streak takes no part in the formation of its walls. These views are at variance with those of Keibel, Pohlmann, and other authorities, and certainly the suggestion that the bladder is closed ventrally by the fusion of the lips of the primitive streak receives no support from the recent work on this subject. Although making the statement that " the vitelline orifice . . . may be situated almost in the perineum," Keith offers no reason for this very unexpected position of a structure which should open at the umbilicus, nor does he make any reference to the histology of the area which intervenes between the umbilical cord and the orifice of the small intestine. As will be shown later, the nature of this area is of the greatest importance in determining the nature of the anomaly.

Wood Jones (2) re-advocates the " Berstungstheorie," and believes that the whole condition is due to overdistention and rupture of the allantois. This takes place before the closure of the neurenteric canal, and so accounts for the associated spina bifida. He makes no attempt to prove that at this early stage the mesonephros is capable of active excretion, nor does he explain why the allantois ruptures into the yolk-sac instead of to the exterior. Further, rupture of the allantois would necessarily involve a tearing of the umbilical cord, and, as has been shown, that structure was perfectly normal in the case recorded in the present paper. I have been unable to trace the authority for the statement that " such accounts as are available agree that a sort of skirt of membranes is attached, on the one hand, around the margins of the exposed red area, and, on the other, to the placenta," but certainly no such condition was present in the case here

recorded. There is another objection to be put forward from the purely mechanical standpoint. If the internal pressure is sufficiently great to prevent the closure of the neurenteric canal, how is it possible for the normal separation of bladder and gut to go on undisturbed, as shown by Wood Jones in his figs. 10 and 11 ?

Extroversion of the bladder, complicated by the presence of openings into the alimentary canal, can be most easily and most satisfactorily explained by rupture of the cloacal membrane occurring at an abnormally early period. If such a rupture occurred during or immediately after the formation of the tail-fold, it would expose the dorsal and lateral walls of the cloaca or hind-gut. As the lateral walls of the cloaca are concerned in the formation of the bladder, it is in keeping with this explanation to find that the lateral parts of the extroverted area in the present case are histologically identical with bladder wall. The central part of the extroverted area should represent those parts of the alimentary canal which are normally formed from the hind-gut or cloaca. As this area has been shown to represent the terminal part of the ileum and the whole of the large intestine, it would appear at first sight as if the above hypothesis were untenable. It is therefore necessary, before proceeding further, to endeavour to determine how large a part the hind-gut takes in the formation of the adult alimentary canal. In an embryo of 13–14 primitive segments (Embryo Pfannenstiel III., fig. ·526, *Keibel and Mall's Manual of Human Embryology*) the origin of the allantois lies opposite the 14th primitive segment, practically at the junction of mid- and hind-gut. In an embryo of 23 primitive segments (Embryo R. Meyer 300, fig. 531a, *Keibel and Mall's Manual of Human Embryology*) the origin of the allantois lies opposite the 23rd primitive segment, while the caudal end of the mid-gut lies opposite the 12th segment. Opposite segments 13–22 there is a part of the alimentary canal which connects the mid-gut with the cloaca, and, from the figures given by Lewis (25), it seems almost certain that the cæcum appears on this part at a slightly later stage. Careful consideration of the available reconstruction models and figures leads to the opinion that, in the growth of the alimentary canal, the region in connexion with the yolk-sac remains practically a fixed point, and that the areas on each side are areas of active growth—*i.e.* the fore-gut and the hind-gut are responsible for practically the whole of the adult alimentary canal.

Abnormally early and excessive rupture of the cloacal membrane exposes the dorsal wall of the hind-gut, which is destined to form the terminal part of the ileum (caudal to the usual site of a Meckel's diverticulum) and the whole of the large intestine. The destruction of

the ventral wall and the exposure of the dorsal wall apparently constitute a condition which greatly restricts the growth of the hind-gut, and the tailward-growing mesodermal septum fails, so that the subdivision of the cloaca is not carried out.

The presence in this and in other cases of a tubular part of the large intestine is a difficulty which requires to be considered. It is possible that it represents persistence of the post-anal gut. In Doran's (15) specimen, however, there was, in addition to a tubular part of large intestine, a small canal, lined by mucous membrane, which opened on the extroverted area and also in the groin. If Keith (1) is correct in his identification of this structure as the persistent post-anal gut, a different explanation must be sought to account for the formation of the tubular part of the large intestine.

Pohlmann (23) believes that, normally, the tailward-growing mesodermal septum is the active agent in shutting off the bladder from the gut, and he holds that the lateral folds of Rathke are more apparent than real. The subdivision is completed by the fusion of this septum with the mesodermal bar, which invades the cloacal membrane and separates it into urogenital and anal segments. It should be remembered that this frontal septum is not horizontal, but crescentic in outline, and that the failure of its central part does not necessarily involve its lateral parts. In order to account for the formation of a tubular part of the large intestine in these cases of extroversion, it is necessary to assume that the central part of the frontal septum fails to develop, and that, under these abnormal conditions, its lateral parts grow inwards and fuse with one another and the mesodermal bar in the perineum. In this way the caudad part of the bladder is separated from the caudad part of the gut, while the two remain undivided in their cephalad portions. At present this explanation cannot be definitely proved, but the conditions found suggest that it is very probably correct. It should be pointed out, however, that this same difficulty is present in the explanations offered by Keith and all the other writers save Wood Jones—who has his own views with regard to the formation of the terminal portion of the alimentary canal,—and that none of these authorities has made any attempt to overcome it.

The histological nature of the area which lies cephalad to the opening of the small intestine and caudad to the umbilicus gives strong support to the explanation offered in this paper. If the opening into the alimentary canal is really the vitello-intestinal duct, as Sequeira (20), Doran (15), Keith (1), and others hold, then the presence of skin on the surface of this area requires to be explained. The vitello-intestinal duct, when patent, invariably opens at the umbilicus, and it is impossible for it to open else-

where, except in the event of pathological lesions. The assumption that the proximal part of the umbilical cord has been taken into the anterior abdominal wall during the process of growth would provide a way out of the difficulty, but no proof has yet been brought forward in its support. The histological findings, however, are in perfect accordance with the present explanation, for, the cloacal membrane having ruptured up to the point of the allantois, the umbilical cord is left intact, together with a small area on the anterior abdominal wall caudad to the umbilicus. If, at a later date, some observer is able to demonstrate the presence of bladder mucous membrane, intervening between the orifice of the small intestine and the umbilical cord, then the case for abnormally early and excessive rupture of the cloacal membrane will be established beyond doubt.

Summary.

(1) Epispadias is due to rupture of the urogenital part of the cloacal membrane at a site cephalad instead of caudad to the genital tubercle.

(2) Pure extroversion of the bladder, together with epispadias, is due to an excessive degree of the same rupture.

(3) Extroversion of the bladder, complicated by intestinal openings on the extroverted area, is due to rupture of the cloacal membrane. This rupture may occur at any time between the first appearance of the membrane and the completion of the subdivision of the cloaca. The period at which it takes place will determine the variety of the anomaly; thus it is suggested that the rupture occurred very early in the case recorded in this paper, and at a later period in the case described by Emrys-Roberts and Paterson (18).

(4) Spina bifida and paired diverticula at or near the surface orifice of the large intestine are not constant features of cases of extroversion of the bladder, complicated by intestinal openings on the extroverted area.

(5) The primitive hind-gut gives origin to a much larger part of the alimentary canal than is generally supposed, whereas the mid-gut forms very much less than is usually ascribed to it.

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