The Embryology of Gut Rotation

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Until today, the puzzling spectrum of midgut "malrotations" is commonly explained by an "impaired" process of rotation of the midgut. However, a closer look at the literature reveals that the description of this "process of rotation" is rather schematic and is aimed more at explaining pathological findings, while detailed proper embryological investigations are still rare. Despite recent trials, good animals models that would allow the comparison of normal and abnormal midgut development are still missing. In the first part of this article, the "normal process of rotation," as it is described in the literature, is presented and critically analyzed. In general, it is a shortcoming that reliable illustrations of these crucial embryological processes are missing in most of these papers. Therefore, in the second part of this review scanning electron microscopy pictures of the developing midgut are presented in a series of rat embryos. In these pictures clear signs of a process of rotation are missing.

SINCE THE WORK of Mall[1] and Frazer and Robbins,[2] it is generally believed that the normal position of the gut inside the abdominal cavity results after a complex embryological process called "rotation of the midgut loop." Consequently, disorders of the positioning of the gut are called "malrotation."[1,3-5] However, in most textbooks of embryology and pediatric surgery, this process of rotation is described rather schematically. Instructive illustrations representing results of detailed embryological studies of midgut development are sparse. Animal models, which may allow embryological studies in specimen with "malrotations" of the midgut, have recently been discussed but are still controversial.[6,7]

In this review, the embryology of the midgut will be discussed in two sections:

1. The description of "normal midgut development" as it can be found in most textbooks of embryology and pediatric surgery.
2. An "atlas of midgut development" using scanning electron photographs. These pictures give an impression of normal embryonic midgut development in 3D.

"NORMAL" EMBRYOLOGY OF THE MIDGUT

The normal embryology of the midgut is described as it is found in most papers and textbooks of embryology[8,9] and pediatric surgery.[4,10,11]

In humans, the development of the midgut starts with the subdivision of the primitive gut into foregut, midgut, and hindgut at the fourth developmental week.[8,9] At this stage, the midgut is still connected to the yolk sac through the omphaloenteric duct. Many researchers believe that the midgut lies straight in the midline of the embryo in this stage.

The Process of Rotation

This process can be subdivided into two or three subsequent developmental steps.[3,8,9]

1. The early development of the gut anlage into the extraembryonic coelom with a sagittal orientation of the primitive loop (approx. fourth week of development in humans). Many researchers believe that this herniation (physiological umbilical hernia) results because the gut grows too fast in relation to the abdominal cavity of the embryo.[3] In this stage, the first rotation of the gut anlage inside the extraembryonic coelom takes place. It is 90° in a counterclockwise direction around the axis of the mesentery vessels (approx. eighth week of development in humans). As a result, the midgut loop is now horizontally orientated with the small gut to the right and the colorectum to the left.
2. "Return of the gut" into the abdominal cavity (approx. tenth week of development in humans).

At the tenth week of development, the extraembryonic part of the gut enters the abdominal cavity. The details of this process are still unclear. Some authors believe that the process of rotation ends at this stage with another rotation in an anticlockwise fashion (180°).[11] As a result, the flexura duodeni is pushed into a position below and to the left of the root of the mesentery while the cecum and the colon are forced to the right side of the abdominal cavity, thus crossing over the mesenteric root.

The end result of these two rotations is a complete rotation of 270°. In the following step, the cecum grows downwards from the upper quadrant of the right abdominal cavity into the right iliac fossa.

In contrast to this description, Grob[3] subdivides the last rotation of 180° into two steps of 90° each.

Remarks

1. This description of this process of rotation is schematic. Good illustrations of important developmental steps are rare. The reason is that most descriptions of the embryology of the midgut were done in order to better explain the background of the pa-

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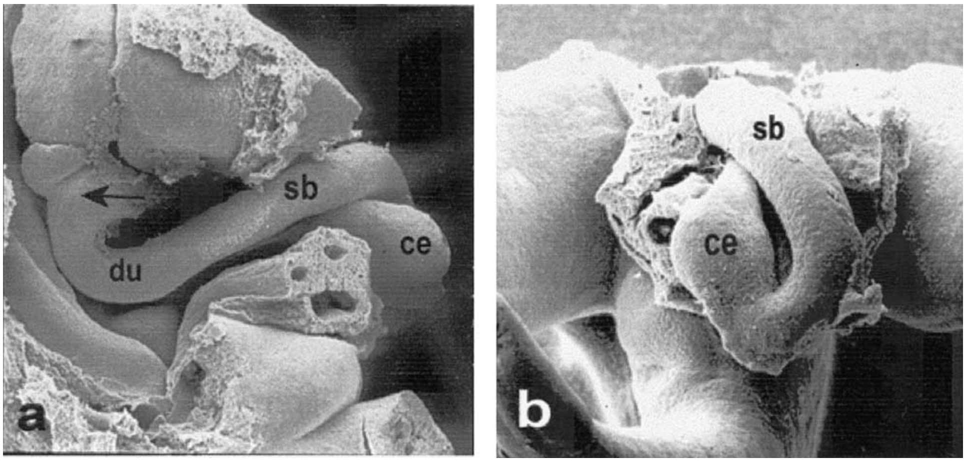


Fig 1. **Midgut of a 13-day-old rat embryo. (a) view from the right, (b) view from ventral. Note the "physiological herniation" of the tip of the bowel loop (ce) into the coelom of the umbilicus. du = anlage of the duodenum, sb = small bowel, ce = cecum. The arrow indicates the pyloric area.**

thology of malrotation than to explain the embryology of the midgut.

2. Many clinicians as well as embryologists believe that congenital malformations in general are best explained by a process of inhibition of normal embryonic development. The theory of rotation of the midgut is a good example for this assumption. Most workers in the field believe that this process of rotation can be hampered at any stage resulting in the known spectrum of malrotations. It is a shortcoming of this theory, however, that these "normal forms" of rotation only exist in schematic drawings. They have never been demonstrated in real embryos.
3. Furthermore, it is another popular assumption that the morphology of normal embryological stages can be mimicked by the morphology of pathological conditions,[12] indicating that that malformations represent "frozen" stages of normal embryos. As a result, the understanding of the development of the intraabdominal position of the gut is highly hypothetical: they represent interesting interpretations of pathological anatomical findings. They are not the result of proper embryological studies.
4. Most schematic drawings indicate that, in the conventional theory, the rotation of the foregut is thought to take place in an "en bloc" fashion. However, it remains completely obscure which force should be responsible for this developmental movement.

OBSERVATION ON THE MIDGUT DEVELOPMENT IN RAT EMBRYOS

In order to demonstrate normal gut development, we used staged rat embryos, which were studied by means of a scanning electron microscope (SEM). In this study, the youngest embryo was aged 13 days and the oldest 18 days. Using microsurgical techniques, the gut loops inside the abdomen and in the extraembryonal coelom were exposed.

In short, the following observations were made:

1. In young embryos (day 13/14) the midgut can be easily identified as a loop (Fig 1a,b). This loop can be subdivided in: (a) a central (dorsal) part (b) an umbilical (ventral) part and (c) a straight part. In this stage, the colon is already shorter than the "small" gut.
2. In 14-day-old rat embryos, the small gut elongates, thus pushing the cecum inside the umbilical coelom

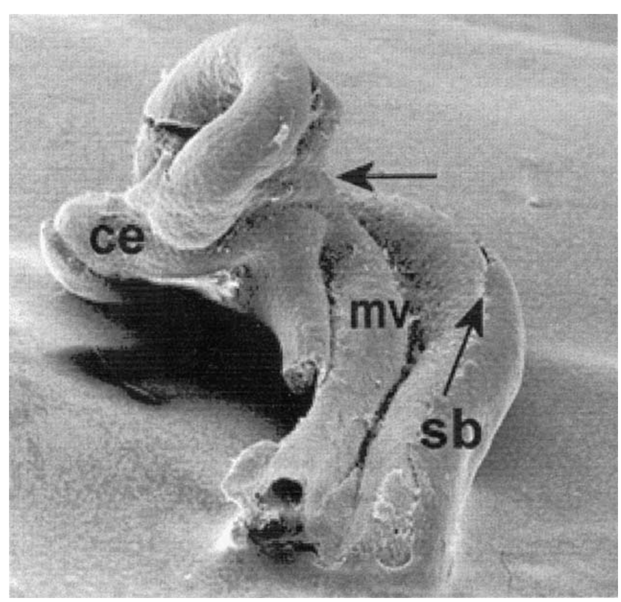


Fig 2. **Midgut of a 14 days old rat embryo, view from dorsal. Arrows indicate the direction of longitudinal growth of the small bowel (sb). As a result, the cecum (ce) is pushed to the left, mimicking "rotation".**

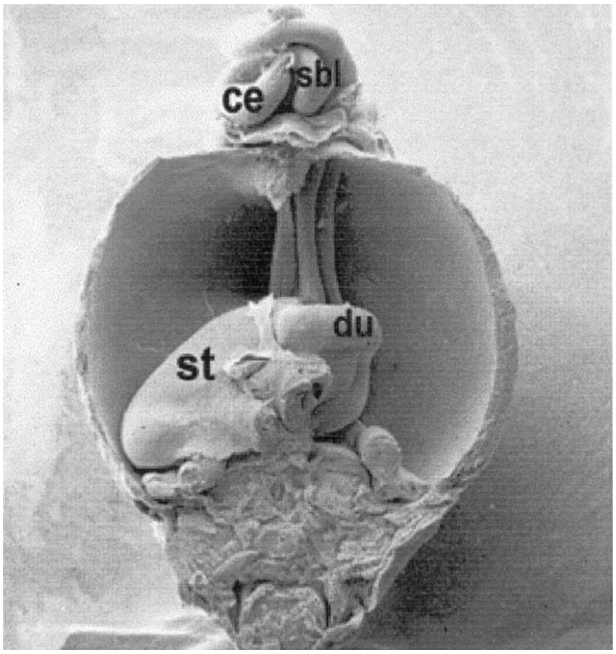


Fig 3. Abdominal cavity and midgut of a 15-day-old rat embryo. The 3 parts of the midgut are easily identifiable. In the central part, the stomach (st) and the duodenum (du) are seen. Ventrally (umbilical part), small bowel loops (sbl), and the cecum (ce) are found in side the umbilical cord.

to the left (so-called "first rotation" of the gut, Fig 2).

3. In a 15-day-old rat embryo the the 3 distinct parts of the gut loop are clearly discernable (Fig. 3).
   a) in the central (dorsal) part, the duodenum is the main feature. Local growth of the duodenal loop forces the tip of the duodenojejunal area beneath the root of the mesentery, which thus reaches its final anatomical position (Fig 4a, b)
   b) In the umbilical part (ventral part) inside the umbilical coelom, gut loops develop due to rapid lengthening of the small gut. The position of the cecum is changing frequently. This seems to be a phenomenon secondary to the growth of the intraumbilical loops (Fig 5a, b).
   c) In the straight intraabdominal part, growth activities are minimal at this time point. Root (Figs 3 and 5b).
4. At day 17, the so-called "return" of the umbilical midgut starts in rat embryos (Fig 6). This process is paralleled by the appearance of loops inside the abdominal cavity also, which seem to stem from local growth of jejunal loops (Fig. 4b). The area of the abdominal cavity into which the loops from the umbilicus return varies initially. Obviously, the actual size of the liver and other neighboring organs influences this developmental step. Interestingly, not the cecum but the terminal ileum is the final loop that enters the abdominal cavity (Fig 7).
5. Due to minimal growth activities, the active contribution of the colorectal part to the development of the midgut loop is only small. The main part of the colorectum remains inside the abdominal cavity and only the coecum can be found inside the umbilical coelom (Fig 5b). This is in contrast to the assumption that major parts of the colon can be found inside the umbilicus.[10] In the 18-day-old rat embryo, the cecum enters the abdominal cavity and takes a ventral position close to the abdominal wall and the liver. We never saw the cecum (Fig 7) in the left abdominal cavity or in a more dorsal position as it is suggested by some schematic drawings.
6. The straight (intraabdominal) part shows, as the colorectum, only minimal developmental activities. This is surprising because rotation, if occurring, should result in clearly notable morphological changes in this area (Fig 5b).

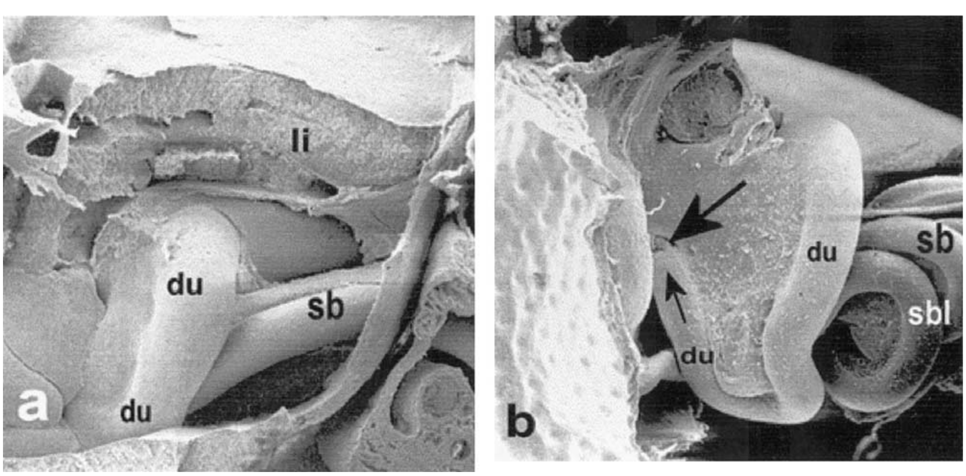
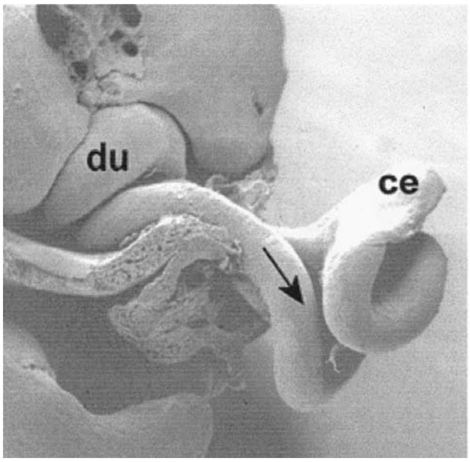


Fig 4. Close up of the duodenal region. (a) Rat embryo 15 days old (b) rat embryo 17 days old. Longitudinal growth of the duodenum (smaller arrow, du) forces the tip of the duodenojejunal loop beneath the mesenteric root (large arrow). sb = small bowel, li = liver Note the formation of bowel loops (sbl) in situ in the 17-day-old embryo.



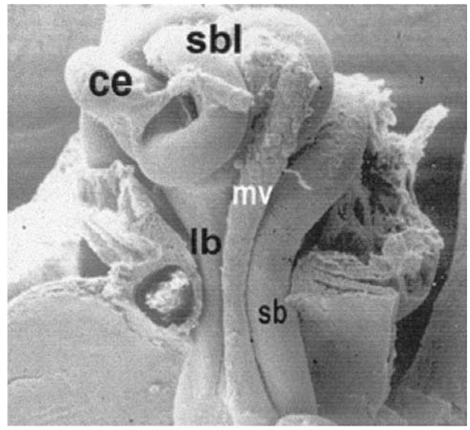


Fig 5. Close up of the umbilical (ventral) region of the midgut loop. (a) View from ventral, embryo approx. 15 days old. Longitudinal growth of the small bowel (arrow) leads to the formation of loops inside the umbilical cord. The cecum (ce) moves passively. (b) View from cranial: note the changed position of the cecum (ce). The umbilical cord is filled with small bowel loops. Note that signs of rotation around the axis of the mesenteric vessel (mv) are missing. Lb = large bowel, sb = small bowel.

Remarks

1. Our study indicates that the final position of the gut inside the abdominal cavity depends on 2 distinct embryological processes: (a) first, the development of the duodenal loop and its rapid growth by longitudinal lengthening in the early phases of development. As a result, the tip of the doudenojejunal loop is pushed beneath the root of the mesentery. It is obvious that this movement is not the result of any rotation. (b) The return of the gut into the abdominal cavity. In all of our embryos, the cecum entered the right abdominal cavity and was found ventrally close to the abdominal wall. The reason for this behavior remains unclear. We can assume, however, that "free space" in the abdominal cavity is minimal. Thus, the cecum enters into a position where space allows.
2. Gut lengthening takes place mainly in the small gut. This results in the formation of loops inside the umbilical cord and, later, inside the abdominal cavity. Through these growth activities, the cecum is pushed into various positions inside the umbilical cord. This movement must not be mixed up with rotation. In this stage, a rotation around the axis of the mesenteric root never takes place.
3. Our observations clearly indicate that mass rotation

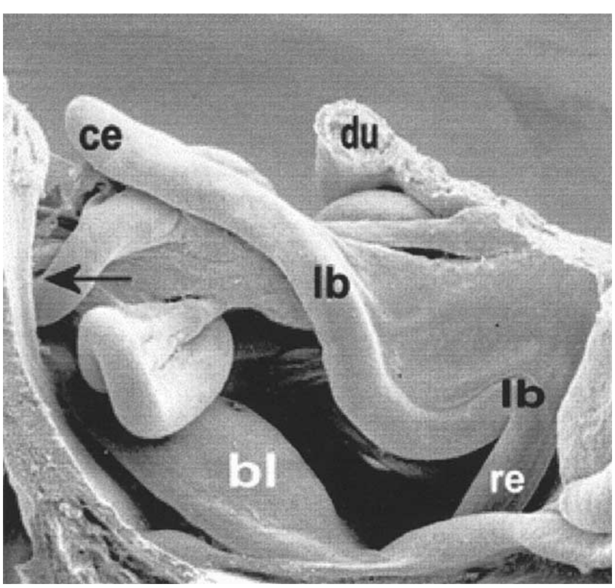


Fig 6. Midgut of a rat embryo, approx. 17.5 days old. View from left, lateral. The colon (ce, co) is entirely inside the abdominal cavity. The cecum (ce) lies close to the ventral abdominal wall. Re = rectum. The arrow points to the last loop inside the umbilical cord (terminal ileum). bl = bladder.

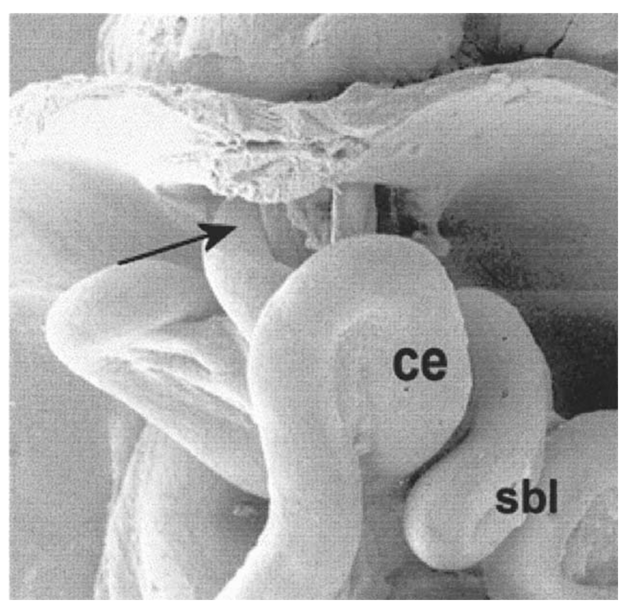


Fig 7. Close up of the ventral part of the midgut loop. Note the position of the cecum in the right abdominal cavity. The arrow points to the terminal ileum which is still inside the umbilical cord. Sbl = small bowel loops.

of the whole midgut does not take place as indicated by numerous sketches.

CONCLUSIONS

In newborns, the normal position of the gut seems to depend on two distinct embryological processes. Of these, the proper development of the duodenal loop seems to be of major importance. This loop appears through localized growth and lengthening of the duodenum in an early period of development. Further growth pushes the tip of the duodenojejunal loop beneath the mesenteric root, which then reaches its normal position left to the spine. This process seems to be crucial for the normal arrangement of the gut inside the abdominal cavity. This is backed up by clinical observations in cases of malrotations[13]: in the vast majority, the duodenal loop presents with an abnormal course, while the position of the cecum is less indicative for the presence of malrotation. Thus we conclude that in all forms of "isolated" malrotations the improper formation of the duodenal loop is the crucial factor.

The other important developmental step is the return of the intestines from the umbilicus into the abdominal cavity. During this developmental phase the cecum immediately reaches its final position in the right side of the abdomen. However, this is not the result of growth activities but rather that of passiveness.

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