Persistent Right Umbilical Vein as a Result of Vitamin Deficiency During Gestation

By I. W. Monie, M. M. Nelson and H. M. Evans

Of the two umbilical veins formed in young rat embryos, the right regresses early while the left persists until birth. In a number of rat fetuses from mothers subjected to a transitory deficiency of pteroylglutamic ("folic") acid during pregnancy, this pattern was reversed and the right, instead of the left, umbilical vein persisted until birth. In such cases, the ductus venosus was always absent. No record of persistent right umbilical vein has been found in the literature.

A TRANSITORY deficiency of pteroylglutamic acid (PGA or folic acid) from the ninth to eleventh days of gestation resulted in multiple abnormalities in 99 per cent of rat fetuses examined on the twenty-first day, one day prior to parturition. Macroscopically, 57 per cent of these abnormal fetuses exhibited cardiovascular anomalies such as persistent interventricular foramen, persistent truncus arteriosus, right-sided aorta and anomalous subclavian arteries. While tracing the development of such abnormalities in younger embryos from mothers on the same PGA-deficient regimen, an anomaly not previously recognized—persistence of the right umbilical vein—was encountered in a number of instances. Since no reference to persistent right umbilical vein has been found in the literature, the following remarks on its nature and possible significance may be of interest.

MATERIALS AND METHODS

Rat fetuses (Long-Evans strain) ranging from 10- to 21-days fetal age* from mothers maintained on the PGA-deficient regimen† from the ninth to eleventh days of gestation resulted in multiple abnormalities in 99 per cent of rat fetuses examined on the twenty-first day, one day prior to parturition.† Macroscopically, 57 per cent of these abnormal fetuses exhibited cardiovascular anomalies such as persistent interventricular foramen, persistent truncus arteriosus, right-sided aorta and anomalous subclavian arteries. While tracing the development of such abnormalities in younger embryos from mothers on the same PGA-deficient regimen, an anomaly not previously recognized—persistence of the right umbilical vein—was encountered in a number of instances. Since no reference to persistent right umbilical vein has been found in the literature, the following remarks on its nature and possible significance may be of interest.

† Previous studies have shown that there are no significant differences, macroscopically or microscopically, between embryos from mothers fed a stock diet and those from mothers maintained on a PGA-supplemented diet.

RESULTS

In order to determine the origin of persistent right umbilical vein, it was necessary to trace the development of the vitelline and umbilical veins in control and PGA-deficient embryos of 10-days fetal age and older.

In both the control and the PGA-deficient embryos of the tenth day of gestation, the umbilical veins were rudimentary contrasting with the vitelline veins which were well established and terminated in the sinus venosus. In the 11-day controls the right umbilical vein ended in the sinus venosus and was of much greater caliber than the left umbilical vein which joined the corresponding vitelline vein within the liver. Traces of the earlier connection of the left umbilical vein with the left duct of Cuvier or the left posterior cardinal vein were discernible in a few control specimens. The location of the ductus venosus could be determined in all 11-day control fetuses. In 3 of the 5 PGA-deficient specimens of this age, the caliber of the right umbilical vein was either equal to, or only slightly larger than, that of the left umbilical vein; the other 2 PGA-deficient embryos resembled the controls. In the 12-day controls the right umbilical vein was still much larger than the left umbilical vein and blood from the latter now reached

* The day of finding sperm in the vagina is considered to be day zero.
† The PGA-deficient, PGA-supplemented, and the stock diets are the same as those used by Baird and associates.
Fig. 1. Diagrams, based on graphic reconstructions, depicting the stages of development of the vitelline and umbilical veins in normal rat fetuses on the tenth (a), eleventh (b), twelfth (c) and thirteenth (d) days of gestation. Veins are indicated as follows: 
- CV — common vitelline
- LAC — left anterior cardinal
- LPC — left posterior cardinal
- LU — left umbilical
- LV — left vitelline
- PV — portal
- PVC — posterior vena cava
- RAC — right anterior cardinal
- RPC — right posterior cardinal
- RU — right umbilical
- RV — right vitelline
- UR — umbilical recess
- SV — sinus venosus

The striated vessel represents the ductus venosus. The alimentary canal is shown in black. The developing liver is indicated by crosses and stippling.

The posterior vena cava through the cranial portion of the left vitelline vein and the ductus venosus. In addition, the portal vein had formed from portions of the vitelline veins and anastomoses between them (fig. 1e). Each of the 5 12-day PGA-deficient embryos showed dominance of the right umbilical vein and the channel connecting the left umbilical and the left vitelline veins was poorly formed.

In the 13-day control embryos the right umbilical vein had almost entirely disappeared while the left umbilical vein was markedly enlarged. The left umbilical vein, the portal vein, the ductus venosus, and the posterior vena cava presented the relationships which are maintained until birth (figs. 1d and 2a). Frequently, in control embryos of this and subsequent stages, the caudal portion of the right umbilical vein persisted as a body wall vein emptying into the left umbilical vein. During the period of its existence as a functional channel through the eleventh and twelfth days of pregnancy, the right umbilical vein was observed to be essentially a body wall vessel having only minor connections with the hepatic sinuses; in this respect, it differed markedly from the left umbilical vein which, by the eleventh day, was intimately connected with the venous sinuses of the liver.

Of the 33 PGA-deficient fetuses of 14- to 21-days fetal age, 11 showed persistence of the right umbilical vein (figs. 1b, 1c, 2b and 2c). All presented the following characteristics: (1) the persisting right umbilical vein left the body wall and coursed over the cranial aspect of the diaphragm to terminate in the posterior vena cava immediately caudal to the heart; (2) the left umbilical vein was either absent or represented by a few small vessels within the body wall; (3) the ductus venosus was absent; (4) the caliber of the intrahepatic portion of the posterior vena cava was noticeably reduced, especially in the older embryos. It was observed that, in the absence of the ductus venosus, the formation of the liver appeared normal and the
vascular pattern similar to that found post-natally. In the 21-day PGA-deficient fetuses a persistent right umbilical vein could be detected by dissection under low magnification.

In the 11 PGA-deficient embryos showing persistent right umbilical vein the following additional cardiovascular abnormalities were encountered: single pulmonary artery (9); persistent interventricular foramen (6); anomalous termination of the pulmonary veins (5); distally arising right or left subclavian artery (4); right-sided aorta (3); defective interatrial septum (3); pulmonary stenosis* (2). Absence of the ductus arteriosus, persistent truncus arteriosus, diminutive right ventricle,* persistent ductus caroticus,* and ectopia cordis, were each observed once. While these abnormalities were not peculiar to fetuses with a persistent right umbilical vein, the frequency of pulmonary arterial and venous anomalies, and defective interatrial septum was slightly greater in embryos with this anomaly than in those without.

**DISCUSSION**

In general, the development and fate of the vitelline and umbilical veins in the Long-Evans rat resemble those of other mammals. However, in this strain, at least, the connections between the right umbilical vein and the liver sinuses are always much less marked than in the pig where the right umbilical vein ultimately discharges all its blood into the hepatic channels of the right side. In fetal rats of the present study the right umbilical vein, during its brief existence, remains fundamentally a body-wall vein. It is this characteristic which enables it to pursue a course cranial to the diaphragm when it fails to regress. Conceivably, the path taken by a persistent right umbilical vein depends upon the developmental peculiarities of the species considered.

The descriptions and illustrations of His* suggest that the fate of the right umbilical vein in the human embryo resembles that described for the pig. In the later study of Mall,* however, there are conflicting statements in this respect and his illustrations of sectioned embryos and reconstructions indicate that in man the development and regression of the right umbilical vein may resemble that of the rat, or perhaps occupy a category somewhere between that of rat and pig. If this is so, then a persistent right umbilical vein in the human fetus would likely present features similar to those observed in the present study.

The factors which result in the relatively sudden regression of the right umbilical vein in control rat fetuses between the twelfth and thirteenth days of gestation are difficult to elucidate, but one or more of the following may play some role: 1. Between the twelfth and thirteenth days of pregnancy, the enlarging liver may compress and consequently occlude the right umbilical vein as it courses through the body wall to join the posterior vena cava. The left umbilical vein, no longer running in the body wall for any great distance, would suffer less compression and constitute a more suitable pathway for blood returning to the embryo from the placenta. 2. Diminution in the volume of the blood conveyed by the left vitelline vein between the twelfth and thirteenth days of pregnancy may permit an increase in the caliber of the left umbilical vein with which it is in close contact. 3. Change in the angle of divergence of the right and left umbilical veins from the parent vessel just prior to the thirteenth day of pregnancy may favor the latter with a greater blood volume. In the PGA-deficient embryos of the present study, retarded or arrested development before the thirteenth day probably has disturbed one or more of these factors.

While it is possible that persistent right umbilical vein could produce hemodynamic disturbances initiating the formation of other cardiovascular abnormalities, the present study, so far, presents no conclusive evidence in this regard. Study of this aspect, however, is continuing.

Since persistent right umbilical vein could occur in the human subject, a routine check for it should be undertaken at autopsy, especially when other cardiovascular abnormalities are present. This anomaly, of course, would be detectable only in fetuses, newborns or infants,
as after birth a persistent right umbilical vein will gradually atrophy and disappear.

**Summary**

Persistent right umbilical vein has been encountered in 11 of 33 pteroylglutamic acid deficient rat embryos of 14- to 21-days fetal age. Retarded or arrested development from the transitory pteroylglutamic acid deficiency apparently disturbed the usual regression of the right umbilical vein between the twelfth and thirteenth days of gestation.

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**Summario in Interlingua**

Persistente venas dextero-umbilical esseva constatate in 11 ex 33 embryones de ratta, a etates fetal de inter 14 e 21 dies, post gestation a carentia de acido pteroylglutamic. Le transition del acido esseva apparentemente le causa de un retardation o arresto de disveloppamento que obstrueva le normal regression del vena dextero-umbilical inter le dece-secunde e le dece-tertie die.

**References**


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