

## CHAPTER 1

### Knotted umbilical cords

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“These vessels, whose origin is already known, wind around each other, like the twigs which form the handle of a basket. Sometime the arteries creep round the vein, like ivy round a tree; and sometimes the vein does the same round the arteries. The vein often folds itself into a kind of loops of different lengths, or forms itself into a species of knots subject to become varicose... The cord from its great length, sometimes get tied into one or more knots. These do not prevent the ordinary development of the foetus nor occasion its death as imagined by some” Baudelocque (1789).<sup>1</sup>

#### 1. Introduction

To the delight of topologists, there are many examples of knots in Nature starting at the level of DNA, proteins, polymers, fish, cables and magnetic braids in the solar corona.<sup>2,3,4,5,6,7,8,9</sup> The purpose of this Note is to discuss and document the formation of knots in umbilical cords, a biological system which exhibits knots and that has seemingly eluded the scrutiny of mathematicians and physicists.

#### 2. Description

An umbilical cord is a cordlike structure in the pregnant female mammal connecting the placenta to the abdominal wall of the fetus. Its primary function is to carry oxygen and blood to the fetus and return waste products. In

pregnant human females, it is normally composed of two arteries and one vein.<sup>10</sup> The umbilical vein carries oxygenated blood from the placenta to the fetus while the umbilical arteries carry deoxygenated blood and wastes from the fetus back to the placenta. The arterial vessels are embedded in a sturdy gel-like structure known as the Wharton's jelly. The vein is twisted around the arteries and the arteries are twisted within the cords to form a triple helix. Typical diameters of an umbilical cord at delivery are around 1.7cm.<sup>a</sup> The length of the umbilical cord at birth (38 weeks) averages<sup>12</sup> 57.4cm with standard deviation 12.6cm but on rare occasions cords as long as 300cm and as short as 6.7cm have been observed.<sup>b</sup> Cords below 40cm occur only in 6% of the cases and are known as short cords. Short cords may cause traction, placental abruption and even cord rupture during vaginal delivery and are associated with many different problems at birth (such as low Apgar scores and hypotonia) and neurological abnormalities later in life. Cords must be sufficiently long (at least 32cm) as to allow the fetus to exit safely the womb. However, if a cord becomes too long it can loop around foetal parts and produce distress through cord compression.

### 3. Knots

The feature of interest for this Note is the possibility of knot formation in umbilical cords. Physicians use the word knot for two different structures. The so-called "false knots" correspond to the looping of the umbilical vessels due to high vascular torsion inside the Wharton's Jelly of the umbilical cord (See Figure 1). Their bulky appearance is sometime mistaken for true knots. A common superstition is that the number of false knots determines the number of children the mother is to have. However, they have little clinical significance, no interesting topology, and will not be discussed further. The "true knots" are knots in the common sense (see Figure 2)<sup>14</sup> but not in the restrictive mathematical sense since, obviously, the cord is not closed. However, there is no ambiguity in the definition of a mathematical knot for an umbilical cord since it is usually localized and pulled tight. One can virtually close the knot by first pulling the end of the cord so that it is contained inside a sphere with its ends on the sphere and imagining a tube connecting the two ends of the cord without any intersection with

<sup>a</sup>Unless specified otherwise, the data used in this paper is taken from Benirschke and Kaufmann (2000).<sup>11</sup>

<sup>b</sup>Leonardo Da Vinci remarked that the typical length of the umbilical cord at birth is equal to the length of the newborn infant, a rather good estimate.<sup>13</sup>

the sphere itself. To avoid pointless arguments, when referring to knots, we assume here that the central curve of the cord has been closed away from the knot in such a manner.



Fig. 1. A false knot is an enlargement of the umbilical cord due to excessive vascular growth. Picture Courtesy of the University of Utah Placental Bank (Reproductive Genetics Research Lab.)

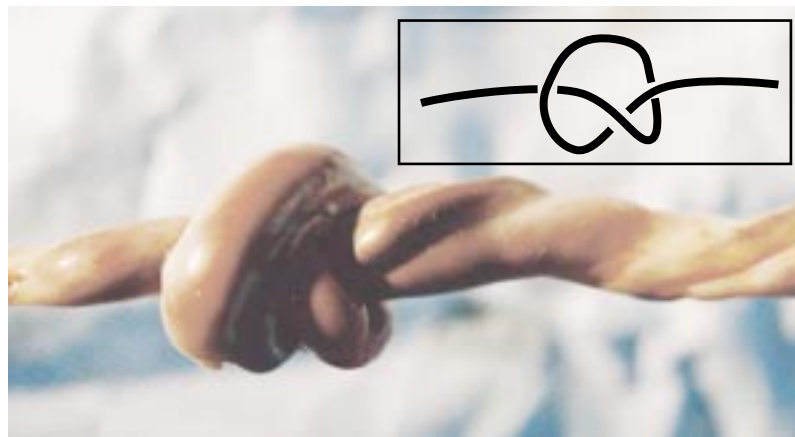


Fig. 2. A true knot occurs when the fetus passes through a loop and forms a knot. Copyright ©1996 Massachusetts Medical Society. All rights reserved.

#### 4. History

Umbilical knots are a rather peculiar and puzzling feature of the umbilical cord. They have attracted the attention of physicians and midwives for centuries and have been discussed in the medical literature extensively. Prior to 1948, more than 150 papers were written on the subject as cited in the review papers by Browne<sup>15</sup> (1923), Lundgren and Boice<sup>16</sup> (1939), Hennessy<sup>17</sup> (1944), and Spivack<sup>18</sup> (1946). Most of these articles are published cases, that is, anecdotal accounts of observed knots in umbilical cords. The earliest paper addressing exclusively the problem of umbilical knots is due to M. Baudelocque who published in 1842 an article<sup>c</sup> entitled “Sur les noeuds du cordon ombilical”<sup>19</sup> Baudelocque’s paper relates his own observations and discusses earlier work by J. L. Baudelocque, William Smellie (See Figure 3) and Mauriceau on the clinical significance of knotted cords and their formation. He argues that the knot is likely to be formed at birth (“It is difficult to conceive that the cord can knot itself up to three times at the same place”) and that it does not affect the outcome of pregnancy (“If a dead infant has a knotted umbilical cord, one should look for another cause of death”). Unbeknown to the modern medical literature, it seems that the earliest report of knots in umbilical cord is to be found in the work of Louise Bourgeois dating back to 1609.<sup>20</sup> In there, she described how she delivered to a baby with a knotted umbilical cord (“le nombril noué a droit noeud”), the woman had complained of belly pains days before giving birth and Bourgeois concluded that the umbilical cord must have passed around the fetus during this time of “great agitation”. She thought the event was so extraordinary that she offered to produce witnesses to corroborate her account.<sup>d</sup>

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<sup>c</sup>This paper is cited in Hennessy<sup>17</sup> but wrongly attributed to Jean-Louis Baudelocque (1745-1810). J.-L. Baudelocque was considered the leading French obstetrician of his time. He attended Napoleon’s wife, Marie Thérèse and published the important treatise “L’art des accouchements” in 1789 in which knotted umbilical cords is also discussed (see quotation above). The Baudelocque family has produced many obstetricians and is still remembered in Paris’ renowned Clinique Baudelocque, one of the first public health clinics ever established (1890).

<sup>d</sup>Louise Bourgeois (1563-1636) was a midwife and attended queen Marie de Medicis for six deliveries. Her Observations is the first book of obstetrics written in French by a woman. Her remarkable life and work has been rediscovered recently and is the object of many interesting publications.<sup>21,22,23</sup>

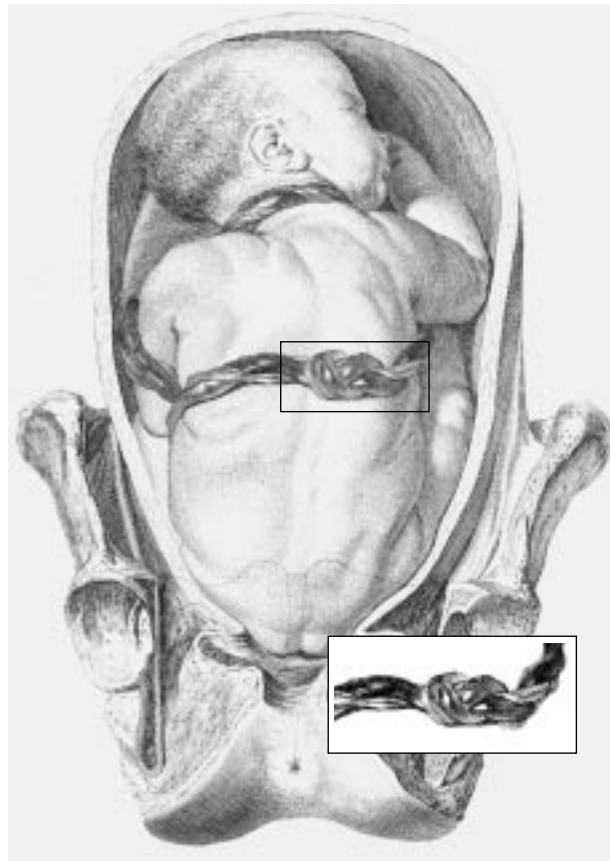


Fig. 3. Table XXIX from Smellie's "An abridgement of the practice of midwifery: and a set of anatomical tables with explanations" (1786). Note also the nuchal coil (the loop around the neck) typical of long umbilical cords. Smellie found the problem sufficiently interesting to discuss it in four different places in his book and include an engraving of a knot. William Smellie (1698-1763) was the most famous and best known teacher of man-midwives in London. He published three treatises on midwifery and was virulently critiqued by English writers opposed to the practice of midwifery by men.

### 5. Knotting frequency

How often are knotted umbilical cords observed? True knots are an uncommon but not rare occurrence. Most papers cite the frequency of knot formation as being between 0.3% and 2.1% of all pregnancies. The earlier studies date back to Chantreuil's thesis in 1875. Over the last 125 years, more than 15 studies on knotting frequencies have been published (see Ta-

ble 1). The most recent studies published over the last 3 years with rigorous statistical controls all seem to agree that the frequency is close to 1% (the grand total is 2,104 cases for 214,124 birth, that is a frequency of about 1.0%).

Authors	(# cases)/(# birth)	Frequency
Chantreuil (1875) <sup>16</sup>	6/1,000	0.6%
Mundé (1879) <sup>16</sup>	2/1,000	0.2%
Von Hecker (1925) <sup>15</sup>	115/31,590	0.4%
Terlizzi and Rossi (1959) <sup>24</sup>	48/15,416	0.3%
Dippel (1964) <sup>25</sup>	21/1,009	2.1%
Spellacy <i>et al.</i> (1966) <sup>26</sup>	180/17,190	1.0%
Recasens <i>et al.</i> (1968) <sup>24</sup>	5/800	0.6%
Hartge (1979) <sup>24</sup>	33/3,400	1%
Blickstein <i>et al</i> (1987) <sup>27</sup>	57/4,650	1.2%
McLennan <i>et al</i> (1988) <sup>28</sup>	6/1,115	0.5%
Sepulveda <i>et al</i> (1995) <sup>29</sup>	18/5,575	0.3%
Joura <i>et al</i> (1998) <sup>30</sup>	286/22,531	1.3%
Sornes (2000) <sup>31</sup>	216/22,012	1.0%
Hershkovitz <i>et al</i> (2001) <sup>32</sup>	841/69,139	1.2%
Airas and Heinonen (2002) <sup>33</sup>	288/23,0272	1.2%
<b>TOTAL</b>	<b>2,104/214,124</b>	<b>1.0%</b>

Table 1. Frequencies of observed knots. Since the methodology varies between all these studies, the total is only given as an indication of the most likely frequency of knotting.

## 6. Contributing factors

Almost all studies conclude that the mean cord length is higher in knotted cords than in normal cords (*e.g.* 84cm versus 59cm from Sornes<sup>31</sup> (2000)). Airas and Heinonen (2002) found that the risk factors associated with true knot formation are multiparity (2 or more pregnancies), previous miscarriages, and obesity.<sup>33</sup> Similarly, Hershkovitz *et al.* identified the following groups at risk: grandmultiparous women (5 or more pregnancies), pregnancies complicated with hydramnios (excess of amniotic fluid), patient

who underwent genetic amniocentesis (a prenatal test in which a small amount of amniotic fluid is removed and examined) and those with chronic hypertension.<sup>32</sup> Male gender was also found to be a significant contributor to knot formation.

These risk factors point to three basic simple chief causes to knot formation: (1) the cord length: Increased fetal activity is associated with long umbilical cords (this is related to the interesting assumption that one of the stimuli for growth in cords is the tension generated through fetal activity<sup>34</sup>), also males have slightly longer cords than females and knots are commonly found in Chimpanzees who have a relatively much longer cord<sup>35</sup>; (2) large uterine volume: Factors such as multiparity, hydramnios, obesity, and diabetes are all associated with large uterine volume or lax uterine wall; (3) high fetal activity: amniocentesis is known to produce large fetal activity. Therefore, these studies suggest that the two relevant geometric features are: long cords and large uterine volume and that the important dynamical feature is fetal activity. These effects can be combined into the following simple model.

## 7. A simple model

To simplify the purely geometrical problem of knot formation we consider a free floating ball of radius  $R$  attached to a string of length  $L$  of negligible thickness and anchored at one point. The ball is free to move randomly in a 3 dimensional space with the constraint that the length of the string remains constant (See Figure 4.A). Will the ball eventually pass through a loop and knot itself? Clearly, the string must be long enough since if  $L/R < \lambda_{\text{crit}} = 2\pi$ , the string cannot slide around the sphere to create a trefoil knot. Since the thickness of the string is considered negligible, the only relevant parameter in the problem is the ratio  $\lambda = L/R$ . Intuitively, if  $\lambda$  is large enough, we expect that knotting will occur frequently and, conversely as  $\lambda \rightarrow \lambda_{\text{crit}}$ , no knotting will be observed. The precise manner in which the knotting frequency depends on  $\lambda$  is not known. However, similar problems have been extensively studied in Brownian motion.<sup>36,37,38,39,40,41</sup> These studies reveal that the probability of forming a knot in self-avoiding polygonal walks increases with the length  $n$  of the polygon as

$$P(n) = 1 - e^{-\alpha n + o(n)} \quad (1)$$

for some positive constant  $\alpha$ . Therefore, it is reasonable to expect that the situation in our model will be similar and that the likelihood of knot

formation increases with the parameter  $\lambda$ . Depending on the geometry, the critical value of  $\lambda$  may be different. For instance, if a string of length  $L$  is attached on a cylinder of height  $2h$  and radius  $r$ , the minimal length to pass the cylinder around the loop is  $l + 2\pi r$  where  $h \leq l \leq 2h$ .

Fetuses are not perfect spheres and different choices can be made for an effective radius  $R$ . Here we give two different choices roughly corresponding to an upper and a lower bound for the problem. First, as an upper bound, we use the weight of the fetus and compute the radius (referred to as the “ball radius”) of the sphere with equal weight (assuming that the density of the fetus is close to that of water). Second as a lower bound, we use the crown-rump length as the diameter of our ball. In Figure 5 we show the evolution of the parameter  $\lambda$  along the pregnancy for these two choices of radii. The dotted line corresponds to  $\lambda = 2\pi$ , that is, if the fetus was a perfect sphere with diameter equal to the crown-rump length, the only geometric possibility of knot formation for average umbilical cords and fetuses would occur between 10 and 15 weeks. The most important features of Figure 5 is the peak appearing at 12-13 week of gestation and the increase of  $\lambda$  between 9 and 15 weeks.

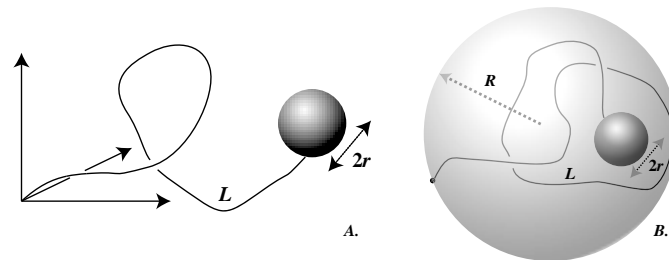


Fig. 4. In the first model (A), a ball attached to a string is free to move in a three-dimensional space. The string is fixed at one point and the ball performs random motion, dragging the string behind itself. The goal of this model is to understand the interplay between the motion of the ball and the constraint due to the string on the formation of knots. In the second model (B), the same ball is attached to a string itself attached to the inside surface of a sphere. This model introduces a new length in the problem (the radius of the outer sphere) and is aimed at understanding the effect of the amniotic sac volume on the formation of knots.

A fetus is not allowed to move freely in space, its motion is restricted by the amniotic sac. The smaller the sac with respect to the size of the fetus, the less likely the fetus will be able to move around and form loops. Eventually, close to gestation (typically after 20 weeks), very few large scale



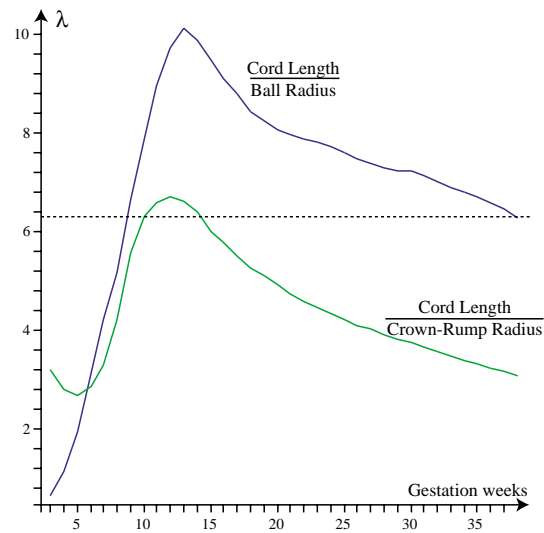


Fig. 5. Evolution of the ratios cord length to ball radius and crown-rump length as a function of gestation time (counted in weeks). The ball radius corresponds to the equivalent radius of a sphere of density one of equal fetus weight. The dotted line corresponds to the critical value  $\lambda_{\text{crit}} = 2\pi$ . That is, if the fetus was a perfect sphere with radius given by half the crown-rump length, knotting could only occur in a very small window of time around week 13.

motion is possible. Ideally, we can look at it as restricting the motion of our ball into a larger sphere (See Figure 4.B). To quantify this effect, we show on Figure 6, the ratio of the placenta radius to the ball radius. Here again, we clearly see a peak at week 13 followed by a sharp decay and a plateau around 20 weeks where fetus motion will be impeded by the sac. This simple analysis suggests that the time where knot formation is most likely to occur is between 9 and 18 weeks with a peak around 13-14 week. Furthermore, if we assume that the increase in probability for knot formation follows a similar law as the one given by Equation (1), we see that small increases in the length of the umbilical cord will result in a large increase in the probability of knot formation.

How does this geometric prediction compare to the accepted knowledge in the medical literature? It is usually believed that knot formation occurs between 9 and 12 weeks' gestation.<sup>32</sup> Blickstein *et al.*<sup>27</sup> argue that knot formation should occur between week 9 and week 28 (when cord length does not increase significantly). Our analysis is also consistent with the

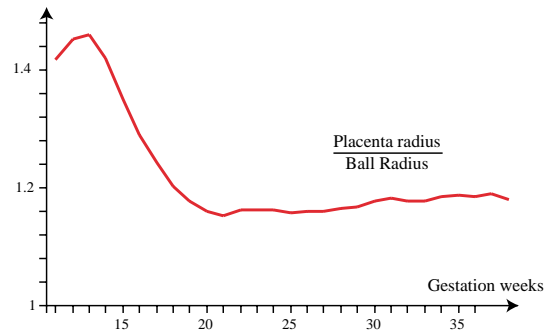


Fig. 6. Evolution of the placenta radius to the ball radius as a function of gestation time (in week). After 20 weeks, the relative room for fetal motion does not change.

onset of large scale motions of the fetus: “By 8 to 10 weeks, the fetus typically exhibits a series of abrupt movements characterized by sudden arching of the back and extension of the limbs. These movements cause the fetus to rise up in the amniotic fluid pool and then to sink slowly at completion of the movement”<sup>42</sup> Finally, the correlation with patients who underwent amniocentesis is also consistent with these results since this test is usually performed between week 15 and 18.

This analysis does not exclude the possibility of knot formation during labor when the fetus, during ejection, is passed through a loop. However, Browne<sup>15</sup> argues that these knots could easily be detected from knots formed earlier as they should not retain their shape when untight. If a true knot forms itself in the second trimester, the shape of the knot is completely set during further growth even when the cord is not pulled.

## 8. Clinical significance

A central question for physicians is the relevance of knots for the final outcome of the pregnancy: “defining a high risk group of patients for true knot of cord is of utmost importance in order to decrease perinatal morbidity and morbidity”.<sup>32</sup> This question has been hotly debated since the first paper by Baudelocque (see quotes above). The risks could be multiple. First, if the cord is pulled too tight it could compress itself and impairs perfusion so that oxygen and nutrient could not reach the fetus, possibly triggering asphyxia and an increase in cardiac load<sup>43</sup> potentially leading to fetal distress. To test this idea, Browne<sup>15</sup> conducted experiments on the perfusion of cords. In his experiment, he collected a fresh umbilical cord and made a

slack knot, then he attached a weight to the cord to simulate tension and perfused it with increasing pressure until circulation was established. His *in vitro* experiment showed that “even a slack knot may be sufficient to interfere with, if not completely to obstruct, the cord circulation”. Modern statistical analyses by Airas and Heinonen<sup>33</sup> have shown that fetuses with umbilical knots have a four-fold increased risk of stillbirth during pregnancy, showing a clear association between fetal demise and cord knots, a finding supported by other studies.<sup>30,31</sup> However, it is not clear in these cases that the umbilical knot was the main reason for fetal death since asphyxia and increased cardiac load can be caused by nuchal coils which are themselves correlated with long cords and henceforth umbilical knots. Sornes<sup>31</sup> argues that: “the mere presence of of a knot on the cord cannot in my opinion be a ‘cause of death’. When these cases occur, a more thorough investigation into the whole of the placenta, and the umbilical cord in its entire length, is called for in order to elucidate the real cause of death.” Moreover, these findings may not be clinically significant since: (1) umbilical knots are extremely difficult to detect by ultrasonography;<sup>29</sup> (2) if a knot is detected, it is not clear what medical care could be given to prevent the tightening of the cord and fetal death associated with asphyxia.

The second risk associated with umbilical knots is the possibility of cord tightening during delivery when the cord is stretched. However, cord knots does not seem to affect birth since the Apgar scores and the level of obstetrical intervention are equal.<sup>28,30,31</sup>

Whereas knot formation is relatively begin in singletons, it becomes significant for the so-called MoMo twins (monoamniotic, monochorionic twins).<sup>44</sup> These MoMo twins are usually monozygotic and share the same uterine sac without any membrane to keep them apart. This is by itself a rare occurrence in twins (about 1 to 2%) but when it presents itself there is a high mortality rate as high as 50-62% and congenital anomalies in 15-20% of cases due to entanglement of the two cords (see Figure 7).

## 9. Complex and multiple knots

Most of the umbilical knots observed are not properly described or classified. Since trefoil knot are the simplest and easiest to make (passing once through as single loop), it is likely that the vast majority of umbilical knots are trefoil. Nevertheless, more complex and multiple knots have also observed. The only comprehensive statistical analysis of multiple knots was performed by Sornes<sup>31</sup> who observed 11 cases of double knots, 201 cases



Fig. 7. Cord entanglement in MoMo twins. This is a very serious condition with high mortality rate. Picture Courtesy of the University of Utah Placental Bank (Reproductive Genetics Research Lab.)

of simple knots in 22012 births. Therefore, the probability of forming a double knot is about  $68/10000$  much larger than the probability of finding two different cords with a single knot (that is about  $(1\%)^2 = 1/10000$ ). This is not surprising since a long cord in a large intrauterine volume has a higher probability of forming a single and hence a second knot. Different authors report multiple or complex knots found in cords. Beside the usual trefoil knot ( $3_1$  in the standard notation), the figure-eight knot<sup>11</sup> ( $4_1$ ) and the  $5_2$  knot have also been observed (remarkably, in this last case, the knot could be observed by ultrasonography<sup>45</sup>). Multiple knots also come with various topologies such as a double trefoil knot<sup>28</sup>, a trefoil knot and a figure-eight knot<sup>46</sup> (see Figure 8), and the most elaborate knot reported: a double figure-eight knot<sup>47</sup> (in this case the authors also tried to find a mechanistic explanation of the knot formation and realized that it could be obtained if the fetus passed through a double twisted loop—see also Hartge<sup>24</sup> for similar mechanisms for simpler knots).

## 10. Handedness and perversion

Umbilical cords have also a very interesting fine geometric structure. The arteries are longer than the vein which is itself longer than the jelly and they are wrapped around each other so that the umbilical cord forms a triple helix. The handedness of this helical structure is another puzzling feature of the umbilical cord that has been the object of many studies<sup>48,49</sup> and was

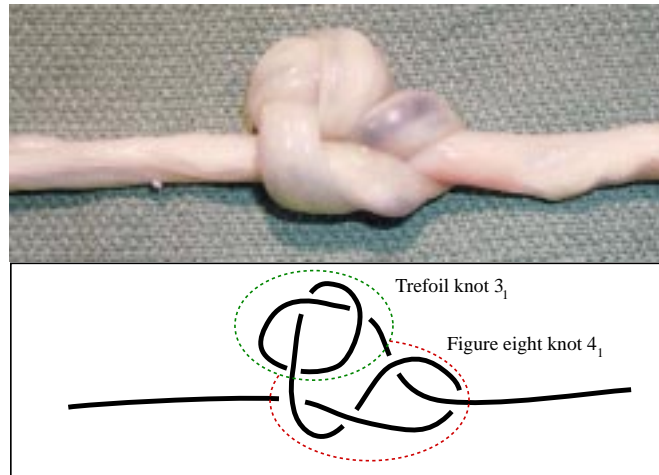


Fig. 8. An example of complex knot in an umbilical cord, a composition of an eight-knot with a trefoil knot. The infant was in good condition, without any clinical evidence of intrapartum asphyxia. Copyright ©1996 Massachusetts Medical Society. All rights reserved.

first discussed by Berengerius in 1521. The umbilical cord has up to to 40 helical turns and handedness can be observed as early as 42 days' gestation.<sup>12</sup> Umbilical cords can be either left-handed, right-handed, straight or with mixed helicity.<sup>50</sup> The ratio of left-handed to right-handed cords is about 7 to 1 similar to the average ratio of right-handed to left-handed adults. However, there is no statistical correlation between the handedness of the cord and hand preferences.<sup>51</sup> An interesting feature that can shed light on the mechanism that selects handedness in cords is the existence of cords with both left and right handed structures. These particular cords with mixed handedness account for 2% to 26% of all cases.<sup>49,52</sup> The transition from left to right handedness is a common occurrence in filamentary structures and is known as *perversion*. It is found in the formation of tendrils in vines,<sup>53,54</sup> in bacterial flagella,<sup>55,56</sup> in the shape of certain bacteria such as spirochetes,<sup>57</sup> in some mutant forms of *B. subtilis*,<sup>58</sup> and in the microscopic structure of cotton fibers.<sup>59</sup> The mechanics and mathematics of perversion has been discussed in length by Goriely, Tabor and McMillen<sup>60,61</sup> who showed that the inversion of helicity if caused by both differential growth and twist blockage of the filamentary structure constraining the filament to writhe and shape itself as helices with zero total twist (the twist of each left and right helices canceling each other). However, to date, there is no

model for the growth of umbilical cords that would explain the difference or handedness, its inversion or even the occurrence of helicity. Both genetic and mechanical factors seem important as indicated by the correlation between umbilical cord helicity in monozygotic twins<sup>48</sup> and experiments on the effect of tension on fetal activity in laboratory rats.<sup>13,62</sup>

## 11. Conclusions

The formation of knots in umbilical cords is an uncommon feature of the umbilical cord that has intrigued scientists for centuries. As early as the 18th century, it was suggested that excessively long cords are the most likely to form knots. Modern data and simple mathematical ideas supports this view and suggest that the formation of a knot is mostly a geometric and dynamical event rather than a physiological pathology. Therefore knotted umbilical cords provide us with a simple and beautiful system to motivate and illustrate the theory of physical knots in long chains.

Mathematicians love knots, they are a simple and elegant construction and knot theory has tentacular connections to various branches of mathematics. However, despite the fact that the microscopic world is mostly filamentary, physical knots in nature are scarce but involved in important processes (such as the ones found in DNA molecules). Most typical ratios of length scales or physical blockage prevent the formation of knots which can, as in the case of umbilical knots, create serious problems and malfunctions. The understanding of mechanisms and geometrical features that prevent knots from forming in many filaments but allow them in particular systems could be a fascinating new chapter in the theory of physical knots.

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