A Conversation About Gut Immaturity, Feeding, Fussiness, and Colic

Editor's Note: This is a transcript of a webinar delivered in English in September 2024. It has been edited for clarity.

Newborn Infant Crying and Fussing: What Is Normal vs Abnormal?

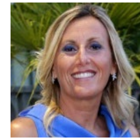
Michael J. Wilsey, Jr, MD: We're going to start out talking about newborn infant crying and fussiness. What is normal vs abnormal? And when talking infant colic and fussiness, you know, in infants, crying is normal, especially in the first few months of life. A baby may cry up to 1 to 3 hours per day. The crying can be related to hunger, discomfort, tiredness or the baby's general adjustment to the world around them. Babies lack the ability to self-soothe before 3 months of age, and their crying can be a natural response to the communication tool during this period of time.

Normal physiologic crying, there can be bouts of intense crying, that is normal, and it's described as the period of purple crying. It's a normal developmental phase in healthy infants, typically between 2 weeks and 4 months of age, that peaks around 2 months of age. And during this time, babies may cry for extended periods of time, often in the evening, and can be difficult to soothe. Though this phase sometimes is confused with colic, purple crying is considered a normal part of infant development. It is not a medical condition. It helps parents understand that excessive crying during this period of time is expected and will pass, typically by about 4 months of age. This differs from organic crying and excessive crying that can be due to hunger, illness, fever, other identifiable causes.

Infant colic is distinguished by more intense crying and prolonged crying spells, which we're going to talk about. Colic typically is defined by the rule of 3, crying for more than 3 hours a day, more than 3 times a week for at least 3 weeks. The crying episodes in colic are often inconsolable, usually occur late in the afternoon or in the evening, these intense screaming spells. Colic babies also show signs of clenching their fists, curling up their legs towards their belly and appear to be in discomfort. And understanding the differences between normal crying and colic crying can help parents manage expectations and seek appropriate support, when needed.

What are the effects of excessive crying in infants on caregivers and family? Well, we know that parents of babies with excessive crying have increased risk of postpartum depression, increased anxiety and distress, sometimes can have difficulty breastfeeding and have also infant/mother bonding disconnect.

Potential long-term outcomes of excessive crying, children that have had, in colic and excessive crying, increased risk of behavioral problems in childhood, increased risk of functional disorders later on in life. There's been association with migraine headaches in infants with excessive crying as well as shaken baby syndrome is at a higher incidence in infants with excessive crying.



Flavia Indrio, MD: How do you explain functional gastrointestinal disorders, like infant colic, to the caregivers?

Michael J. Wilsey, Jr, MD: With functional gastrointestinal disorders, like infant colic—conditions where babies experience distress or discomfort in their digestive system but without any identifying medical causes or structural issues—I explain to parents and caregivers that colic is common, often self-limited where infants cry excessively, often in the evening time and this crying is usually not due to illness, but may be related to developing digestive symptoms. And I share my own personal anecdotal experience. Both my daughters were super-colicky, with that intense screaming and how it can really affect parents and the family. I emphasize that while colic can be stressful it typically resolves on its own between 3 to 6 months of age. And importantly, I reassure them that their baby is healthy and that this phase is temporary.

Flavia Indrio, MD: As you know very well, being a pediatrician, the baby is crying constantly. How can we say what is normal, what is excessive?

Michael J. Wilsey, Jr, MD: Oftentimes, I'll let parents know that they'll get to know the baby's cry. You know, there's the hunger cry, the waah, waah. There's the upset cry, waah, and then there's pedal to the metal screaming fits that happen usually between the witching hours of 5:00 and 10:00 at night. And I try to differentiate normal from excessive crying by discussing both the duration and the pattern of crying. For normal crying, I explain that it's normal and expected for babies to cry 1 to 3 hours a day, and this is how they communicate hunger, tiredness, discomfort, that they need their diaper changed, maybe they need to be burped and they're generally consolable. Excessive crying, such as colic, follows the rule of 3: crying for more than 3 hours a day, more than 3 times a week and for more than 3 weeks. Crying is often more intense, unpredictable and often difficult to soothe.

Flavia Indrio, MD: Regarding the possibility to cow's milk protein allergy or lactose intolerance as a source of crying, what sign do you look for?

Michael J. Wilsey, Jr, MD: I often get a detailed history, particularly with cow's milk protein allergy. The family history of

allergies, asthma, eggs and seasonal allergic rhinitis and then I also ask about symptoms. You know, is there any blood or mucous in the stool, persistent diarrhea, rashes or eczema, very itchy skin, poor weight gain, feeding difficulties, excessive gassiness and fussiness. Sometimes you can have reflux symptoms that don't respond to reflux measures. And so those can be symptoms of a possible cow's milk protein allergy and then I recommend dietary elimination for the mother who's breastfeeding or trying hypoallergic formula in a bottle-fed baby and monitor for symptom improvement.

Flavia Indrio, MD: What about lactose intolerance?

Michael J. Wilsey, Jr, MD: With lactose, I don't see as much lactose intolerance, at least in the United States. You know, congenital lactase deficiency is rather rare and mothers will often, if their baby is breastfed or they're bottle-fed, they'll switch formulas before they come to see us.

Flavia Indrio, MD: This is something we have to underline to the parents. Lactose intolerance is a very rare condition. There is no need to avoid lactose in the formula or if the lactose is generally present in the breast milk. This is something we need to emphasize. Do you ever consider the quantity of crying in addition to the quality of crying when diagnosing colic? This rule of 3 … but the problem is, is the mother staying with the clock, watching, at this time, the hours?

Michael J. Wilsey, Jr, MD: Again, it's a rule of 3, but not all babies read the textbooks. But again, looking at both the quantity, how intense and the amount of crying and the quality, the severity of crying. And again, as you mentioned, the rule of 3—3 hours a day, 3 times a week for more than 3 weeks—that gives some guidelines that this may be excessive crying like colic, but also pay attention to the screaming, that intense pedal to the metal, difficult to console which often is high-pitched, unconsolable, occurs in the late afternoon and evening. And these factors help differentiate between normal crying and excessive crying.

Assessing and Measuring Developmental Outcomes

Flavia Indrio, MD: Now we're going to focus on newborn crying and the connection to gut immaturity. The problem of colic, as a functional gastrointestinal disorder, is a complex disorder that is multifactorial. Multifactorial means that there are some gastrointestinal causes and nongastrointestinal causes. Of course, for gastrointestinal causes, we have, what could be cow's milk allergy or the main reason of the inflammation due to this diagnosis. Of course, there are psychosocial factors, when the caregiver is stressed and depressed.

And then there is also a neurobiological cause. What does this mean? It means the maturity of the central nervous system. But we will see that these 2 causes, at least the gastrointestinal disorder and central nervous system disorder, are connected to each other, because we will talk later about this gut-brain communication.

Exactly what is this gut-brain microbiota axis and this neuroendocrine signaling? As I was telling you before, the gut and the brain, they are absolutely connected in a way that the brain can influence the gut function, but also, on the other way around, the gut can influence the brain function and maturation. Exactly, there are a lot of signals that go back and forth from the brain to the gut that are especially the cytokine, the inflammation cytokine, the neuroendocrine hormones, and this kind of signal can change and disrupt the intestinal permeability, increasing and changing the colonization of the brain, that can alter the bile acid composition and can increase the visceral hypersensitivity. What does this mean? It means that any baby affected by colic has a threshold of pain into the gut that is lower than normal children and this is due to this complex relationship between the gut and the brain. And it's not that simple because the system is complex and there is more than 1 factor involved.

If we go into detail in this story of the dysbiosis, there have been a lot of studies published and it's not the last one, but for sure, it's one of the most important, and it is that a scientist from the Netherlands, she took the colicky baby and compared the non-colicky baby and she just checked, without any intervention, what were the colonization of those babies? The baby with colic showed a slower colonization rate, less diversity and stability, a low butyrate-producing species and a low anti-inflammatory species and a high gas-producing and proinflammatory species.

Now, if this is the egg or the chicken, nobody can tell. If this is the cause or if this is the effect, nobody can tell. For sure, what we can tell is that there is a dysbiosis, that there is an inflammation, that there is something that is interrupting the colonization of those babies, changing dramatically the gut-brain communication.

Michael J. Wilsey, Jr, MD: You talked about the brain-gut axis and the microbiome and the role in functional gastrointestinal disorders are getting more attention. How do you explain this concept to patients and families?

Flavia Indrio, MD: This is not that simple because generally I try to tell the mother or the parents, I generally say, look, the baby is going to mature. The brain and the gut, they are going in together, hand to hand, to reach the final maturation. If something happens to the brain of the baby, if the baby just feels the distress of the mother or then something is changing in the intestines. They are connected. I try to explain how these

functions are connected and take care more of, let's say, a psychological factor because the baby's feeling so much, the anxiety and the feeling of the parents, truly not what they want to show him but what they really think in their heart.

Michael J. Wilsey, Jr, MD: How can parents and caregivers promote a healthy microbiome in infants?

Flavia Indrio, MD: This is also a very, very good and difficult question. Microbiome, it's a complex stepwise process of colonization. There are a lot of factors that influence it. First of all, I would suggest not to use antibiotics during the first day or even intrapartum and, of course, one preference over the other is to go to a vaginal delivery which is better than a cesarean birth. And also breastfeeding. This is the first step. We have different steps, so prenatally, not to use antibiotics for the mother during pregnancy. Using vaginal delivery instead of choosing a cesarean delivery, and use breast milk. These 3 criteria, at least, will help in the proper colonization in the baby.

Michael J. Wilsey, Jr, MD: Is there a role for prophylactic probiotics in preventing the development of functional gastrointestinal disorders?

Flavia Indrio, MD: This is a quite debatable statement because, in the literature, if we go through the literature, there is only 1 study I performed 10 years ago in Italy. It was quite a big study, around 500 children included. They were randomized to have probiotic, *Lactobacilli reuteri* DSM17938 or a placebo since the very first 7 days of life. This study showed that the use of prophylactic, not in treatment, prophylactic, so before the baby showed the colic or regurgitation or constipation, so whatsoever functional gastrointestinal disorder, there was efficacy. But as everybody knows, the study needs to be repeated and so far, no one has repeated it. What I can tell you is that now we are analyzing more than 8,000 children in Italy, analyzing the data with artificial intelligence, with an algorithm, just to identify the risk factor of the functional gastrointestinal disorder. Let me tell you, it's not only microbiome. There are other factors, but wait until that paper is published.

Clinical Management Strategies for Infantile Colic

Flavia Indrio, MD: Now is the time to talk about clinical management strategies for infantile colic. The problem of this is that, first of all, we have to make a diagnosis because a proper diagnosis allows us to administer proper treatment. First of all, we have to follow the rule for criteria so that the days when the baby is crying, well it's not exactly that we stay with the time, 3 hours a day, 3 days a week. When the baby's crying at the same time and we cannot even have any possibility to stop it. We do the physical and clinical intervention. First of all, we have to exclude other disease. The baby has to be otherwise healthy. What does otherwise healthy mean? No fever, no fracture or suspicion of fracture of abuse, no other sign of infection. Then we go to a differential diagnosis because we have talked previously about the possibility of allergy, non-IgE-mediated cow's milk allergy or also to soy products. And then we have to go through the history of the baby, family history of allergy. And then again, lactose overload or malabsorption is not that one that we need. Lactose intolerance is a very rare condition. Lactose overload is something that is not so rare. It's just temporary. After 3 or 4 days, lactase is called inducted enzyme. You need as much as is available. It's just temporary.

And we have also to check if there is gastroesophageal reflux disease or the baby has an injury. And once we have done the diagnosis, then we go to the proper treatment approach.

Michael J. Wilsey, Jr, MD: What questions do you ask parents and caregivers who present with concerns of excessive colic and crying?

Flavia Indrio, MD: Generally, I ask what is the time when the baby's crying because, generally, this baby has got the crisis of crying always at the same time. That is intestinal because simply this excessive air that is overloading into the intestine is just having some eructation. Generally, this colicky baby is always crying at the same time and, as Dr. Wilsey also stated before, it's different crying. The crying of the colic is inconsolable. You cannot possibly stop it.

Michael J. Wilsey, Jr, MD: What warning signs or red flags do you look for when evaluating an infant with excessive crying?

Flavia Indrio, MD: Red flags and warning signs are extremely important. I told you already, first of all, fever. If the baby has got fever. If the baby has got any sign of infection, urinary tract infection. We have to look for this. For instance, the weight gain, if the baby is not gaining weight, if the baby is also, you look for some abuse sign like a fracture or the cranial evaluation, if there is like an external hypertension. You have to look at these red flags, but basically weight gain, fever, trauma.

Michael J. Wilsey, Jr, MD: Also look for like bloody stools and eczema in those babies.

Flavia Indrio, MD: Bloody stools, yes.

Michael J. Wilsey, Jr, MD: When you see these warning signs, what are your next steps for these patients?

Flavia Indrio, MD: when you see these warning signs, then you are allowed to go farther in investigation because if you don't see these warning signs, no further investigations are needed.

First, you can go for lab tests, microbial tests to look for infection. You can go to urine tests, to see if there is a urinary infection and you go to a more detailed history and you can go farther with laboratory tests. Again, I want to stress this concept, process, the laboratory tests when you're quite sure there is colic, functional gastrointestinal disorder, there is no need to take the baby under the line on this. You can go through the evaluation of the blood and the stool or calprotectin or other signs, but if you are quite sure the functional gastrointestinal disorder, colic, is the diagnosis, please don't take this baby anywhere.

Michael J. Wilsey, Jr, MD: You have now a baby who's growing well and no warning signs, what reassurance do you give parents and caregivers of this infant with colic?

Flavia Indrio, MD: First of all, from not my experience only but also the literature, these parents need to be informed and educated when they visit. This is the first one. Even if we look at the meta-analysis, you know, just all the science story and stuff, the reassurance is basically compared with the probiotic in the better approach. You reassure the parents, you say that this disease will not last forever and that the baby is healthy, it's a healthy baby. It's a physiological condition related to maturation. I just teach them to handle the baby when it's crying, not to shake it, just to try to console it, just to relax themselves so the baby will feel they're relaxed. Do not overfeed the baby because the baby, whenever it's crying, is always asking for consolation with sucking. The mother, one of the main mistakes is this: the mother gives milk or breast milk or bottle feed because she says, but the baby is sucking. The baby, the only things he can do after crying is sucking. That's it. That's the only things he can do. Don't overfeed the baby. Just reassure, take it easy, ask for help, from the father or some other family member, if there's any, you know, it's just, that it will take teamwork.

Michael J. Wilsey, Jr, MD: I love that you demonstrate colic comfort measures while they're there, in front of them. That can be very reassuring. And regarding probiotics in your clinical practice, do you recommend probiotics for infants, whether the parents ask for them or not, and if so, why or why not?

Flavia Indrio, MD: This is also quite debated. Probiotics are used and their efficacy has been demonstrated so many times, not only with several randomized controlled trials, with meta-analysis, because the probiotics make at least something related to dysbiosis and to just modulate the dysbiosis, but more the inflammation of the intestine. Now, there are also the nonresponders. You have to be clear with the parents, say look, this probiotic has the possibility to cure the colic, but that doesn't mean that your baby will be cured by this product because there are also the nonresponders to treatment. You have a chance to give probiotics to this baby and you have a possibility to treat your baby. The probiotics need to be specifically strain-related into the guidance. We just finished the ESPGHAN guidelines where there are 2 kind of strains that have been included, 1 is the *Lactobacillus reuteri* DSM17938 that reduced the crying time for a baby, but at least after 1 week of treatment. This is another thing that we have to be clear with the parents. This is not like Tylenol, it's not efficacy in 1 hour, in 2 hours. You need time. You need to supplement the baby for 1 week and then you can see if they are better or not better.

Also, a combination of *Bifidobacterium animalis* BB12. These 2 strains are the most efficacious. Now, I have to be clear that, in the guidelines, these 2 strains have been shown to be efficacioius more in the breast-fed baby because the number of formula-fed babies included in the study was not sufficient to evaluate for efficacy. But I can say that they work also in my study, with this huge study, I did the subgroup analysis and they work also in the formula-fed baby. They work better in the breast milk with formula because breast milk is a very complex biological system and in the breast milk there are already HMOs that can enhance the effect of the probiotic.

Michael J. Wilsey, Jr, MD: For your breastfeeding mothers who want to try maternal, some dietary measures and elimination, how do you counsel those parents?

Flavia Indrio, MD: Do not eliminate anything from the breast-fed mother. At least except if the mother has a history of allergy or the baby can show some history of allergy, then you are allowed to. The mother is to have a normal diet, a diet for a mother who is breastfeeding and please don't do any maternal diet modification unless it's like healthy food, but this is for everybody. It's not only for colicky babies. And again, only if you have a suspicion of allergy diet.

Michael J. Wilsey, Jr, MD: How does your approach to colic management differ from breast-fed infants, like you discussed, and formula-fed infants?

Flavia Indrio, MD: Breast milk is a very complex biological system. No one can just reach the complexity and the efficacy of breast milk, any formula, any probiotic, anything. Even the baby who is breastfeeding, so the question could be, okay, but in the breast-fed already we do have the probiotics, but we don't know which are the concentration of that kind of strain that we have efficacy, like *Lactobacillus reuteri* or the *Bifidobacterium*. So again, there is no different approach. The only approach that I strongly suggest to the breastfeeding mother, please do not overfeed because that is much more simple to give the breast milk for a mother who is breastfeeding

when the baby's crying. For the formula-fed infants, they have to prepare, they know exactly how much the baby took, like 100 mL or whatsoever. The mother that is breastfeeding, she never knows how much the baby took. In that line, so okay, the baby's hungry, I give more. This is the main mistake that the breastfeeding mother makes, the overfeeding.

Assessing and Measuring Developmental Outcomes

Michael J. Wilsey, Jr, MD: What about caregiver reassurance and educational support? What can we do as clinicians? Well, studies show that when we educate families about infant colic, families and parents report improved well-being after receiving support and education from clinicians independent of whether the crying is improved or not. And clinicians can empower parents and improve self-efficacy by counseling caregivers on how to evaluate infants for illness and injury. You know, when I always have parents in the office, I'll say go through the 5 things if the baby's crying. Are they hungry? Do they need to burp? To change their diaper? Are they cold or do they just need some attention? Do they need to be held? And number 2, methods to settle and soothe infants, shushing, swaying, swaddling which we'll talk about. Identifying excessive crying, that it may not be because something's wrong, right? And so that babies cry, it's how they communicate and it's a normal physiologic process. We talk about the difference between normal crying and excessive crying. And maintaining their own well-being and coping skills, particularly with infants, with parents that are struggling with the new baby or first-time parents, always encourage them to nurture the love that brought them into this world. You know, to go out to find support, to go out on a date, to help support the individual and the parents itself. Also, available resources and support, both online and from community and relatives, you know, to help deal with the challenges of having a baby with infant colic.

What are some soothing and feeding techniques to help with infant colic? Well, the 5 S's, swaddling, shushing, swaying, swinging, warm baths, sometimes on the side-lying position. Both my daughters had colic, one really did well in the swing, for the other, swaddling was the key. And each child is different. Some of the worst colic I ever saw, my godson, his mother put him in the car and drove him around the neighborhood to help, that constant noise to help soothe and settle down. Feeding techniques can be helpful. Feeding in the upright position, limiting feeding times to about 10 minutes. Oftentimes, pacing can be helpful as well. Some babies are aggressive eaters, especially bottle-fed babies. Being able to pull the bottle out of the mouth and burp frequently, avoid overfeeding as was mentioned before, sometimes decreasing the size of the nipple opening to prevent overfeeding and really encouraging parents to experiment with options. You know, each child is uniquely different and responds to different techniques and ways to soothe colic.

Flavia Indrio, MD: What are your favorite techniques for soothing colicky infants to share with parents?

Michael J. Wilsey, Jr, MD: As discussed earlier, a lot of displaying and showing parents colicky techniques. I love nothing more when a baby comes in and is crying and I can take the baby, swaddle and shush in my arms as I'm talking with the family and it settles down. And that way, the parents believe that it's possible and it's not something seriously wrong. Oftentimes, I'll demonstrate in our clinic, in our office, the swaddling technique, side-lying position, I often like to hold the baby, you know, between the legs and have the belly support on the arm, the American football hold, as we call it in the United States, and that can be very helpful. Sometimes holding in a supine position and going back and forth. For some babies, it just takes about 10 or 12 times and then they settle down. That is beautiful when we're able to display that. Swinging, gentle rocking, sometimes just giving the baby a pacifier, you know, sucking can help. We mentioned car rides and stroller walks can be helpful. Carrying the baby sometimes with a snuggly, so the baby can feel voice reverberate through and just have a connection to the parent as well.

Flavia Indrio, MD: What resources do you recommend to caregivers who are struggling with colic?

Michael J. Wilsey, Jr, MD: I think the first thing we start out with is meeting with their healthcare provider, with their pediatrician. That should be the first point of contact with any concerns about colic to make sure it's not something more serious. And then support groups, in-person and that can be family, that can be parents. First of all, as a parent of 2 children with colic, older siblings are very helpful and that was our experience. And now there's support groups that are available, both in-person and online. Lots of great books and resources. One of the classics is the *Happiest Baby on the Block* by Dr. Harvey Karp and he talked about the 5 S's, shushing, swaying, swaddling, side-lying position, and also sucking, you know, having a pacifier to help soothe because babies can cry and they can suck. Using that to help settle down. There's lots of great websites. In the United States, the American Academy of Pediatrics has a terrific website, and most major children's hospitals have lots of useful information, providing evidence-based advice on colic. In addition, nowadays, there's lots of apps in addition. There are sleep sounds and music that have heartbeat, shushing, womb noises, white noise that can be helpful. For our breastfeeding babies that are struggling, I'll often have the mother meet with a lactation consultant to see if it's a latching, maybe it's a forceful letdown to see what are

the challenges that a mother is experiencing. And then lastly, especially now that a younger generation of parents are coming up and are really connected with social media, there's lots of social media support. Both online and Instagram and others to find emotional support and practical tips from parents who have walked that path and can share. I have 3 young adult children who learned how to cook from TikTok videos and so there's others, videos that can be educational and reassuring. Oftentimes, parents can find quick tips, easy to apply tips. A lot of tutorials online. I love demonstrating colic comfort techniques and then reassuring them that you can go to lots of platforms, such as YouTube, to be able to, in the middle of the night when the baby's crying and they can't remember what Dr. Wilsey had said, to be able to go through, including proper swaddling techniques and baby massage and things as well as parenting blogs. Lots of parents will share their journey online with colic and growth that can be helpful and starting out with the pediatrician, but also there's a lot of supports that parents can find to help walk that path when trying soothing colic techniques.

Flavia Indrio, MD: When do you recommend additional mental health support, such as cognitive behavioral therapy, to the caregivers of infants with colic?

Michael J. Wilsey, Jr, MD: I think that starts with a discernment, right? Really connecting with your families. A first-time visit may or may not accomplish this, unless the parents are just overwhelmed and that's the thing. Life feels overwhelming, right, and my ability to parent, sometimes with first-time parenting, all these fears can come in. Sometimes, they can lead to postpartum depression, severe stress and finding support. I think mental health support is much more open than it was just even 15 or 20 years ago. If there's increased risk of just parental burnout feelings, and I think you get that as a healthcare provider. You know, parents who are struggling, may not have the support of an extended family, of sisters, of grandparents there to support them. If you notice difficulty bonding, you know, the mom is disconnected, if she's feeling overwhelmed, poor eye contact, being able, I think we, as healthcare givers, we have great influence and help by saying this is important. And being there for the family members, for the parents, you are not alone, and also, there's light at the end of the tunnel. Part of the things that we can do is to educate that this is a limiting process and it's going to get better, often between 3 to 6 months of age. And if the caregiver's thought of really getting a history, of course, of harming themselves or the baby, those are times that emergency intervention can be sought.

Key Takeaways

Michael J. Wilsey, Jr, MD: Key takeaways from our discussion are that although colic, a self-limited condition, has potentially serious effects on caregiver well-being, colic is a functional GI disorder that's diagnosed based on a thorough clinical history and physical examination to rule out organic etiologies. The causes of colic are multifactorial and associated with a complex interplay between infants and their environments. The gut immaturity and dysbiosis may contribute to visceral hypersensitivity, gas production and distention, and inflammation. And probiotics, like Professor Indrio had discussed, have been shown to improve symptoms of colic. And caregiver reassurance and education are important components of colic management.

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