Current topic**Infantile colic revisited**

R S ILLINGWORTH

More than 30 years ago, with the help of the *Index Medicus*, I reviewed the world's published reports on evening colic.¹ Since then the *Index Medicus* has listed about two papers a year, with no advance in our understanding, but with the coming and going of a highly effective drug, dicyclomine hydrochloride.

The early term 'three months' colic' confused many, who interpreted it as meaning colic beginning at age 3 months. I prefer the term 'evening colic', because of its characteristic circadian rhythm of pain in the early evening. Similar attacks of pain may occur during the day in the older infant, at around 6 months of age, but this may or may not be the same condition. The term 'infantile colic' became popular, but is too all embracing, and in the minds of many includes troublesome crying for any reason—hunger, thirst, overheating, an itch, fatigue, allergy, boredom—but above all, crying which promptly stops when the baby is picked up and loved. Some (other than me) would add overfeeding as a cause. A sensible term is 'paroxysmal fussing'.² I am told that in India and the Punjab it was called 'sanjhana', and was deemed to be due to the evening gods.

Definition

The classic picture as described by Joe Brennemann of Chicago,³ Benjamin Spock,⁴ and others, was that of a well, thriving baby who in the early evening, for no apparent reason, develops paroxysms, beginning with flushing of the face, a frown, drawing up of the legs, followed in a few seconds by high pitched screaming, suddenly ending in a few minutes, and followed in a few minutes by another paroxysm. The attacks recur for up to two or three hours. In the attack the baby is unconsolable, there are loud borborygmi, and the pain is relieved by the passage of flatus from the rectum (not from the stomach), by the passage of a stool, or, it is said, by an enema. The above description is that of moderate or severe cases. In milder ones there is merely otherwise unexplained intermittent fussiness in the evenings. The attacks begin in the first week or two and cease by the age of 2, 3, or occasionally 4 months. It has

been said^{5 6} that the onset is delayed in preterm babies.

The condition is common, but because of imprecise definition, figures for its incidence⁷ are of little value.

Aetiology

Psychological factors. A popular view, especially among psychiatrists, is that the colic is due to the mother's psychological problems, excessive anxiety, picking the baby up unnecessarily (and bouncing him after a feed) and 'misinterpretation of infant cries leading to ineffective responses'-Taubman;⁸ but Taubman's definition of colic was inadequate. Wessel,² using a satisfactory definition of colic, thought that 'family tension' was an important factor. Lakin,⁹ in a study of 20 mothers of babies with colic and controls without colic, found 'poorer parent child relationships, greater intrapersonal conflict, conflict over role acceptance, concern about inadequacy as a female, poor marital adjustment, and less motherly love'. On the other hand Paradise,¹⁰ with his characteristic thoroughness, found no connection with emotional problems. He found that the mothers were stable, cheerful, and feminine. On the basis of clinical impression, I have never noticed characteristic features in the mothers; nor have other paediatricians.¹¹ None of the psychiatrists who blame the mother for causing the colic made any attempt to explain exactly how the mother causes the infant to have pain that is obviously of intestinal origin. Neither do they seem to realise that mothers, particularly in the evening when they are tired after a hard day's work, are likely to be upset by the baby's obvious pain and their inability to console him. If the colic were due to maternal anxiety, one would expect it to occur more often in the case of the first born. Though there is some disagreement,^{2 12} there is good evidence that this is not the case.^{1 5 10 11} I suggest that a mother's anxiety is not the cause but the result of the colic.

Several have suggested that the baby's tempera-

ment is the cause,¹³ or his sensory threshold for pain.¹⁴ This is a reasonable suggestion, but the temperament does not necessarily cause the colic: the temperament and colic may both be due to other factors. In the many hundreds of colicky babies whom I have seen, I have failed to notice anything characteristic about their temperament. Bruce¹⁵ seemed to suggest that the baby with colic is a malingerer; he wrote 'I feel sure of one thing: the infants are usually not in as much pain as they appear to be, or as their parents think they are'.

Allergy. It is difficult to interpret the many papers on allergy to cows' milk as a cause of colic, because of the lack of satisfactory criteria.^{16 17} The Malmö workers^{18 19} defined colic as paroxysms of severe crying with abdominal distension and frequent sucking. I have not found that abdominal distension or frequent sucking are notable features of evening colic: radiological studies during attacks of colic did not show gaseous intestinal distension.¹

In one study,¹⁸ 60 infants were fed on either a cows' milk or soya formula. Eleven babies were free from colic on soya, 32 were no better when given both cows' milk and soya, but lost their symptoms when fed on hydrolysed casein. Seventeen were no better when tried on a cows' milk free formula or soya. A third of those free from colic on the milk free diet developed colic again when challenged with milk. In a later study,¹⁹ 66 mothers of 66 breast fed babies who had colic were tried on a milk free diet; 35 babies lost their colic but developed it again when the mothers were challenged with cows' milk. Ten mothers were given cows' milk whey capsules and nine of their babies then developed colic.

Le Blanc²⁰ regarded the Malmö work¹⁸ as not statistically significant, and himself found that a soya formula without cows' milk did not help. Evans,²¹ in a double blind study of 20 breast fed babies, did not find that elimination of cows' milk from the mother's diet prevented the colic: he argued that the relevant factor in the mother's diet was not cows' milk but a variety of foodstuffs. Liebman,²² with a satisfactory definition of evening colic, found that lactose intolerance was not a factor; as for cows' milk protein, he found no difference in the babies' IgE or radioallergosorbent test results (cows' milk protein) when compared with controls.

In my view, the Malmö workers showed that allergy to cows' milk protein or to soya could cause abdominal pain in infants: but I am not satisfied that it is a common cause of evening colic. If allergy were an important factor for evening colic, one would expect that there would be a significant incidence of allergy in the family, of other manifestations of allergy in the infant, such as eczema or asthma, or

other evidence that the baby's colic would cease when the mother avoided cows' milk. There is much evidence against this.^{1 2 10-12 22 23 33} This does not exclude allergy, but it makes it less likely.

There is a difference of opinion as to whether infantile colic is more frequent in breast fed babies. My impression is that it is so. Others had the same opinion,^{3 4} and some disagreed.^{5 12}

Passive smoking. A French report²⁴ suggested that some cases of colic were due to the baby inhaling tobacco smoke. It has been shown²⁵⁻²⁷ that nicotine and cotinine are found in considerable quantities in the infant's saliva, urine, and serum when exposed to passive smoking, or when taking breast milk from a mother who smokes. These findings should be investigated, but may prove to be irrelevant.

Other factors. Various workers^{1 2 10-12} have found that infantile colic is not related to the mother's age, parity, or social class, or to the baby's mode of delivery, prematurity, birthweight, deficient or excessive weight gain, vomiting, diarrhoea, constipation, number of stools, sex, gastric flatulence, or hypertonia. Thomas²⁸ argued that the colic was due to drugs taken by the mother in labour, but Whicelow²⁹ criticised this on the grounds of lack of adequate diagnostic criteria. It has been shown that colic is not related to plasma progesterone concentration.³⁰

A theory and a call for research

The symptoms of evening colic, with the rhythmical paroxysms, the loud borborygmi, the relief by the passage of flatus per rectum, or by the passage of a stool or an enema, must surely indicate an intestinal origin, as Brennemann and other suggested long ago. Perhaps there is intestinal spasm. A Swedish study²³ reported colonic hyperperistalsis and increased rectal pressure, responding to an anticholinergic drug, methyl scopolamine nitrate. The fact that another anticholinergic drug, dicyclomine, was strikingly successful in preventing evening colic, suggests clues for research. Perhaps other anticholinergic drugs, such as propantheline, would be effective. An anticholinergic drug would reduce gut motility and slow transit time.

I believe that the enigma of evening colic now calls for fundamental combined physiological and clinical research. The role of vasoactive intestinal polypeptide (VIP) and gut hormones (for example motilin, enteroglucagon, neurotensin, and opioids) deserves investigation. The VIP is thought to mediate relaxation of the gut musculature,³¹ inhibit peristaltic reflex, and cause gastric relaxation,³² and

it has been implicated in many intestinal conditions associated with diarrhoea, such as the ganglioneuroma. The intestinal opioid peptides³⁴ are also concerned with gut motility. Two constipated adults, one of whom had been constipated from childhood, promptly responded to the specific opioid antagonist naloxone.

The intestinal prostaglandins have a profound effect on the transport of water and electrolytes through the intestine, and on intestinal motor function.^{31 35 36} Injection into volunteers caused abdominal colic.³⁵ Raised prostaglandin E was shown in an adult with functional intestinal obstruction.³⁷ An Israeli report³⁸ linked prostaglandin with diarrhoea of different causes. Dodge in Cardiff³⁹ showed that in the benign 'toddler's diarrhoea' there were raised prostaglandins, especially PGF₂ α and that the diarrhoea was inhibited by prostaglandin inhibitors, indomethacin, or aspirin. It is of interest that Murray Davidson⁴⁰ wrote that infantile colic predisposes to later functional gastrointestinal problems, and Jorup²³ wrote that 40% of infants with colic later had diarrhoea or pains of 'spastic colon'. But in a 13 year follow up study of 30 babies with colic,⁴¹ only one had recurrent abdominal pain in later childhood. A report from Finland⁴² noted a previous history of infantile colic in 12 of 27 children in a clinic for toddler's diarrhoea.

I believe that intestinal physiology may provide the clue to the enigma of infantile colic (and incidentally to otherwise unexplained constipation in infants and perhaps to recurrent-abdominal pain in the young school child).

Treatment

In my review¹¹ I listed the numerous treatments advocated in the published reports. Later,⁴³ I described a controlled trial of the anticholinergic drug, dicyclomine hydrochloride, indicating that it was strikingly successful in preventing evening colic. This has since been confirmed in Australia⁴⁴ and the USA.⁴⁵ Provided that the child had the classic picture of evening colic, as described, I have virtually never known the drug fail to provide relief—and the experience included many scores of infants. I am unable to understand the experience of one doctor⁴⁶ who found it ineffective—but he did not name the criteria for his diagnoses.

Most regrettably, the drug has been withdrawn after reports of possible untoward reactions. In one report⁴⁷ two children apparently had an immediate hypersensitivity reaction with respiratory difficulty. Two letters following this report^{46 48} described two possibly similar cases. I could not interpret their importance because of the absence of the necessary

details. According to one of these letters,⁴⁸ the child had received a mixture of dimethicone and dicyclomine, and the writer chose to attribute the symptoms to the dicyclomine. The manufacturers told me that the Committee on Safety of Medicine had received 15 to 20 reports of similar symptoms, and the report of a 'cot death' of an ill triplet. It is not possible to assess those reports without knowledge of the children's condition before the drug was given, its dosage, and the time interval between the administration and the onset of the symptoms. Two writers^{2 45 49} described an episode of rapid breathing before an attack of colic. I have no experience of this sequence, but did not specifically ask about such symptoms. In another paper⁴⁹ infantile colic was linked to a 'near miss sudden infant death'.

I know of no drug that is always free of side effects. Millions of doses of dicyclomine have been given for over 30 years without trouble. I feel sure that the drug was grossly over prescribed, for it seemed to be regarded as a panacea for crying, whatever the cause. Mothers are exhausted and worried by a baby's unconsolable crying—a symptom that may lead to non-accidental injury; and infants suffer severe discomfort. We can now no longer prevent it as the only effective drug known has been withdrawn—presumably because of the fear of litigation. But the fear of litigation is a poor reason for causing human suffering.

A widely used drug for infantile colic is dimethicone, consisting of silica, sold under several trade names (for example Asilone, Dentinox colic drops), sometimes combined with dicyclomine, aluminium hydroxide, or magnesium oxide. All the oral preparations listed in *MIMS* carry the warning that it is either not recommended at all for children, or not for those under 1 month of age. It has been used to relieve abdominal distension in adults^{50 51}—it was thought to accelerate the transit of intestinal gas, but had no effect on the volume of gas recovered, or the number of flatus passages. In another report, quoted by Martindale,⁵² it was found to be of no value for gastrointestinal flatulence. In a double blind crossover study of 27 cases of infantile colic⁵³ it was ineffective in relieving the symptoms. I find it difficult to understand how a suspension containing 15 to 30 mg of an unabsorbable preparation of silica in about 350 cm of intestine would prevent or relieve the pain which one presumes is caused by intestinal spasm or functional obstruction.

Innumerable other drugs continue to be used for infantile colic. O'Donovan and Bradstock⁵⁴ tried four drug regimens—homatropine with phenobarbitone and alcohol, phenobarbitone and alcohol, alcohol alone, or a placebo; all the first three,

probably because of the alcohol, were better than the placebo. Some doctors prescribe gripe water: perhaps it achieves something because of its alcohol content. A patient of mine had been given regular doses of whisky for his colic. In developing countries I have seen scars of multiple abdominal incisions to let the pain escape. A paediatrician⁵⁵ found that his own children responded only to a rocking cradle or a ride in his car.

I agree with O'Donovan and Bradstock, that 'if we knew what we were treating, perhaps the therapy would be more successful. When the majority of patients improve no matter what is done for them, the uncritical therapist will conclude that his treatment is effective'.

Conclusion

The time has come for basic physiological research into infantile colic; but an essential preliminary is a precise clinical diagnosis; as precise as it can be in the absence of any laboratory tests to confirm it. Cases should satisfy the criteria suggested, but exclude (in the first place) similar cases in older infants, because other factors, such as allergy, may be more likely then and so might confuse the picture. The method of feeding, breast or formula, and the age of the child, should be recorded as it is a self limiting condition, resolving by about 3 months of age. Infantile colic may well prove to have a multifactorial causation, like so many other medical conditions, with the end result evening colic; but what we then want to know is what is the nature of the final common pathway that culminates in colic.

I will conclude by paraphrasing the final comment by Prensky⁵⁶ in his discussion of the unfounded scare concerning the dangers of pertussis vaccine 'This 50 year old controversy, punctuated by limited clinical studies and testimonials, will remain a monument to the ineffective nature of anecdotal reports'.

References

- Illingworth RS. 'Three months' colic'. *Arch Dis Child* 1954;**29**:165-74.
- Wessel MA, Cobb JC, Jackson EB, Harris GS, Detwiler AC. Paroxysmal fussing in infancy, sometimes called colic. *Pediatrics* 1954;**14**:421-35.
- Brennemann J. Breast feeding and mixed feeding. *Practice of Pediatrics* 1943;**1**:chapter 25.
- Spock B. Etiological factors in hypertrophic pyloric stenosis and infantile colic. *Psychosom Med* 1944;**6**:162-5.
- Meyer JE, Thaler MM. Colic in low birth weight babies. *Am J Dis Child* 1971;**122**:25-7.
- Pierce P. Delayed onset of 'three months' colic in premature infants. *Am J Dis Child* 1948;**75**:190-2.
- Hide DW, Guyer BM. Prevalence of infantile colic. *Arch Dis Child* 1982;**57**:559-60.
- Taubman B. Clinical trial of the treatment of colic by modification of parent-infant interaction. *Pediatrics* 1984;**74**:998-1003.
- Lakin M. *Monogr Soc Res Child Dev* 1957;**22**:7-15.
- Paradise JL. Maternal and other factors in the aetiology of infantile colic. *JAMA* 1966;**197**:191-9.
- Weissbluth M. *Cry babies—coping with colic*. New York: Arbor House Publishing, 1984.
- Stahlberg M. Infantile colic—occurrence and risk factors. *Eur J Pediatr* 1984;**143**:108-11.
- Barr RG, Kramer MS, Pless IB, Boisjoly C, Le Duc DG. Feeding and temperament predispose to cry/fuss behavior at 6 weeks. *Am J Dis Child* 1983;**137**:541.
- Carey WB. Clinical application of infant temperament measurement. *J Pediatr* 1983;**103**:935-6.
- Bruce JW. Infantile colic. *Pediatr Clin North Am* 1961;**8**:143-5.
- Townley RRW. Colic and cow's milk allergy. *Aust Paediatr J* 1977;**13**:259-60.
- Harris MJ, Petts V, Penny R. Cow's milk allergy as a cause of infantile colic: immunofluorescent studies on jejunal mucosa. *Aust Paediatr J* 1977;**13**:276-81.
- Lothe L, Lindberg T, Jakobsson I. Cow's milk formula as a cause of infantile colic. *Pediatrics* 1982;**70**:7-10.
- Jakobsson I, Lindberg T. Cow's milk proteins cause infantile colic in breast fed infants: a double blind crossover study. *Pediatrics* 1983;**71**:268-71.
- Le Blanc MH. Soy formula doesn't help colic. *Pediatrics* 1983;**71**:299-300.
- Evans RW, Fergusson DM, Allardice RA, Taylor B. Maternal diet and infantile colic in breast fed infants. *Lancet* 1981;**i**:1340-2.
- Liebman WM. Infantile colic. Association with lactose and milk intolerance. *JAMA* 1981;**245**:732-3.
- Jorup S. Colonic hyperperistalsis in neurolabile infants. *Acta Paediatrica* 1952;**Suppl** 85:1-110.
- Said G, Patois E, Lellouch J. Infantile colic and parental smoking. *Br Med J* 1984;**ii**:660.
- Luck W, Nau H. Exposure of the fetus, neonate and nursed infant to nicotine and cotinine from maternal smoking. *N Engl J Med* 1984;**311**:672.
- Woodward A, Miles H, Grgurinovich N. Cotinine in the urine of smokers' infants. *Am J Obst Gynecol* 1984;**150**:236-44.
- Greenberg RA, Haley NJ, Etzel RA, Loda FA. Measuring the exposure of infants to tobacco smoke: nicotine and cotinine in urine and saliva. *N Engl J Med* 1984;**310**:1075-8.
- Thomas DB. Aetiological association in infantile colic: an hypothesis. *Aust Paediatr J* 1981;**17**:292-5.
- Whichelow MJ. Infant colic and drugs during labour. *Lancet* 1981;**i**:777.
- Weissbluth M, Green OC. Plasma progesterone concentration in infants in relation to infantile colic. *J Pediatr* 1983;**103**:935-6.
- Rask-Madsen J, Bukhave K. Prostaglandins and intestinal secretion. In: Turnberg LA, ed. *Intestinal secretion*. London: Smith Kline and French, 1982:76-83.
- Dimaline R, Dockray GJ. Intestinal VIP: current status as an intestinal regulatory polypeptide. In: Turnberg LA, ed. *Intestinal secretion*. London: Smith Kline and French, 1982:45.
- Hemmings WA. Maternal diet and colicky breast fed babies. *Lancet* 1981;**ii**:418-9.
- Kreek M, Schaefer RA, Hahn EF, Fishman J. Naloxone, a specific opioid antagonist, reverses chronic idiopathic constipation. *Lancet* 1983;**i**:261-2.
- Cummings JF, Newman A, Misiewicz JJ, Milton-Thompson GJ, Billings JA. Effect of intravenous prostaglandin E₂ on small intestinal function in man. *Nature* 1973;**243**:169-71.
- Bennett A, Flesher B. Prostaglandins and the gastrointestinal tract. *Gastroenterology* 1970;**59**:790-800.
- Luderer JR, Demers LM, Bonnem EM, Saleem A, Jeffries GH. Elevated prostaglandin E in idiopathic pseudo-obstruction. *N Engl J Med* 1976;**295**:1179.

- ³⁸ Korman SH, Berant M, Alon U. Review: prostaglandins in diarrheal states. *Isr J Med Sci* 1981;**17**:1109-13.
- ³⁹ Dodge JA, Hamdi IA, Burns GM, Yamashiro Y. Toddler diarrhoea and prostaglandins. *Arch Dis Child* 1981;**56**:705-7.
- ⁴⁰ Davidson M. Paroxysmal fussing. In: Rudolph AM, ed. *Pediatrics*. 16th ed. New York: Appleton Century Crofts, 1977:1011.
- ⁴¹ Joseph AY, Lupu GH. No relation between evening colic and later recurrent abdominal pain. *Am J Dis Child* 1984;**138**:990-1.
- ⁴² Savilahti E, Simell O. Chronic nonspecific diarrhoea. *Arch Dis Child* 1985;**60**:452-6.
- ⁴³ Illingworth RS. Evening colic in infants. A double-blind trial of dicyclomine hydrochloride. *Lancet* 1959;**ii**:119-20.
- ⁴⁴ Grunseit F. Evaluation of the efficacy of dicyclomine hydrochloride (Merbentyl) syrup in the treatment of infant colic. *Curr Med Res Opin* 1977;**5**:258-61.
- ⁴⁵ Weissbluth MD, Christoffel KK, Todd Davis A. Treatment of infantile colic with dicyclomine hydrochloride. *J Pediatr* 1984;**104**:951-5.
- ⁴⁶ Edwards PDL. Dicyclomine in babies. *Br Med J* 1984;**i**:1230.
- ⁴⁷ Williams J, Watkin-Jones R. Dicyclomine: worrying symptoms associated with its use in some small babies. *Br Med J* 1984;**i**:901.
- ⁴⁸ Spoudeas H, Shribman S. Dicyclomine in babies. *Br Med J* 1984;**i**:1230.
- ⁴⁹ Weissbluth M. Infantile colic and near-miss sudden infant death syndrome. *Med Hypotheses* 1981;**7**:1193-9.
- ⁵⁰ Gibstein A, Cooper JJ, Wiscot AL, Rosenthal AH. Prevention of postoperative abdominal distension and discomfort with simethicone. *Obstet Gynecol* 1971;**38**:386-90.
- ⁵¹ Danhof IE, Stavola JJ. Accelerated transit of intestinal gas with simethicone. *Obstet Gynecol* 1974;**44**:148-54.
- ⁵² Martindale. *The extra pharmacopoeia*. London: Pharmaceutical Press, 1975;**17**:80.
- ⁵³ Danielsson B, Hwang CP. Treatment of infantile colic with surface active substance (simethicone). *Acta Paediatr Scand* 1985;**74**:446-50.
- ⁵⁴ O'Donovan JC, Bradstock AS. The failure of conventional drug therapy in the management of infantile colic. *Am J Dis Child* 1979;**133**:999-1001.
- ⁵⁵ White PJ. Management of infantile colic. *Am J Dis Child* 1979;**133**:995-6.
- ⁵⁶ Prenskey AL. Pertussis vaccine. *Dev Med Child Neurol* 1974;**16**:539-43.

Correspondence to Professor R Illingworth, 8 Harley Road, Sheffield S11 9SD.