

# The unsettled baby: crying out for an integrated, multidisciplinary primary care approach

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One in five babies has parent-reported cry–fuss problems.<sup>1</sup> These unsettled babies are at increased risk of premature breastfeeding cessation,<sup>2</sup> child abuse<sup>3</sup> and long-term psychological disturbances,<sup>4,5</sup> and their mothers are at increased risk of postnatal depression.<sup>6,7</sup> But help for these infants and their families remains piecemeal, despite the prevalence and significance of the problem. Parents continue to receive conflicting advice about caring for their unsettled baby from the primary, secondary and tertiary sectors. General practitioners, paediatricians and community child health nurses, working in isolation from each other, are frustrated by the long waits that families face in accessing multidisciplinary help in the tertiary sector, including access to lactation clinics, early parenting centres, and services for perinatal anxiety and depression.<sup>8</sup>

Although organic disturbance is implicated in only 5% of cases,<sup>9</sup> concerned clinicians, in the absence of accessible services, may be tempted to apply a simplistic diagnostic approach to this complex problem. Here, we explore three conditions that are often mistakenly diagnosed in unsettled babies, and the risks associated with misdiagnosis. We argue that the current climate of health system reform offers an important opportunity for rethinking our management of unsettled babies and their mothers, and that designing and evaluating an integrated, team-delivered primary care intervention for unsettled babies and their mothers is a priority.

## The rise and fall of gastro-oesophageal reflux disease

From the mid 1980s, the prevalence of the diagnosis of “reflux” in otherwise well crying babies began to rise. Previously, these babies had been diagnosed with “wind” or “colic”, and families battled through months of distress with minimal support. The diagnoses of reflux, gastro-oesophageal reflux, or gastro-oesophageal reflux disease (GORD) brought exhausted mothers relief from the tendency to self-blame, as well as access to support from both health professionals and community self-help groups. Yet there is no evidence that the cluster of signs in unsettled babies commonly attributed to “reflux” — failure to thrive, aversive feeding behaviour, regurgitation, sleep disturbance, back-arching, flexion of knees and hips, tense abdomen, and clenched fists — correlate with acid-peptic GORD.<sup>10–12</sup> For each of these signs, other causes are common.

For example, failure to thrive usually results from inadequate caloric intake. In the first months of life, this is often a result of breastfeeding difficulties, which remain poorly understood by the medical profession.<sup>13</sup> Aversive feeding behaviour derives from a range of feeding difficulties, including poor attachment and positioning when breastfeeding, oral motor dysfunction, sensory processing disorder, and rare anatomical or physiological anomalies.<sup>14,15</sup> If unrecognised and not appropriately managed, feeding difficulties may become entrenched in the long term.<sup>16,17</sup> Regurgitation is a normal physiological process and may occur frequently in the first months of life.<sup>10</sup> Night waking is developmentally normal in infants under 6 months of age.<sup>18</sup> Back-arching, flexion

## ABSTRACT

- Unsettled behaviour in the first few months of life is a common clinical problem, with the associated risks of postnatal depression, premature cessation of breastfeeding, long-term psychological disturbance, and child abuse.
- Parents of new babies complain of difficulty accessing appropriate care and receiving conflicting advice.
- Although organic disturbance is implicated in only 5% of cases, gastro-oesophageal reflux disease, food allergies and lactose intolerance are often mistakenly diagnosed in unsettled babies.
- There is no evidence that acid-suppressive medications help in treating unsettled behaviour and, until the hypothesis that proton-pump inhibitors may predispose to food allergies has been properly investigated, treatment with acid-suppressive medications should be avoided in this population.
- Although unsettled behaviour in infants is commonly a transient neurodevelopmental phenomenon that peaks at 6 weeks of age, failure to diagnose other correctable problems, including breastfeeding difficulty and cows milk allergy, risks entrenching anxiety and disrupted mother–infant interactions in the long term.
- In the current climate of health system reform, the design and evaluation of an integrated, evidence-based, multidisciplinary primary care approach to management of unsettled babies and their mothers is a priority.

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of knees and hips, tense abdomen and clenched fists all form part of the repertoire of the infant’s expression of distress and signal a desire for external regulation of his or her internal state; despite popular perception, this cluster of signs does not necessarily, or even usually, signal pain.<sup>19</sup>

Inappropriate diagnosis of GORD in unsettled babies over the past two decades has had a number of consequences, including:

- Increased risk of breastfeeding cessation due to a failure to identify and correct breastfeeding problems, placing the baby at risk of short-term and long-term effects of breastmilk substitution, including cows milk allergy (CMA),<sup>20</sup> obesity and diabetes.<sup>21</sup>
- Underdiagnosis of correctable disturbance (eg, CMA).<sup>20</sup>
- Failure to identify psychological and sociocultural factors that are related to an infant’s regulation of state (eg, maternal perinatal anxiety and depression, sleeping arrangement, parental responsivity).<sup>6,22</sup>
- Development of parental perception of an infant as a vulnerable child, predisposing to long-term behavioural disturbances.<sup>23</sup>
- Widespread adoption of ineffective and inconvenient interventions (eg, prolonged breastfeeding intervals, holding baby upright after feeds, elevating head of bed, thickened feeds).<sup>24,25</sup>

- Potential harm to the infant from pharmaceutical interventions, with no reduction in crying other than that due to natural history or the placebo effect.<sup>23</sup>

Reported adverse outcomes of pharmaceutical interventions include fatal cardiac arrhythmias secondary to the previously widely prescribed prokinetic agent cisapride,<sup>26</sup> and elevated plasma aluminium levels secondary to antacid therapy.<sup>12</sup> Acid-suppressive medications — both proton-pump inhibitors (PPIs) and H<sub>2</sub>-receptor antagonists — are no better than placebo in the treatment of irritable infants.<sup>12,27</sup> Despite increasing evidence concerning adverse effects of PPIs in both adults and children, and recognition that more research is required to establish the safety of gastric acid suppression in infancy, PPIs continue to be prescribed “off-label” for crying babies from the first weeks of life.<sup>28–31</sup> Still more worryingly, it has been hypothesised that acid-suppressive medications may predispose to eosinophilic oesophagitis (EE), a disease that is emerging worldwide and that appears to be a manifestation of food allergy.<sup>32</sup>

### The rise and rise of food allergies

In our experience, the same cluster of signs previously used to mistakenly diagnose GORD in unsettled babies in their first months of life is now commonly used to diagnose EE or food allergies in this population. We have observed clinically that unsettled babies are often treated with maternal elimination diets and hypoallergenic formulas, in addition to PPIs.

EE is a chronic relapsing disease that progresses to oesophageal strictures and food bolus impaction without treatment. It is diagnosed by endoscopic biopsy, is associated with atopy, and is linked to both cellular and IgE-mediated food allergies (in particular to milk, egg, wheat, and soy).<sup>33</sup> Food allergies may present with failure to thrive, feeding difficulties, vomiting, abdominal pain and dysphagia, and, because EE and food allergies are known to have an uncertain but complex relationship with GORD, PPIs may be prescribed.<sup>34</sup> However, studies cited to support the claim that EE or food allergies (other than CMA) are symptomatic in infancy have been conducted with toddlers and older children, not babies in the first months of life.<sup>35</sup>

It is important to distinguish CMA from other food allergies. CMA is the most common food allergy, particularly in its non-IgE-mediated form, occurring in 2%–3% of children and 0.5% of exclusively breastfed infants.<sup>36</sup> CMA causes infant distress,<sup>20,37</sup> although there are not yet good community-based data concerning its prevalence in unsettled babies in Australia. In contrast to other food allergies, most children grow out of non-IgE-mediated CMA. In an exclusively breastfed, unsettled baby, this diagnosis is confirmed by a 2-week maternal elimination diet; and in an unsettled, formula-fed baby, by use of hypoallergenic formula.<sup>20</sup>

There is little evidence that low-allergen diets for breastfeeding mothers resolve parent-reported crying in infants,<sup>22,38</sup> other than in the case of maternal elimination of dietary cows milk protein. There is clearer, but not universally accepted, evidence that hypoallergenic formula may reduce crying in some formula-fed infants.<sup>22,39</sup> Maternal elimination diets for food allergies may be extensive and difficult to maintain, placing mothers at risk of nutritional deficiencies<sup>20</sup> and promoting anxiety in a population already at risk of perinatal anxiety and depression.<sup>6,7</sup>

Merwat and Spechler have argued that when gastric pH is raised by acid suppression, the usual breakdown of allergens by peptic digestion is unable to occur.<sup>32</sup> PPIs increase gastrointesti-

nal mucosal permeability, which may increase uptake of these undegraded peptide allergens, causing immune sensitisation. They hypothesise that this mechanism explains the complicated link between EE and GORD, and point out that the time course of the introduction and subsequent widespread usage of PPIs fits well with the emergence of EE.<sup>32</sup> If their hypothesis proves correct, inappropriate diagnosis of GORD or food allergies in irritable infants, and resultant treatment with a PPI, could result in lifelong morbidity.

### The froth and bubble of lactose intolerance

Another trend in the medical approach to unsettled babies has been to diagnose lactose intolerance, and prescribe either lactase or a lactose-free formula. While a decline in lactase-specific activity commonly occurs as early as 3–5 years of age in humans, congenital lactase deficiency is extremely rare.<sup>40</sup> High-volume breastfeeds with low fat content may result in a functional lactose overload in breastfed babies in the first weeks and months of life, causing an irritable infant with tympanic abdomen, excess flatus and explosive stools. Although functional lactose overload signals a correctable breastfeeding problem and is resolved by appropriate breastfeeding management,<sup>41,42</sup> it may not be identified by health professionals due to knowledge deficits concerning lactation.<sup>13</sup> For example, a randomised controlled trial demonstrating that lactase helped settle some infants did not consider offering breastfeeding management for functional lactose overload in the breastfed babies, nor that the instruction to express foremilk might be a confounder.<sup>43</sup>

Babies may acquire a transient, secondary lactose intolerance. This results from damage to the intestinal villi, most commonly due to gastroenteritis or CMA. Breastmilk substitution predisposes to both.<sup>20,21</sup> Weaning is not indicated in breastfed babies with secondary lactose intolerance, although probiotics and CMA maternal elimination diet may have a role.<sup>44</sup> In formula-fed infants, secondary lactose intolerance may respond to lactose-free formula, although babies with CMA who are mistakenly diagnosed with lactose intolerance could experience perpetuation of their gut lesion, as lactose-free formula contains cows milk protein.

An unsettled breastfed baby with a functional lactose overload who is mistakenly diagnosed with lactose intolerance is at risk of being inappropriately weaned.<sup>2</sup> Breastmilk substitution puts the infant at risk of developing gastroenteritis or CMA,<sup>20,21</sup> which then puts him or her at risk of developing a true, secondary lactose intolerance.

### Paradigm shift

These three diagnoses that are often inappropriately applied to unsettled babies show the potential harm of a simplistic, or reductionist, approach to this complex problem. However, 5% of unsettled infants do have an organic disturbance. Infant crying is commonly a normal state or a transient developmental problem that peaks at 6 weeks and resolves by 3–4 months of age. An approach that focuses only on interventions to support maternal coping may fail to identify correctable clinical problems, including breastfeeding difficulty, resulting in adverse outcomes such as unnecessary disruption of mother–infant interactions and, in some cases, entrenchment of anxiety and behavioural abnormalities in the long term.

Unsettled baby research is undergoing a paradigm shift, congruent with the paradigm shift in primary care research more generally — that is, from a reductionist to a systemic approach.<sup>45</sup>

Unsettled infants are a heterogeneous population with a multifactorial aetiology, and any approach to managing them should reflect this.<sup>22</sup> Tertiary units in Australia offer multidisciplinary residential interventions that appear effective but are costly to implement and can never hope to meet the needs of all families who experience infant cry–fuss problems. By the time unsettled babies and their mothers are admitted to an early parenting centre, at least half have tried other health service interventions, and abnormal mother–child dynamics may already be entrenched.<sup>46</sup> A cost analysis of the problem of infant unsettledness has not yet been performed in Australia, despite it being the most common presentation to the GP in the first months of life<sup>47</sup> (in the context of an average of 7.7 GP consultations for mothers and babies in the infant's first 6 months).<sup>48</sup> In a 2001 cost analysis in the United Kingdom, health professional time devoted to dealing with unsettled infants aged 1–3 months was found to cost the National Health Service £66 million annually.<sup>49</sup>

The Australian Government is currently advocating multidisciplinary primary care service provision.<sup>50</sup> The Australian National Breastfeeding Strategy 2010–2015 advocates collaborative partnerships between lactation services and health professionals,<sup>51</sup> and the 2009 report of the Maternity Services Review identifies the need for research into effective and collaborative models of postnatal care.<sup>52</sup> This climate of health system reform offers a timely opportunity to prioritise the development of a team-delivered primary care program for unsettled babies and their mothers. Such a program needs to be integrated and evidence-based, taking into account the multiple aetiologies of unsettledness in infants, if we are to optimise the outcomes and minimise the costs of this complex problem.

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### Competing interests

None identified.

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