REVIEW ARTICLE

Lactobacillus Therapy for Acute Infectious Diarrhea in Children: A Meta-analysis

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ABSTRACT. *Objective.* **Childhood diarrhea accounts for substantial morbidity and mortality worldwide. Multiple studies in children have shown that *Lactobacillus*, administered orally, may have antidiarrheal properties. We conducted a meta-analysis of randomized, controlled studies to assess whether treatment with *Lactobacillus* improves clinical outcomes in children with acute infectious diarrhea.**

Methods. **Studies were sought in bibliographic databases of traditional biomedical as well as complementary and alternative medicine literature published from 1966 to 2000. Search terms were "competitive inhibition," "diarrhea," "gastroenteritis," "*Lactobacillus*," "probiotic," "rotavirus," and "yog(h)urt." We included studies that were adequately randomized, blinded, controlled trials in which the treatment group received *Lactobacillus* and the control group received an adequate placebo and that reported clinical outcome measures of diarrhea intensity. These inclusion criteria were applied by blind review and consensus. The original search yielded 26 studies, 9 of which met the criteria. Multiple observers independently extracted study characteristics and clinical outcomes. Data sufficient to perform meta-analysis of the effect of *Lactobacillus* on diarrhea duration and diarrhea frequency on day 2 were contained in 7 and 3 of the included studies, respectively.**

Results. **Summary point estimates indicate a reduction in diarrhea duration of 0.7 days (95% confidence interval: 0.3–1.2 days) and a reduction in diarrhea frequency of 1.6 stools on day 2 of treatment (95% confidence interval: 0.7–2.6 fewer stools) in the participants who received *Lactobacillus* compared with those who received placebo. Details of treatment protocols varied among the studies. A preplanned subanalysis suggests a dose-effect relationship.**

Conclusion. **The results of this meta-analysis suggest that *Lactobacillus* is safe and effective as a treatment for children with acute infectious diarrhea. *Pediatrics* 2002; 109:678–684; *gastroenteritis, infectious diarrhea,* Lactobacillus, *meta-analysis, rotavirus.***

ABBREVIATIONS. ID, acute infectious diarrhea; ORS, oral rehydration solution; CI, confidence interval.

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Diarrhea is common among children and contributes substantially to pediatric morbidity and mortality worldwide. In the United States, an estimated 21 million to 37 million episodes of diarrhea occur among 16.5 million children younger than 5 years of age annually.[1] Three million physician visits per year are related to diarrhea,[1] as are 163 000 hospitalizations, or 13% of all hospitalizations for children in this age group.[2] Given the ubiquity of acute infectious diarrhea (ID) and its associated burdens on children, families, and the health care system, all parties desire a therapy that is safe, relatively inexpensive, and effective in ameliorating the course of illness.

For at least a century, researchers have hypothesized that live bacterial cultures, such as those found in yogurt, may help treat and prevent diarrhea.[3] The bacterial genus *Lactobacillus*, which is found in normal human intestinal and perineal flora, has been studied frequently in children with regard to its antidiarrheal properties since the 1960s.[4,5] Studies published in the world literature have concluded that *Lactobacillus* is indeed safe and effective in treating and preventing ID; antibiotic-associated diarrhea; and diarrhea in children who are unusually susceptible as a result of poor nutrition, impaired immune status, or frequent exposure to pathogens. Despite these reports, health professionals in the United States do not routinely recommend *Lactobacillus*,[6] perhaps believing that its effectiveness has not yet been proved.[7,8] We therefore conducted a meta-analysis of existing randomized, controlled studies to test the hypothesis that treatment with *Lactobacillus* improves clinical outcomes in children with ID.

METHODS

Data Sources

We sought trials that involved human subjects in the traditional biomedical literature as well as the complementary and alternative medicine literature. To this end, the following databases were searched: from 1966 to 2000, Medline, PubMed, EMBase, CCTR (Cochrane Controlled Trials Register), DARE (Database of Abstracts of Reviews of Effectiveness), CINAHL (Cumulative Index to Nursing and Allied Health); from 1985 to 2000, AMED (Allied and Alternative Medicine), MANTIS (Manual, Alternative and Natural Therapy), Complementary and Alternative Medicine Citation Index, and AltHealthWatch. The search terms for the disease/therapy pairing used to interrogate the databases were "diarrhea," "gastroenteritis," or "rotavirus," in combination with "competitive inhibition," "*Lactobacillus*," "probiotic," or "yog(h)urt." Search terms were modified slightly to correspond to the subject

headings and tree structures of some databases. We also sought trials in reference sections of other clinical trials and review articles. Key investigators in the field were contacted and asked to provide other known clinical trials.

Study Selection

We first limited the entire set of trials to original studies that involved *Lactobacillus* treatment of ID in children, in which clinical outcomes were reported. Studies included in the meta-analysis were adequately randomized, blinded, controlled trials in which the treatment group received *Lactobacillus* (any species or strain) and the control group received a suitable placebo. A killed *Lactobacillus* species was considered unsuitable as a placebo, because there is evidence that this agent itself may have antidiarrheal properties.[9–11] Randomization was considered adequate when a study was described as randomized, even if the precise randomization method was not reported. When *Lactobacillus* and control were indistinguishable and when the individuals who recorded clinical data were blinded as to which treatment was given to which subjects, blinding was considered adequate. Because no consensus exists regarding a consistent definition of diarrhea, the manner in which diarrhea was defined was not a criterion for inclusion or exclusion. Studies in which patients had received recent antibiotics were excluded. No language restrictions were used in the literature search or selection process.

The studies that originated from the database search were examined by 2 of the authors (C.F. and M.M.G.). These authors independently read only the methods section of the studies and were blinded to all information about the author, site, journal, year, or title of each study. Two authors (C.W.V.N. and D.A.C.) resolved any disagreements regarding the inclusion of studies, which arose infrequently and were attributable to reader misunderstanding rather than to true differences of opinion. Study results were not weighted on the basis of assessments of quality.[12]

Outcome Measures

The primary outcome measures were the characteristics of the clinical course of diarrhea. Diarrhea was defined variously in the studies as an increase in duration or frequency of diarrhea, increase in volume of stool, or decrease in consistency of stool, as noted by caregivers or investigators. Diarrhea was considered to be infectious by clinical diagnosis, with or without confirmation by laboratory testing. Subjects with bloody as well as nonbloody diarrhea were described in the included studies.

Because 1 or more measures of diarrhea intensity were used in the studies, we presumed a priori that the best measure of diarrhea intensity has components of duration (days of diarrhea), frequency (number of stools per day), and amount (volume of diarrheal stool). We abstracted data from each study using outcomes that best approximated these 3 components (duration, frequency, and amount).

A secondary outcome was whether subjects received additional medical intervention, such as intravenous fluid administration, or additional contact with a health care provider in an ambulatory or inpatient setting. We also noted any reports of adverse reactions as a result of treatment.

Data Extraction

The full articles of all studies that met the inclusion criteria were translated into English, if necessary, and reviewed. Data were extracted independently by 2 authors (C.F. and M.M.G.) with subsequent verification by a third author (C.W.V.N.). Each study was examined for sample size, study site, patient demographics, strain of *Lactobacillus*, definitions of diarrhea, infectious pathogens, adverse effects, and the outcome measures described above. Disagreements, which were infrequent and were entirely attributable to misreading by 1 of the authors, were resolved by clarifying discussion, rereading, and consensus.

Statistical Methods

The studies were analyzed separately for each measure of diarrhea intensity. Measurements of diarrhea duration were converted to days, maintaining the number of significant digits in the original units of time. Diarrhea frequency was reported as the number of loose stools per day. We calculated an absolute difference between the *Lactobacillus* and control groups for each of the outcomes in each study. Given that the distribution of duration and frequency of diarrhea may be right-skewed (as a result of potential long-duration or high-frequency cases), inferences based on an assumed normal distribution are not ensured. Although nonparametric analysis would be preferable, we did not have access to original data and therefore could analyze only the means reported in the studies. Nevertheless, summary estimates of the effects of *Lactobacillus* across the studies are likely to be more accurate and stable than in any of the individual studies. Summary measures were determined by a random effects model because of significant heterogeneity of point estimates among the studies. In the meta-analysis, outcomes across the included studies were examined for evidence of publication bias using the Begg and Mazumdar[13] adjusted rank correlation test and the Egger et al[14] regression asymmetry test. The dose-response relationship was tested using least-squares linear regression of the log of the dose used in each study and the mean change in diarrhea duration measured in days.

Subanalyses were planned a priori to discern modification of reductions in diarrhea intensity by subject age group, use of adjunctive therapy such as oral rehydration solution (ORS), strain of *Lactobacillus*, dose and duration of *Lactobacillus* treatment, location of subject population, whether the patients were ambulatory or inpatients, and infectious agent. All analyses were performed using Stata 7.0 (Stata Corp, College Station, TX).[25]

RESULTS

Study Selection

The initial search for studies involving *Lactobacillus* treatment of ID in children yielded 26 journal articles (as of August 1, 2000). A search of the Medical Editors' Trial Amnesty did not detect any relevant unpublished studies. Eleven studies[10,16–25] met inclusion criteria on the basis of examination of the methods sections. Fifteen studies were excluded because they were not controlled,[5,26–28] were not randomized,[5,26–29] were not blinded,[5,26–28,30] had no placebo group,[5,26–28,31–36] had an inadequate placebo group (killed *Lactobacillus*),[25] or had exclusion[11] or reallocation[37] of subjects after randomization. Two other studies were subsequently excluded from the meta-analysis because of methodological issues discovered on examination of the entire article. One of these articles reported data from a subanalysis only,[24] and the other reported aggregated data (subjects had either ID or antibiotic-associated diarrhea).[25]

Study Characteristics

Characteristics of the included studies are described in Table 1. Eight of the 9 included studies involved inpatients exclusively,[10,17–23] and 1 study[16] was a multicenter trial with a minority of outpatient subjects. Subjects in all 9 studies received at least ORS in addition to *Lactobacillus* or control as a part of the experimental protocol. Some subjects in 4 of the studies also received intravenous fluids.[19,21–23] Diarrhea duration and frequency of diarrheal stools on day 2 of treatment were the only clinical outcomes reported in multiple studies. We were therefore not able to examine stool amount or frequency of diarrhea stools at other times as outcome measures.

One study[16] that examined children who had ID and were receiving ORS did not follow clinical outcomes of subjects who became ill enough during the course of the study to require intravenous fluids. With this study protocol, a small and equal propor-

TABLE 1. Characteristics of Included Studies Comparing *Lactobacillus* and Control in the Treatment of ID in Children

Study	Country	Age of Subjects (Months)	Pathogen*	*Lactobacillus* treatment			Diarrhea Duration Defined as Time to:
				Strain	Dose (cfu)	Vehicle	
Simakachorn et al,[10] 2000	Thailand	3–24	48% rotavirus 1% bacterial 51% not identified	Killed *L acid*	10^{10} twice daily for 5 doses	Fermented culture medium	2 formed stools or 12 h without stool
Guandalini et al,[16] 2000	Ten countries†	1–36	35% rotavirus 18% bacterial 13% other 34% not identified	*L GG*	10^{10}/250 mL as tolerated for 4–6 h, then *ad lib*	ORS	Last fluid stool
Shornikova et al,[17] 1997	Finland	6–36	75% rotavirus 25% not identified	*L reuteri*	10^{10}–10^{11} daily for 5 days or until discharge	Milk powder and reconstituting fluid	Last watery stool
Shornikova et al,[18] 1997	Finland	6–36	Rotavirus exclusively‡	*L reuteri*	10^{10}–10^{11} daily up to 5 days	Lactose and reconstituting fluid	Last watery stool
Shornikova et al,[19] 1997	Russia	1–36	28% rotavirus 21% bacterial 51% not identified	*L GG*	5×10^9 twice daily for 5 days	Reconstituting fluid	Last watery stool
Raza et al,[22] 1995	Pakistan	1–24	22% rotavirus 78% not identified	*L GG*	10^{10}–10^{11} twice daily for 2 days	ORS	Not reported
Kaila et al,[20] 1992	Finland	7–37	Rotavirus exclusively‡	*L GG*	10^{10}–10^{11} twice daily for 5 days	Fermented milk product	Last watery stool
Pearce et al,[21] 1974	Canada	<36	100% not identified	*L acid/L bulg*	$\geq 10^8$, 4–8 doses per day until discharge	Capsule added to oral fluid	First 8-h period without diarrhea
Chicoine et al,[23] 1973	Canada	<2–>36	Nonbacterial exclusively§	*L acid/L bulg*	10^9 every 8–12 h	Capsule	First normal stool

L GG indicates *Lactobacillus GG*; *L reuteri*, *Lactobacillus reuteri*; *L acid*, *Lactobacillus acidophilus*; *L acid/L bulg*, a probiotic mixture including *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, and a *Streptococcus* species (either *S thermophilus* or *S lactis*); cfu, colony-forming units.

* Bacterial pathogens include *Campylobacter* species, *Escherichia coli*, *Salmonella* species, *Shigella* species, *Yersinia* species; other pathogens include protozoa and mixed pathogens.

† Italy, Egypt, Portugal, Netherlands, Croatia, Slovenia, Greece, United Kingdom, Poland, Israel.

‡ This study enrolled only subjects who were known to have rotavirus infection.

§ This study enrolled only subjects who were known to have normal bacterial stool cultures.

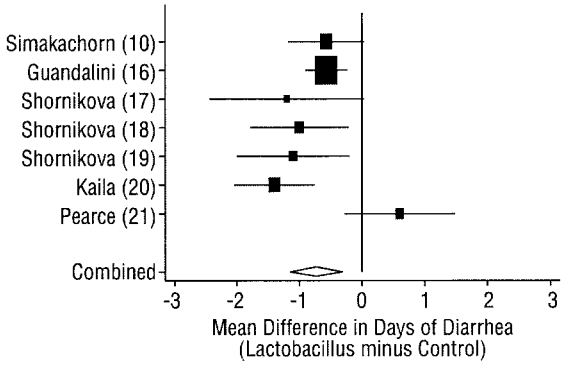

Fig 1. Diarrhea duration. Summary point estimate of reduction in diarrhea duration in 7 included studies that reported mean reduction and variance. Box size is proportional to the inverse of the magnitude of the study variance.

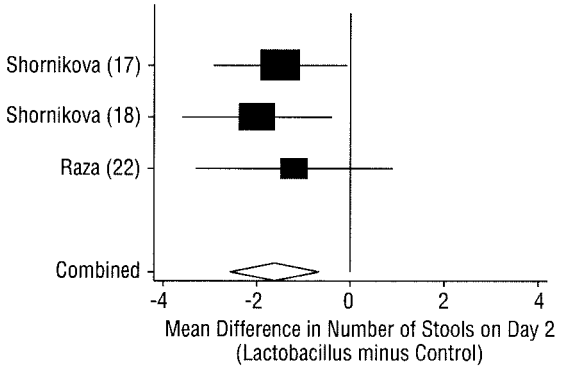

Fig 2. Diarrhea frequency. Summary point estimate of reduction in diarrhea frequency on day 2 in 3 included studies that reported mean reduction and variance. Box size is proportional to the inverse of the magnitude of the study variance.

tion of subjects were removed from the *Lactobacillus* and control groups. Omission of these data made an intention-to-treat analysis impossible. However, recalculation of the meta-analysis without this study did not result in a significantly different point estimate for reduction of diarrhea duration (0.8 days; 95% confidence interval [CI]: 0.2–1.3 days).

Reduction of Diarrhea

The summary point estimate from the meta-analysis indicates a significant reduction in diarrhea duration of 0.7 days (95% CI: 0.3–1.2 days) in subjects who were given *Lactobacillus* compared with control subjects (Fig 1). Only 7 studies reported variance in the measurement of diarrhea duration (Table 2).[10,16–21] We could not calculate variance because individual subject data were not available, so only these 7 studies could be included in the meta-analysis to estimate the effect of *Lactobacillus* on duration. Similarly, only 3 studies reported variance in the measurement of diarrhea frequency on day 2 of treatment (Table 2).[17,18,22] The summary point estimate for frequency for these 3 studies was 1.6 fewer stools in subjects who were given *Lactobacillus* than in control subjects (95% CI: 0.7–2.6 fewer stools; Fig 2). No publication bias was detected.

Preplanned Subanalyses

Preplanned subanalyses were performed only when the study characteristic of interest was reported in 3 or more studies. When the studies that were performed in developed countries were analyzed,[16–18,20,21] the summary point estimate showed a decrease of 0.8 days of diarrhea (95% CI: 0.1–1.5 days) in subjects who were given *Lactobacillus* compared with control subjects. Studies that used only live *Lactobacillus* preparations[16–21] also demonstrated a reduction in diarrhea duration of 0.8 days (95% CI: 0.3–1.3 days), whereas studies that included subjects with ID of all causes (not just rotavirus)[10,16,17,19,21] demonstrated reduction of diarrhea duration of 0.5 days (95% CI: 0.1–1.0 days). We could not infer any effects of various *Lactobacillus* strains because of heterogeneity of study results.

In all included studies, adverse reactions that were consistent with signs and symptoms usually associated with ID occurred equally in patients who received *Lactobacillus* and those who received placebo, except in 2 studies that reported decreased vomiting in the *Lactobacillus* group.[17,22] One study[22] reported adverse reactions outside the usual clinical spectrum of ID: myoclonic jerks were noted in 1 patient in the *Lactobacillus* group and 1 patient in the control group. The analysis of subjects who required additional interventions was not possible, as insufficient data were reported.

Dose-Response Relationship

A dose-response relationship appears across the 8 included studies that reported diarrhea duration. A

TABLE 2. Diarrhea Intensity Outcomes in Included Studies Comparing *Lactobacillus* and Control in the Treatment of ID in Children

Study	Number of Subjects		Duration of Diarrhea (Mean Days [SD])		Frequency on Day 2 (Mean Stools/Day [SD])	
	Lactobacillus	Control	*Lactobacillus*	Control	*Lactobacillus*	Control
Simakachorn et al,[10] 2000	37	36	1.81 (1.08)	2.38 (1.51)	nr	nr
Guandalini et al,[16] 2000	134	126	2.43 (1.15)	3.00 (1.49)	nr	nr
Shornikova et al,[17] 1997	19	21	1.7 (1.6)	2.9 (2.3)	1.0 (2.3)	2.5 (2.3)
Shornikova et al,[18] 1997	21	25	1.5 (1.1)	2.5 (1.5)	1.8 (2.7)	3.8 (2.8)
Shornikova et al,[19] 1997	59	64	2.7 (2.2)	3.8 (2.8)	1.5	3.0
Raza et al,[22] 1995	19	17	nr	nr	5.8 (3.1)	7.0 (3.3)
Kaila et al,[20] 1992	22	17	1.1 (0.6)	2.5 (1.4)	nr	nr
Pearce et al,[21] 1974	53	41	2.7 (2.5)	2.1 (1.6)	nr	nr
Chicoine et al,[23] 1973	27	27	2.5	2.8	3.4	3.3

SD indicates standard deviation; nr, not reported.

significant positive linear association exists between the log of the *Lactobacillus* dose and the reduction in diarrhea duration in days ($P < .01$; Fig 3).

DISCUSSION

The results of this meta-analysis suggest that *Lactobacillus* is safe and effective as a treatment for ID in children, reducing diarrhea duration by approximately two thirds of a day and reducing the frequency of diarrhea on the second day of treatment by 1 to 2 stools. Furthermore, our preplanned subanalyses suggest that all children with ID, rather than just a subset, may benefit from *Lactobacillus*. Specific indications and limited use of *Lactobacillus* in children with ID have been proposed in the *Lactobacillus* literature.[9,16,19,22,24] We did not find, however, that the effect of *Lactobacillus* on diarrhea duration was modified by country of study or live versus killed *Lactobacillus* preparation. We also found that *Lactobacillus* therapy benefited not only cases with documented rotavirus diarrhea but also cases of ID caused by a variety of pathogens, as would be found in ambulatory clinical settings.

Exactly how *Lactobacillus* exerts its probiotic effect is unclear. Some have postulated that *Lactobacillus* enhances the immune response,[20] elaborates antimicrobial substances,[38–40] and occupies intestinal mucosal sites, inhibiting the attachment and growth of pathogenic organisms by achieving competitive exclusion and microbial balance.[41] The dose-effect relationship noted in this meta-analysis suggests that *Lactobacillus* is most effective above a threshold dose (10 billion colony-forming units during the first 48 hours) that reduces diarrhea duration by more than half of 1 day. Although this relationship could support any of the postulated mechanisms, it has been shown that a similar dose of 10^{10} to 10^{11} colony-forming units of the species *Lactobacillus GG* results in colonization of the intestine and inhibition of attachment by pathogens.[42] Higher doses of *Lactobacillus* may lead to a shorter duration of diarrhea. Careful thought is warranted, however, in applying the concept of dose-response relationship to a probiotic agent that, in the case of live *Lactobacillus*, can replicate. The proposed mechanisms may also explain observations that credited *Lactobacillus* with the ability to prevent antibiotic-associated diarrhea[43,44] and traveler's diarrhea.[45,46] Children who are susceptible to the development of diarrhea as a result of poor nutrition, impaired immune status, or frequent exposure to infectious agents have also been shown to benefit from *Lactobacillus* administration.[34,47–49]

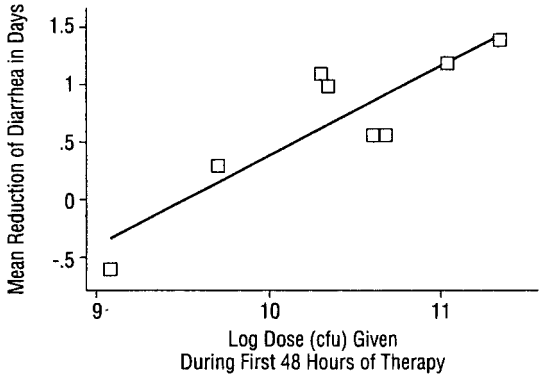

Fig 3. Dose-effect relationship between *Lactobacillus* dose and reduction in diarrhea duration in 8 included studies that reported diarrhea duration as an outcome. Cfu, colony-forming units.

Several issues should be kept in mind when evaluating these findings. First, the methods of the included studies differed as to how diarrhea was defined, how diarrhea intensity was measured, which strain of *Lactobacillus* was used, and how *Lactobacillus* was administered. Despite these differences, the studies did suggest a consistent conclusion, showing significant reductions in duration and frequency of diarrhea in children who were given *Lactobacillus*, even when we accounted for possible heterogeneous treatment effects across the studies. Second, the subjects in the studies were almost exclusively inpatients. *Lactobacillus*-associated reductions in diarrhea intensity might be less pronounced in children who are not sick enough to require hospitalization. However, most subjects in the included studies required only oral rehydration, and some studies excluded children with severe dehydration before enrollment.[10,18] The conclusions from this meta-analysis may therefore be plausibly generalized to ambulatory populations with diarrhea. Moreover, diarrhea durations reported in these studies are consistent with the usual course of childhood ID,[50] regardless of the severity of illness or location of patient care. In outpatients, the use of *Lactobacillus* may in fact serve to prevent hospitalization and other adverse outcomes. Third, although none of the included studies was performed in the United States, most originated in developed countries, with incidences and causes of ID similar to those in the United States.[50] Extension of the conclusions of this meta-analysis to children in the United States is therefore reasonable. Fourth, most subjects were children younger than 3 years. Younger children are more susceptible to clinical consequences of ID and thus may have the most to gain from *Lactobacillus* administration. Fifth, we had determined measures of diarrhea intensity a priori that we believed would best relate to the clinical burden of diarrhea. For example, a large amount or frequency of diarrheal stool, regardless of duration of illness, might have a close association with the likelihood of dehydration and subsequent medical intervention or with socioeconomic burden such as parental days of work lost or number of diapers purchased. We were constrained, however, by the outcomes most commonly reported in the studies, namely diarrhea duration and frequency. Finally, publication bias remains a concern, although there was no statistical evidence of its presence. Specifically, we note that this meta-analysis includes studies funded by pharmaceutical and food companies, raising the possibility that sources of funding with vested interests may have biased toward submission and publication of only those studies that found therapy to be beneficial.

These limitations suggest additional research. For example, a large randomized and controlled trial, funded by a nonvested party, could test whether

high-dose *Lactobacillus* is an effective treatment for ID in an ambulatory pediatric population, as no such study has been published. Use of consistent measures of diarrhea intensity would help prevent the challenges of interpretation presented by the variety of measures used in the studies included in this meta-analysis. An outpatient pediatric population and consistent diarrhea intensity measures could also be applied to studies in children with other gastrointestinal disorders and studies examining other treatments.

Should *Lactobacillus* be used to treat children with ID? Our results indicate that *Lactobacillus* seems safe and reasonably effective in reducing diarrhea duration and frequency. A crude family-centered cost analysis would also favor *Lactobacillus* use in children with signs and symptoms of ID. A 48-hour course of a *Lactobacillus* product is commercially available for approximately $10[31] and on average could save approximately 17 hours of caring for a sick child with diarrhea, and 1 to 2 diapers. This framework may help a physician counsel a specific patient's family when the patient receives a diagnosis of ID. We conclude that *Lactobacillus* can be recommended in the treatment of children with ID.

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THIS NEW CHALLENGE TO PEER REVIEW COULD/WILL BE A DISASTER!

Peer review certainly has its critics, and it takes time, but it's certainly better than letting public relations departments and the public judge science on instant advertising in the press and on TV.

Biotech Firms Bypass Journals to Make News

"It used to be that a scientific breakthrough was taken seriously only if it first appeared in a peer-reviewed journal. But in the race to grab the spotlight, some companies are rushing to release information via esoteric publications that have less-stringent criteria or in news releases.

The upshot: investors and the public may be led to believe certain claims that could later prove to be exaggerated. 'It undermines public trust in science if key results are released without peer review,' says Philip Campbell, editor-in-chief of *Nature*, a 133-year-old British research journal that has published the likes of Charles Darwin.

PPL—which shot to fame in 1997 after helping clone Dolly the sheep— insists it didn't know about Immerge's imminent publication. Although it accepts that peer review of experiments 'is the gold standard' in scientific publishing, the company says it is often forced to override the convention. 'We're a public company and we decided to make a limited press release . . . as soon as we felt that we had something [stock] price-sensitive,' says Alan Colman, PPL's research director. In the high-stakes world of stem cells and cloning, he adds, 'people don't have time to hang around and wait for a peer review'. . .

. . . Advanced Cell Technology, Inc said it had created a human embryo clone. It reported the details in an obscure 2-year-old Internet-based publication called *e-biomed: The Journal of Regenerative Medicine*. The paper, which was peer-reviewed, was widely hailed as a landmark and hit the front page of newspapers around the world, including *The Wall Street Journal*.

. . . But there is now a chorus of detractors who point to serious potential flaws in the experiment. Advanced Cell's cloned embryo, these scientists say, had divided into just 6 cells after 5 days, and then died."

Naik G. *Wall Street Journal*. January 28, 2002

Noted by JFL, MD