E. coli O157:H7 in hay- or grain-fed cattle

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Would feeding hay to cows instead of grain solve or reduce the E. coli O157:H7 problem? The NY Times recently ran an editorial ("Leafy Green Sewage" By Nina Planck, September 21, 2006) that included the statement:

> *"It's* [E. coli O157:H7] *not found in the intestinal tracts of cattle raised on their natural diet of grass, hay and other fibrous forage. No, O157 thrives in a new — that is, recent in the history of animal diets — biological niche: the unnaturally acidic stomachs of beef and dairy cattle fed on grain, the typical ration on most industrial farms."*

A number of local news outlets repeated this claim without discussion of the scientific evidence for or against. The goal of this paper is to provide a summary of the evidence.

The hypothesized impact of hay feeding on *E. coli* O157:H7 in bovines seems to have originated in the late 1990s with a research group at Cornell who published an article in *Science* (Diez-Gonzalez et al, 1998) that has subsequently been widely cited. The senior author wrote several additional papers arguing his hypothesis (Russell et al, 2000a; Russell et al, 2000b), but the key data cited as a test of the hay-feeding hypothesis in cattle appeared to be from the 1998 *Science* paper. In that study, a total of three (n=3) cows were rotated through different diets. No evidence is presented that any of the experimental cows were colonized with *E. coli* O157:H7 at any point during the study. Therefore all inferences made by the authors were based on changes in the naturally-occurring mixed populations of *E. coli* of the normal colonic flora, with the assumption that had *E. coli* O157:H7 been there it would have behaved similarly as the rest of the mixed populations of *E. coli*. Some have criticized this assumption on the grounds that *E. coli* O157:H7 are known to differ in important ways from most of the other *E. coli* flora—more on this later. It is also important to note that, in a mixed generic population, it is difficult to distinguish between an induced change (i.e., strains becoming more acid resistant—as the authors hypothesized) and simple trait selection (those naturally more acid resistant being more likely to survive). The authors hypothesized that *E. coli* O157:H7 with induced acid resistance (were it to occur in cows on grain diets) would more easily make it through the gastric barrier of the human stomach and therefore be more likely to cause disease. Only laboratory data were presented to support the possibility that increased acid resistance can be induced in some strains of *E. coli* O157:H7. In spite of these weaknesses, the finding in the 1998 Science paper of a 1000-fold decline in total *E. coli* and a 1-million-fold reduction in acid resistant *E. coli* among their three cows seemed to be promising pilot data in support of their hypothesis. Unfortunately, their findings --and especially their far reaching conclusions regarding the key significance of grain-based feeds to cattle-- have not been corroborated by numerous scientific papers from research groups around the world.

First, consider that a substantial number of papers by researchers around the world have documented that cattle on pasture or rangeland (i.e., eating grass) have *E. coli* O157:H7 in their feces at prevalences roughly similar to those of confined, grain-fed cattle of a similar age (Sargeant et al, 2000; Fegan et al, 2004b; Renter et al, 2004; Laegreid et al, 1999) . One study (Fegan et al, 2004a) found that a higher prevalence among pastured cattle and, among positive cattle, similar concentrations of *E. coli* O157:H7 in feces. More specifically, several outbreaks and sporadic cases of human disease have resulted from pasture or water contamination with *E. coli* O157:H7 from grazing animals (Ogden et al, 2002; Locking et al, 2006) and several papers have documented environmental contamination with *E. coli* O157:H7 originating from cattle on pasture (Strachan et al, 2002; Ogden et al, 2005; Strachan et al, 2006; Looper et al, 2006). As regards potential for environmental contamination, *E. coli* O157:H7 in pooled slurry (manure, urine, waste water etc) declined faster if the manure originated from cattle fed a grain mix diet (grain + silage) than from cattle fed 100% forage (silage) (McGee et al, 2001).

Second, the assumption of the Cornell researchers in their 1998 paper (Diez-Gonzalez et al, 1998) that *E. coli* O157:H7 is typical of the overall population of colonic *E. coli* has been contradicted by subsequent research. First of all, the location of *E. coli* O157:H7 in the animal is now known to differ from that of most other *E. coli.* Several groups have demonstrated that *E. coli* O157:H7 has a unique predilection for colonization of the recto-anal junction, different from most other *E. coli* that colonize cows (Naylor et al, 2003; Sheng et al, 2004; Low et al, 2005; Greenquist et al, 2005). This is important because bacteria at this site experience a different physico-chemical environment than that experienced by the overall mixed *E. coli* flora of cattle and therefore may be expected to react differently to the effects of different feed regimens. For example, a study in which the acid resistance of the overall mixed population of *E. coli* was compared with that of *E. coli* O157:H7 in animals on all hay or grain-containing diets found that, while diet did affect acid resistance of the overall population of *E. coli*, it had no such effect on acid resistance of *E. coli* O157:H7 (Grauke et al, 2003).

Third, several experimental studies have directly tested the hay vs. grain hypotheses using bovines colonized with *E. coli* O157:H7. A research group at the University of Idaho (Hovde et al, 1999) found no difference in acid resistance of *E. coli* O157:H7 from grain-fed or forage-fed animals and found that *E. coli* O157:H7 was shed in the feces for a longer period by forage fed animals. A second study by the Idaho group (Grauke et al, 2003) failed to find much difference in *E. coli* O157:H7 shedding between grain and hay-fed animals (perhaps even a bit higher in rectums of grain-fed cattle based on Figure 3c, though no P-value was given) but corroborated their previous findings in finding no differences in acid resistance of *E. coli* O157:H7 from cattle on the two diet types. Similar to the first Idaho study, van Beale and others (2004) found that *E. coli* O157:H7 was shed for longer and at higher numbers in feces of forage fed animals compared to grain fed; however, they did not report any comparisons of acid resistance. Another study, never published in a refereed journal, was summarized in a review paper (Callaway et al, 2003). According to the summary, feedlot cattle (high-grain diet) with natural *E. coli* O157:H7 infection were identified and split into a group abruptly switched to all hay and a group that continued on the grain diet. At an unstated time thereafter,

the prevalence of *E. coli* O157:H7 was 52% in the grain fed group and 18% in the hay fed group. Acid resistance was evidently not measured in this unpublished study.

Fourth, although many bench researchers have speculated about the importance of acid resistance of *E. coli* O157:H7 the weight of the evidence suggests that any effect in enhancing survival through the human stomach, and thus decreasing infectious dose, is likely to be small in practice. A recent study using simulated gastric fluid found that *E. coli* O157:H7 suspended in saline prior to mixing with simulated gastric fluid experienced a die-off sufficient to reduce, though not eliminate, the dose reaching the intestine (Templin, 2005). In contrast, the same strains mixed with ground beef experienced a substantially slower die-off, such that the fraction of a consumed dose reaching the small intestine would be expected to be reduced only marginally. This finding suggests that *E. coli* O157:H7 consumed with at least some foods is largely protected from the acid shock encountered in the stomach. Another paper (de Jong et al, 2003) showed that, in an environment with a decreasing pH--such as a recently-filled stomach--any *E. coli* O157:H7 that are not acid adapted when consumed are capable of becoming more acid resistant in as little as 17 minutes, well before gastric pH minimum is reached. Consistent with these findings, despite a very large number of outbreak and sporadic case-control studies, none have reported consumption of antacids, proton pump inhibitors or other medications known to reduce gastric acid production to be significant risk factors for acquiring an *E. coli* O157:H7 infection. (In contrast, in case-control studies on human salmonellosis this association has been fairly commonly reported.) The lack of such a reported association for *E. coli* O157:H7 suggests that the acid stomach barrier is relatively less important for this agent.

In summary, while one cannot rule out a role of cattle diet on affecting exposure and infectivity of *E. coli* O157:H7 to humans, the data available at present demonstrate that cattle on a wide variety of diets (including 100% forage diets) are regularly and similarly colonized with this pathogen. Furthermore the balance of evidence regarding the grain vs. hay feeding hypothesis (Diez-Gonzalez et al, 1998) seems to weigh in favor of rejection. Therefore, statements suggesting that all or most of human disease associated with *E. coli* O157:H7 can be attributed to feeding cattle grain instead of hay (as in the aforementioned NY Times editorial) is not supported by the existing scientific literature.

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