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Adult Lactose Tolerance Is Not an Advantageous Evolutionary Trait

To the Editor.—

I read with great interest the recent article from Fomon¹ in which he refers to the well-known hypothesis that views the variable frequencies of lactase persistence in different human populations and, consequently, the possibility for some adults to feed on milk (lactose tolerance) as an advantageous evolutionary trait that has been genetically determined and brought about through centuries of natural selection. This notion stands as a common statement in current medical literature, and most authors have accepted its validity since the 1970s.^{2,3}

Because adult mammals are lactose-intolerant, this hypothesis is, moreover, based on the low percentage of lactose malabsorption and high enterocyte lactase activity (0–30%) among populations originating in northwestern Europe and in some ethnic groups around the Mediterranean and Near East, in Africa, and on the Indian subcontinent. These people share the longest known tradition of dairying, since humans first domesticated livestock and practiced milk-based pastoralism (6000–9000 years ago), making milk abundant for adults. Accordingly, lactose tolerance is supposed to be due to a genetic mutation for lactase persistence, allowing carriers to have milk as a nutritional resource, especially useful in times of food shortage. For the majority of the world's populations, however, the absence of genetic challenge has meant that no evolution has occurred.

Mutation, in combination with natural selection, is most frequently the mechanism utilized to explain these changes in genetic frequency, assuming that the ancestral state was that of nonpersistence (the normal mammalian state) and that the relevant mutation probably originated before the geographical expansion of modern humans. Mathematical models trying to explain this genetic polymorphism require high selection coefficients and a reasonable starting gene frequency.⁴ Such outstanding genetic change during so short an evolutionary span, as claimed, implies an increase in the survival and fertility rates of the lactase-persistence gene carriers to displace the noncarriers in so few (200–300) generations.

Evidence does not support such a hypothesis; the rate of recurrent mutation needed to explain these changes in the genetic frequencies would be very high, 100 to 1000 the usual ($\sim 10^{-5}$ or 10^{-6} per generation for most loci in most organisms). At these usual rates, mutation without selection would bring about only slow changes in the gene frequency in 250 generations. In addition, individual fitness (the contribution of offspring to the next generation) does not exhibit any difference between lactose-tolerant and lactose-intolerant people; no differences in viability or fertility rates in the prereproductive or reproductive periods have been noticed up to now. Moreover, fitness is greater by far in lactose-intolerant populations, and figures show, curiously, that an increase in lactose-tolerance rates is, in general, paralleled by a decrease in demographic values, and vice versa. There are additional unexplained facts concerning the lactase-persistence polymorphism that the evolutionary hypothesis has been unable to explain, but expounding on them would make this letter too protracted.

However, what is more important is that the rationale of evolutionary analysis tells us that restricting milk to the nursing period of mammals is more efficient (greater fitness) than to share it with older individuals. As Fomon points out, the evolutionary forces are focused on the survival of the mother-offspring unit; postreproductive individuals ("the genetic dustbin"⁵) do not directly contribute to evolutionary changes.

In short, evidence does not support the evolutionary hypothesis of lactase persistence in human adults as a consequence of selection. A founder effect could be a more suitable explanation to

justify this trait, and this mechanism does not need the cooperation of natural selection.

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Does Children's Watching of Television Cause Attention Problems? Retesting the Hypothesis in a Danish Cohort

To the Editor.—

In a recent issue of *Pediatrics*, Christakis et al¹ reported an association between the number of hours of watching television close to 2 and 4 years and parents' report on their children's behavior in early school age.

Based on the findings, the authors suggest that we generally limit young children's television use. This is probably a good idea, but we question whether this report creates additional evidence for this advice.

The authors reported a 9% increase in risk of attention problems for each daily hour of television-watching. The measure of adverse behavior was based on a score of maternal report of child behavior including restlessness, concentration problems, impulsiveness, confusion, and obsession. A similar association was found at both ages of reported television-watching, which would be unexpected if the association was caused by an influence on brain development.

A log-linear association is anticipated, but whether such a relationship is actually present in the data is obscure. This particular strategy of analysis may provide more statistical power, but the assumption of a log-linear association is strong and implies that any additional hour of watching television provides the same log-linear increase in risk, whereas a threshold effect or other nonequidistant associations may very likely be present.

We retested the hypothesis in a part of the Aarhus Birth Cohort, which consists of all children born from 1990 at the Aarhus University Hospital, Denmark. As part of a follow-up program for children born in 1991–1992 and examined at 8 months of age,² participating mothers were asked about their child's television-watching on the day previous to completion of the questionnaire when children were 3½ years old. The relevant child behavior at that age was evaluated by a questionnaire developed for preschoolers by Behar³ based on the Rutter scale.

The behavior of the children was evaluated further at the age of 10 to 11 years by the mother using an "ADHD [attention-deficit/hyperactivity disorder] problem score" based on a selection of 12 questions from the Child Behavior Checklist⁴ identified by their relation to the ADHD diagnosis in a previous Danish study.⁵ The following year, teachers and parents filled in the Strength and Difficulties Questionnaire,⁶ and their reports were summarized to identify probable and likely ADHD cases.⁷

We found no significant association between hours of watching television and behavioral problems in any of the age groups, although the results do not rule out such an effect, especially not for those who spend the longest time in front of the television (Table 1).

US children apparently watch much more television than Danish children, and if there is a threshold level for effect, we may not

TABLE 1. ADHD Relevant Behavior According to Hours of Television-Watching

Hours of Watching Television, Age 3½ y	N	Age 3½ y, Behar score*				Age 10–11 y, ADHD Problem Score†				Age 11–12 y, SDQ Algorithm‡			
		N	%	OR	95% CI	N	%	OR	95% CI	N	%	OR	95% CI
<½	168	9	5	1		16	10	1		9	5	1	
½–1	555	34	6	1.1	0.5–2.4	38	7	0.7	0.4–1.2	32	6	1.0	0.5–2.2
1–1½	346	23	7	1.2	0.6–2.7	25	7	0.7	0.3–1.3	22	6	1.1	0.5–2.4
1½–2	204	23	11	2.2	1.0–4.9	14	7	0.6	0.3–1.4	15	7	1.3	0.6–3.1
>2	76	8	11	2.0	0.8–5.5	9	12	1.2	0.5–3.0	8	11	2.0	0.7–5.5

Logistic regression was adjusted for gender. Shown are singletons born in the Aarhus Birth Cohort 1991–1992 ($N = 1349$). OR indicates odds ratio; 95% CI, 95% confidence interval.

* Sum of >4 on a 4-symptom Lickert-based scale (possible score: 0–8)—hyperactive/distractible scale.³

† An “ADHD problem score” of >5 of 12 selected behavior symptoms (possible score: 0–12) from the Child Behavior Checklist.⁵

‡ Probable and likely ADHD cases based on a combination of parent and teacher reports (Strength and Difficulties Questionnaire [SDQ] score/impact).⁷

be able to detect an association. Our data indicate that a threshold for no effect may exist.

It is a clinical experience that watching television can engage children with ADHD for some time, probably because of the constant visual and auditory stimuli they receive from these media. The parents of these children may therefore be more likely to allow them to watch television for longer periods of time. The children in our study, who were watching >1½ hour of television at the age of 3½ years, were more likely to have ADHD-like behavior already at this age. The direction of causality may very well be the opposite of what is concluded by Christakis et al.

We cannot exclude the possibility that watching television in childhood may cause behavioral problems, but we need better studies to further elucidate this association.

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In Reply.—

We are pleased that Obel et al have tried to replicate our findings in a Danish data set of convenience and happy to reply to their letter. They are surprised that the association between television-viewing and attentional problems that we found was similar at ages 1 and 3. We are not. Many of the children in our study were included in both the age-3 and the age-1 analysis, and in fact the amount of television viewed at age 3 years is highly correlated with the amount viewed earlier.¹ Thus, it is not surprising that television viewed at 3 years and at 1 year had similar odds ratios within the context of our data set. Their next point is that they found an association between television-viewing and behavioral problems in their data set at age 3½ years but not in subsequent years. In reviewing their data, it must first be noted (as they too acknowledge) that Danish children watch considerably less television than US children do. Fewer than 6% of children in their sample watched >2 hours per day at age 3 years as opposed to >50% of US children at the same age.^{2,3} Their analysis therefore has considerably less power than ours did to detect a significant difference at these levels of viewing. In addition, as underpowered as they are, they do report an odds ratio of 2.0 for “probable and likely” ADHD cases at 11 to 12 years. Although this finding is not significant as the 95% confidence interval extends from 0.7 to 5.5, with more data in this range it might have been. Moreover, it is also possible that the kinds of programming available in the

United States and Denmark are different. Different types of children's programming have been shown to vary with respect to the pacing and to lead to differences in children's attention spans at young ages.⁴⁻⁸

Finally, we concur that better research of the effects of television-viewing in this age group is needed. It has been said that "many parents are enlisting the help of a stranger to raise their children."⁹ That stranger's influence warrants more robust study. We are pleased to be part of that effort.

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Effectiveness of Neonatal Intensive Care for Extremely Low Birth Weight Infants

To the Editor.—

I commend Doyle et al^{1,2} for the thorough longitudinal follow-up of their extremely low birth weight infants over 2 decades, which demonstrated greater overall and quality-adjusted survival for the most recently born cohorts. However, I think the authors overinterpreted the outcome data in concluding that these data demonstrate effectiveness and efficiency of neonatal intensive care. The study actually provides little information regarding neonatal intensive care management over the 2 decades and no data specifically relating neonatal management to the improved survival. The provision of neonatal intensive care over these decades has undoubtedly contributed to improved survival, but the influence of neonatal care should not be separated from obstetrical management as has been done in the Doyle et al study.

Specific obstetrical interventions including antenatal corticosteroid use,³ more liberal cesarean section delivery,⁴ and increased

prenatal care⁵ have proven or suggested benefit for survival and decreased morbidity for low birth weight infants. It is likely that over the study period, obstetrical providers increasingly used these and other interventions for pregnancies at marginal gestations. Previous studies have suggested that a change in perception by obstetrical providers, without new technical interventions, may significantly benefit neonatal survival.^{6,7}

It is reassuring that in this geographically defined population, greater survival for extremely low birth weight infants was associated with increased quality-adjusted survival, which has certainly not been universally reported.^{8,9} However, before concluding that this outcome has resulted from effective and efficient neonatal care, prenatal (and perhaps postneonatal) influences and associated costs must be considered in the analysis.

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In Reply.—

Dr Kilbride is concerned that we have overinterpreted the data in our reports of the effectiveness¹ and efficiency² of neonatal intensive care and particularly that we have overlooked the contribution of obstetric interventions. What we have done is to quantitate the overall effectiveness of neonatal intensive care, without trying to measure the individual contributors, including obstetric interventions, to the outcomes. We also incorporated postneonatal care by including any hospitalizations beyond 28 days up to 5 years of age (2 years of age for the 1997 era).

We agree with Dr Kilbride in that obstetric care has changed over the 2 decades of our study and that obstetric decision-making for extremely low birth weight (ELBW; birth weight: 500-999 g) infants is important to their outcome. The overall contribution of obstetric care might be best quantitated in the changes in availability of neonatal intensive care for ELBW infants, the final step in the overall evaluation of neonatal intensive care.³ Availability addresses the issue of whether intensive care is reaching those who need it. We have reported elsewhere on the changing availability of neonatal intensive care for ELBW infants in Victoria, Australia.⁴ As measures of availability, we determined the changes in both the proportion of ELBW infants who were offered intensive care as well as the place of birth of these infants. Over time, the proportions offered intensive care rose substantially

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