

CARDIOVASCULAR DISEASES

Body indices and basic vital signs in *Helicobacter pylori* positive and negative persons

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Abstract. It has been hypothesized that *Helicobacter pylori* (Hp) infection may contribute to reduced stature, risk of hypertension or obesity. The aim was to evaluate body indices in Hp positive and negative persons. A total of 2436 subjects (4–100 years old) were tested for Hp status by ¹³C-urea breath test. Data on height and weight were collected for 84%, and blood pressure for 80% of the study subjects. The prevalence of Hp infection was 41.6%. The odds ratio for a 10-year increase in age was 1.21 (95% CI 1.17–1.25, *p*-value <0.001). Statistically significant negative association of Hp positivity with body height was most pronounced in the younger age groups, while a

positive association of Hp positivity with body mass index was only seen in those aged 15+ years. There was a negative effect of Hp positivity on systolic and diastolic blood pressure in subjects below 25 and a relatively strong positive effect on blood pressure in subjects over 65 years. Residual confounding by social characteristics as a possible explanation for the associations of Hp positivity with height and blood pressure cannot be excluded. Unmeasured factors related to social and family environment may cause the apparent association between Hp positivity and children's growth and blood pressure.

Key words: ¹³C-urea breath test, Height, *Helicobacter pylori*, Hypertension, Weight

Introduction

Helicobacter pylori (Hp) has been recognized as one of the most common chronic bacterial infection in the world. Its prevalence is high in developing

countries (80–90%) and lower in developed ones (<40%) [1, 2]. Hp infection is acquired during early childhood in most individuals. The infection lasts several decades or even life long, with a low spontaneous eradication rate. Hp is a cause of chronic gastritis and may be closely associated with a number of extragastric diseases [2, 3]. In general, any chronic inflammatory conditions can influence health status remote to the site of inflammation. It has been suggested that chronic Hp infection may predispose subjects to the development of malnutrition [4, 5] and growth delay in children [4–7]. On the other hand it has been hypothesized that chronic Hp infection may contributed to hypertension [8–11], lipid metabolism disturbance [9, 12] and obesity [9]. However, published results are rather controversial in current literature. Other authors have found no association of Hp infection or short stature [13–15], hypertension [16, 17], nutritional

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status [15, 18] or obesity [19, 20]. These papers are difficult to be compared as they differ in the individuals studied, design and number of subjects, the diagnostic methods used (serology, ^{13}C -urea breath test, stool antigen tests) and coming from both developed and developing countries. The Czech Republic has medium prevalence of *Helicobacter pylori* infection (~40%) and thus differs from both developed and developing countries. The aim of this study was to evaluate body indices and basic vital signs in Hp positive and negative persons in a representative sample of the general Czech population.

Subjects and methods

Subjects

Hp status was investigated in 2436 persons older than 4 years. These subjects were chosen in a two-step random selection, carried out centrally, in a general population of 30,012 individuals. Nineteen general practitioners (12 for adults and 7 for children) took part in this Project. Recruitment areas fitted well with geographic distribution of population in the Czech Republic, covering cities and towns (8 GPs), smaller towns with surrounding villages (8 GPs) and rural areas (3 GPs). There were no preliminary exclusion criteria.

For 2425 (>99.5%) of these, results of two test samples were available. For the purpose of the current analysis 1,003 subjects who had positive results in both tests or one positive and one borderline (or missing) result are classified as Hp positive. Twenty-five (<1%) subjects with clearly discrepant results (one positive and one negative) were excluded from the evaluation. The rest of the study subjects are considered Hp negative for the purpose of the current analysis.

Urea breath test

Urea breath tests were performed in the morning after overnight fasting. Citric acid solution (3 g dissolved in 150 ml of still water) was used as a test drink. All subjects ingested 100 mg ^{13}C -urea for adults (*Helicobacter Test Hp Plus*, Utandningstester i Sverige AB, Göteborg, Sweden) or 75 mg ^{13}C -urea for children and adolescents (*Helicobacter Test INFAI*, INFAI GmbH, Köln, Germany) dissolved in 50 ml of still water with 1 g citric acid. Baseline and test breath samples were collected in duplicate at time 0 and after 30 min. Tubes with breath samples were sent to a single analytical centre by post and measured within a 1-week period. Breath samples were analysed by means of isotope ratio mass spectrometry (AP 2003, Analytical Precision, United Kingdom). Cut-off was 3.5 (grey zone range 3.3–3.7).

Body indices and basic vital signs

Data on height and weight were collected at the clinics for 84% of the study subjects. Overweight and obesity in adults were defined as body mass index of 25+ and 30+ kg/m², respectively. The definitions of overweight and obesity in children and adolescents aged 4–17 years are based on age and gender-specific cut-off points developed by Cole et al. [21].

Systolic and diastolic blood pressure measurements were performed by a trained nurse in a standard manner [22] at the study clinics and were completed for 80% of the study subjects. The blood pressure was measured in the morning (from 8 to 12 a.m.). Hypertension in adults was defined as systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mm Hg, according to the guidelines of European Society of Hypertension-European Society of Cardiology [22] and the reviewed WHO-International Society of Hypertension guidelines [23]. Hypertension in children and adolescents aged 4–17 years was defined based on the age, gender and height-specific criteria published by the National High Blood Pressure Education Program Working Group on High Blood pressure in Children and Adolescents (2004) [24]. Analyses of associations of Hp positivity with body size and blood pressure were restricted to 79.8% of the sample with data on height, weight, systolic and diastolic blood pressure available. There were no statistically significant differences in the prevalence of Hp positivity, age, gender or nationality between the subjects with all data available and those who had missing data on body size or blood pressure. The subjects excluded from the analyses because of missing data on body size or blood pressure tended, however, to be on average more educated and were more likely to live in large towns.

Questionnaires

Social characteristics are based on data from self-completed questionnaires and include nationality classified as Czech and other, place of residence classified as “village”, “small town with less than 20,000 inhabitants” and “larger town with more than 20,000 inhabitants” and highest level of education achieved. The study subjects’ own education or their parents’ education (if younger than 25 years or still studying) are analysed as categorical variables with four categories (basic or less, vocational training, secondary education, university). Information on social characteristics was available for 99% of the study sample. Information on the study subjects’ smoking habits was also collected in the questionnaire, grouped into three categories of “never”, “past” and current” smokers, and is used in the analyses for those aged 15+.

Statistical analysis

The data was analysed by univariate and multivariate linear and logistic regressions as appropriate, using the STATA package [25]. Multivariate analyses were restricted to those subjects with all relevant data available. Results of analyses stratified by age are presented in this paper to take account of the hypothesised interactions with age of the study subjects.

Study approval and confidentiality of data obtained

The study was approved by the local Ethics committee. All participants got detailed written information about the Project in advance and signed written consent (parents on behalf of their children). For all data obtained, all personal identification information was deleted in compliance with the laws for the protection of confidentiality of the Czech Republic.

Results

Basic descriptive characteristics of the study sample are presented in Table 1. The overall prevalence of Hp positivity in our study was 41.6%. Hp positivity was strongly associated with age of the study subjects. The odds ratio for a 10-year increase in age was 1.21 (95% CI 1.17–1.25, p -value < 0.001). There were no statistically significant gender differences in Hp positivity. The age-adjusted odds ratio for Hp positivity in females compared to males was 0.95 (95% CI 0.81–1.13, p -value 0.577). Only four subjects ($< 0.2\%$) were on long term proton pump inhibitors treatment at the time of our study, of whom two subjects tested as Hp positive and two as Hp negative. Exclusion of these four subjects from analysis did not affect the results appreciably.

We observed a relatively strong and statistically significant negative association of Hp positivity with body height, which was most pronounced, and statistically significant, in the younger age groups (Table 2). Some of this association was explained by further adjustments for place of residence, education and nationality (Table 2).

Hp positivity was also associated with a slightly lower body mass index in children below 15 years (Table 2) and with a higher mean body mass index in subjects over 15 years (Table 2). The associations of Hp positivity with body mass index were relatively little affected by adjustments for social characteristics or smoking (Table 2).

Analyses of overweight and obesity showed a statistically significantly lower prevalence of overweight in Hp positive children and a higher prevalence of overweight and obesity in adults that was of borderline statistical significance (Table 3).

There were marked differences between age groups in how Hp positivity was related to systolic and

diastolic blood pressure. We observed a strong negative effect of Hp positivity on systolic and diastolic blood pressure in subjects below 25 years of age and a relatively strong positive effect on blood pressure in subjects aged 65+ years (Table 4). While the strength of the association between Hp positivity and blood pressure in children was nearly halved on adjustment for body mass index and social characteristics, the strength of the positive association between Hp positivity and blood pressure in oldest subjects was less affected by adjustments for body mass index, social characteristics and smoking, and the negative association between Hp positivity and blood pressure in subjects aged 15–24 became stronger.

Analyses of Hp positivity with hypertension yielded results broadly consistent with analyses of blood pressure (Table 5). Fully adjusted analyses did not show statistically significant associations between Hp positivity and hypertension, with the exception of a positive association of borderline statistical significance seen in the oldest group (Table 5). The statistical interactions of Hp positivity with age in their effect on blood pressure and hypertension were statistically significant, suggesting differential effects, and possibly also different mechanisms, by which Hp positivity is related to blood pressure in different age groups.

We did not observe any statistically significant effects of Hp positivity on pulse rate in any age group (data not shown).

Discussion

The overall prevalence of Hp infection was 41.6% in this study. Hp positivity was strongly associated with age of the study subjects. We observed a relatively strong and statistically significant negative association of Hp positivity with body height, which was most pronounced, and statistically significant, in the youngest age groups (Table 2). Several epidemiological studies showed association between Hp infection and short growth in children [4–7]. However, contradictory data are available on this topic, as other authors did not find any relation [13–15]. Results and conclusions of all published papers (including our findings) must be assessed with caution. It is necessary to distinguish intrinsic shortness and delayed or attenuated growth. Several factors can influence growth and stature, including chronic inflammation, nutrition and several gastrointestinal diseases [26].

Thomas et al. [4] followed 190 children in Gambia from their birth in two cohort studies. Early colonisation with Hp was associated with weight and growth deficit compared to non-infected individuals. No socioeconomic or demographic confounding variables were identified these findings. The deficit was no longer detectable when the children reached age of 5–8 years [4]. Bravo et al. [27] studied 347 Hp

Table 1. Descriptive characteristics of the study sample

Gender and age (years)	Number of subjects	Helicobacter pylori positive	Height (cm)		Body mass index (kg/m ²)		Overweight or obese ^a	Systolic blood pressure (mm Hg)		Diastolic blood pressure (mm Hg)		Resting pulse rate (per min)		Hypertension ^b
			Proportion in %	Mean and std. dev.	Mean and std. dev.	Proportion in %		Mean and std. dev.	Mean and std. dev.	Mean and std. dev.	Mean and std. dev.	Proportion in %		
<i>Males</i>														
4-14	220	28.2	134.7 (17.1)	17.0 (2.6)	14.9	107.5 (10.6)	62.0 (10.4)	85.4 (9.0)	15.9					
15-24	186	30.6	177.9 (9.5)	22.6 (3.6)	23.7	121.8 (11.2)	72.5 (11.0)	74.2 (9.8)	14.7					
25-34	135	34.1	178.0 (6.9)	24.7 (2.8)	42.7	126.3 (11.4)	76.0 (8.6)	72.8 (8.3)	21.3					
35-44	100	46.0	178.0 (6.2)	26.4 (3.7)	67.6	130.9 (13.4)	81.0 (11.2)	73.0 (8.7)	42.6					
45-54	155	45.8	176.8 (6.5)	27.8 (4.4)	74.8	135.3 (15.4)	81.4 (10.0)	75.1 (8.8)	53.3					
55-64	128	60.9	175.7 (6.5)	28.2 (3.7)	78.6	140.6 (14.9)	83.7 (9.5)	74.2 (6.4)	67.0					
65-74	157	50.3	173.2 (6.9)	28.4 (4.1)	81.4	146.4 (17.3)	85.4 (10.3)	73.5 (7.4)	77.2					
75-100	109	61.5	171.1 (6.7)	26.4 (3.9)	66.0	146.8 (21.3)	86.5 (10.9)	74.8 (8.1)	78.5					
Total	1190	42.5	167.9 (19.2)	24.4 (5.4)	50.8	129.9 (19.8)	77.0 (13.3)	74.7 (8.8)	39.7					
<i>Females</i>														
4-14	250	33.2	137.1 (17.4)	17.2 (3.4)	14.0	108.6 (12.6)	63.1 (9.7)	89.6 (12.2)	18.5					
15-24	222	24.8	166.1 (6.9)	21.7 (4.0)	15.2	115.5 (11.1)	70.1 (9.7)	75.9 (12.2)	7.1					
25-34	113	39.8	165.5 (6.9)	23.2 (4.7)	27.1	117.6 (14.6)	72.4 (10.6)	73.0 (9.9)	12.8					
35-44	110	36.4	166.7 (7.6)	24.7 (4.4)	47.4	122.2 (15.3)	77.1 (10.6)	72.6 (8.4)	21.9					
45-54	157	46.5	165.0 (6.1)	26.4 (4.7)	56.2	131.2 (16.2)	79.5 (9.8)	75.0 (10.1)	43.8					
55-64	106	50.0	163.7 (6.1)	29.1 (4.6)	80.0	144.0 (16.6)	86.0 (10.2)	73.9 (7.7)	72.1					
65-74	147	50.3	161.9 (6.6)	28.1 (4.6)	72.4	145.0 (19.5)	84.1 (10.0)	72.4 (7.7)	76.1					
75-100	116	63.8	161.1 (6.2)	26.4 (4.0)	59.4	151.4 (20.3)	85.2 (8.9)	74.9 (8.8)	78.8					
Total	1221	40.7	158.2 (15.3)	23.4 (5.8)	39.8	126.3 (21.7)	75.1 (12.9)	75.4 (10.7)	33.0					

^aBody mass index $25 + \text{kg/m}^2$ in adults; age-specific cut-off points for children and adolescents based on Cole et al. (Ref. 21).^bSystolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg in adults; age-specific cut-off points for children and adolescents based on National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (Ref. 24).

Table 2. Association of *Helicobacter pylori* positivity with height and body mass index, by age group

Age:	Height		Body mass index						
	Mean and std dev. in cm		Regression coefficient with 95% CI and p-value		Mean and std dev. in kg/m ²		Regression coefficient with 95% CI and p-value		
	Hp positive	Hp negative	Adjusted for age and gender	+ Social characteristics	Hp positive	Hp negative	Adjusted for age and gender	+ Social characteristics	
4-14 years (n = 415)	133.1 (17.0)	137.0 (17.3)	-2.1 (-3.7, -0.5)	0.010 (-1.5 (-3.2,0.2))	0.091 (16.7 (3.1)	17.4 (3.0)	-0.5 (-1.1,0.1)	0.082 (-0.6 (-1.3,0.0))	0.043 (-
15-24 years (n = 356)	170.5 (10.5)	171.8 (9.7)	-1.8 (-3.6,0.0)	0.048 (-1.5 (-3.4,0.3))	0.098 (22.9 (4.4)	21.9 (3.6)	0.9 (0.0,1.8)	0.039 (0.8 (-0.1,1.6))	0.092 (0.7 (-0.1,1.6))
25-64 years (n = 772)	170.9 (8.9)	171.9 (8.9)	-1.2 (-2.2, -0.3)	0.009 (-0.7 (-1.6,0.3))	0.162 (26.9 (4.2)	26.0 (4.8)	0.3 (-0.3,0.9)	0.305 (0.1 (-0.5,0.7))	0.657 (0.2 (-0.4,0.8))
65+ years (n = 427)	166.3 (8.2)	167.9 (8.9)	-0.6 (-1.9,0.6)	0.307 (-0.4 (-1.6,0.8))	0.540 (27.5 (4.3)	27.3 (4.2)	0.4 (-0.4,1.2)	0.345 (0.3 (-0.5,1.1))	0.452 (0.4 (-0.4,1.1))
Total 15+ years (n = 1555)	169.3 (9.1)	171.0 (9.3)	-1.1 (-1.8, -0.3)	0.004 (-0.6 (-1.3,0.1))	0.077 (26.5 (4.5)	25.0 (4.8)	0.6 (0.1,1.0)	0.009 (0.4 (0.0,0.9))	0.044 (0.5 (0.0,0.9))

Note: social characteristics include: education (own or parental, if younger than 25 years), nationality and place of residence.

Table 3. Association of *Helicobacter pylori* positivity with overweight and obesity, by age group

Age:	Overweight or obesity ^a		Obesity ^b						
	Prevalence (%) among		Odds ratio with 95% CI and p-value		Prevalence (%) among		Odds ratio with 95% CI and p-value		
	Hp positive	Hp negative	Adjusted for age and gender	+ Social characteristics	+ Smoking	Hp positive	Hp negative	Adjusted for age and gender	+ Social characteristics
4-14 years (n = 415)	8.6	17.4	0.44 (0.22,0.88)	0.021 (0.20,0.88)	0.021 (0.20,0.88)	2.3	2.4	0.88 (0.22,3.52)	0.77 (0.17,3.42)
15-24 years (n = 356)	23.7	18.5	1.32 (0.75,2.34)	0.333 (0.66,2.12)	0.570 (0.66,2.13)	5.1	3.5	1.53 (0.50,4.71)	1.26 (0.40,4.00)
25-64 years (n = 772)	66.0	54.4	1.35 (0.98,1.84)	0.062 (0.90,1.72)	0.183 (0.91,1.73)	22.1	16.8	1.14 (0.78,1.66)	1.02 (0.69,1.50)
65+ years (n = 427)	70.5	70.5	1.11 (0.72,1.72)	0.619 (0.69,1.70)	0.720 (0.72,1.83)	27.0	20.5	1.53 (0.97,2.44)	1.49 (0.93,2.40)
Total 15+ years (n = 1555)	61.6	47.1	1.31 (1.05,1.64)	0.017 (0.98,1.55)	0.071 (0.99,1.57)	21.4	13.6	1.36 (1.03,1.80)	1.27 (0.96,1.68)

^aOverweight or obesity: body mass index 25+ kg/m² in adults; age-specific cut-off points for children from Cole et al. (Ref. 21).

^bObesity: body mass index 30+ kg/m² in adults; age-specific cut-off points for children from Cole et al. (Ref. 21).

Note: social characteristics include: education (own or parental, if younger than 25 years), nationality and place of residence.

Table 5. The effect of *Helicobacter pylori* positivity on hypertension, adjusted for age and gender; with additional adjustments for body mass index and social characteristics

	Hypertension ^a					
	Prevalence (%)		Odds ratio with 95% CI and <i>p</i> -value			
Age:	Hp positive	Hp negative	Adjusted for exact age and gender	+ Body mass index	+ Social characteristics	+ Smoking
4–14 years (n = 379)	13.8	19.5	0.65 (0.36,1.19) 0.161	0.68 (0.37,1.24) 0.210	0.72 (0.37,1.38) 0.324	–
15–24 years (n = 327)	10.1	10.5	0.92 (0.41,2.08) 0.852	0.80 (0.35,1.84) 0.601	0.64 (0.26,1.56) 0.326	0.59 (0.24,1.48) 0.264
25–64 years (n = 757)	46.5	39.5	1.02 (0.74,1.40) 0.899	0.96 (0.69,1.34) 0.830	0.86 (0.61,1.21) 0.377	0.84 (0.60,1.19) 0.337
65+ years (n = 421)	81.6	72.7	1.62 (1.02,2.58) 0.041	1.58 (0.98,2.54) 0.058	1.53 (0.94,2.50) 0.089	1.56 (0.95,2.56) 0.076

^aSystolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg in adults; age-specific cut-off points for children and adolescents based on National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (Ref. 24).

Note: social characteristics include: education (own or parental, if younger than 25 years), nationality and place of residence.

negative children aged 12–60 months (tested by ¹³C-urea breath test). During the prospective follow-up (2.5 years) 105 (30%) children, who were uninfected at the start of the study, acquired Hp infection. Growth velocity in infected children was significantly reduced (0.5 cm per year) [27]. Passaro et al. [28] found that even 2 months after eradication of Hp (assessed by seroconversion) there was a slowing of weight gain in young children. Reasons for this finding remain unclear. However, Naficy et al. [15] did not find such an association among young seroconverted Egyptian children. Hp infection was not associated with malnutrition either [15]. In a study from Guatemala [18], 211 girls aged 5–10 were investigated and their height-for-age was significantly decreased with both Hp infection and lower income level. However, Hp infection did not affect nutritional status of those individuals [18]. Sood et al. [29] having assessed 257 children in a US study, found Hp positive children shorter and lighter compared with non-infected ones. They concluded that differences in anthropometry might be due to socioeconomic and ethnic factors rather than Hp infection [29].

Perri et al. [7] found a strong relationship between Hp infection and short stature in older children, poor socio-economic status and household overcrowding. Several hypotheses were given to explain this association: chronic systemic release of cytokines (tumour necrosis factor alfa in particular) affecting growth, low energy intake and/or malnutrition and low socio-economic background may be the pathogenic mechanisms responsible for short stature [7]. Choe et al. [30] found a significantly lower height among 532 healthy children aged 10–15 having both Hp infection and iron deficiency anaemia. Authors concluded that Hp infection accompanied by iron deficiency anaemia, rather than Hp infection per se, might delay pubertal growth [30]. According to other

studies both Hp infection and short stature are two non-related consequences of low socio-economic status [16]. Growth delay at around the time of puberty in Hp positive children was also found by other authors [6, 7, 31, 32] and could be explained as delayed pubertal growth spurting. Delayed menarche in Hp positive girls [33] is consistent with these findings. Recently, Moayyedi et al. [34] found that Hp infected women (aged 40–49) were 1.4 cm shorter than uninfected ones. Statistically significant difference persisted even after adjusting for age, ethnicity, childhood and present socio-economic status. Despite this, authors concluded that this reduced adult height might be due to residual confounding [34]. Similar findings of reduced height in Hp positive women (but not men) compared to Hp negative ones were described also by Murray et al. [35]. In this large population-based study (4742 subjects aged 12–64) Hp was more common in men (61%) than women (55%) [35].

In our study, Hp positivity was associated with a slightly lower body mass index in children below 15 years and with a higher mean body mass index and a higher prevalence of overweight and obesity in older subjects. In literature, there are both positive [9, 33] and negative [19, 20] reports on association of Hp infection and higher body mass index and/or obesity. Hp eradication has induced increase in body mass index in Japanese industrial workers [36]. According to another studies, Hp eradication improved some nutritional parameters, including gain in body weight [37].

We have also found marked differences between age groups in how Hp positivity was related to systolic and diastolic blood pressure. We observed a strong negative effect of Hp positivity on systolic and diastolic blood pressure in subjects below 25 years of age and a relatively strong positive effect on blood

pressure in subjects over 65-year old (Tables 4 and 5). Controversial data have been published in literature on the association of Hp infection and hypertension with both positive [8–11] and negative [16, 17] results. In a large community-based cross sectional study (1634 Hp positive and 3267 Hp negative persons out of 10,537 subjects enrolled), Hp infection had little effect on blood pressure in the general population, mean systolic blood pressure was higher in Hp infected individuals than in those who were not infected and, although this was significant statistically, the authors concluded that it was unlikely to be clinically important and might be explained by unknown residual confounding factors [17]. Migneco et al. [10] demonstrated a significant decrease in blood pressure values (in particular in the diastolic one) after successful Hp eradication. There are several methodological difficulties in carrying out studies to determine possible relationship between Hp infection and raised blood pressure, there are several other factors that must be considered (weight gain, salt intake, aging, co-morbidity, antihypertensive therapy, compliance of patients etc.) [38]. We can speculate that a negative effect of Hp infection on blood pressure is markedly expressed (in the relative absence of other factors) in younger adults while other factors mentioned above dictate blood pressure in older subjects, both Hp positive and negative.

We cannot exclude residual confounding by social characteristics as a possible explanation for the associations of Hp positivity with height and blood pressure reported in our paper, especially in children. It is plausible that unmeasured factors related to social and family environment may cause the apparent association between Hp positivity and children's growth and blood pressure. On the other hand, associations of Hp positivity with overweight and hypertension in older subjects seem relatively little affected by adjustments for social characteristics or smoking in our study, and the respective underlying mechanisms should be further explored.

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