Does *Helicobacter pylori* protect against asthma and allergy?

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The microbes that persistently colonise their vertebrate hosts are not accidental.[1] Although highly numerous and diverse, there is specificity by site and substantial conservation between individuals. The genus *Helicobacter* includes spiral, highly motile, urease-positive, Gram-negative bacteria that colonise the stomach in many mammals. Each mammal has one or more dominant *Helicobacter* species and they are highly, if not exclusively, host species-specific.[2] Such observations are consistent with the hypothesis that when ancestral mammals diverged from reptiles about 150 million years ago, they contained ancestral helicobacters, which then diverged as their hosts changed. According to this hypothesis, helicobacters represent ancestral biota (flora) in the mammalian stomach. The human-adapted strain is *H pylori*,[3] which has not been reproducibly observed in any animals other than humans and other primates.[3]

Although we can not reliably estimate how long *H pylori* has been in the human stomach, its ancestors may have been present when our humanoid ancestors diverged from other primates about four million years ago. Consistent with this view are results from phylogeographic studies; strong and consistent evidence indicates that our ancestors already were carrying gastric *H pylori* when a group that ultimately populated much of the world last left Africa, more than 58 000 years ago.[4] In any case, *H pylori* has been colonising the stomach of humans since at least Paleolithic times.

In this paper, we examine the evidence concerning the relationship of this ancient member of the human microbiota, and particularly its absence, with the recent and on-going epidemic of asthma and related allergic disorders. We discuss the possibility that gastric *H pylori* colonisation protects against these disorders and that its disappearance has fuelled their rise.

H PYLORI ACQUISITION AND PERSISTENCE

H pylori is acquired, and may be detected, in early childhood usually after the first year of life.[5] Transmission is faecal–oral, oral–oral and vomitus–oral.[6] Once acquired, in the absence of antibiotic use, *H pylori* persists at least for decades, and most often for the full life of its host.[7] *H pylori* strains are highly variable, and several loci affect *H pylori*–host interactions. In particular, strains with an intact *cag* island inject the CagA protein into host gastric epithelial cells;[8] this heightened interaction in relation to *cag*-negative strains affects disease risk.[9 10]

For most of human existence, we have lived in small, intimate groups,[11] in which our microbiota mingled extensively with that of other group members.[12] Under the conditions of poor hygiene that have predominated for most of human existence, transmission of gastro-intestinal microbes has been easily accomplished. In present-day developing countries in which such enteric transmission occurs, *H pylori* is ubiquitous, with estimates for its prevalence in adults exceeding 80%; its presence is possibly nearly universal, when multiple detection methods are used.[7 13] In populations in which *H pylori* is highly prevalent, gastric colonisation with several distinct strains appears common.[14]

H PYLORI IS DISAPPEARING

Despite the substantial evidence for the antiquity and ubiquity of *H pylori* colonisation in humans, it now has become clear that the prevalence of *H pylori* is rapidly decreasing! This is a birth cohort effect, which began in the early 20th century in many developed countries, and accelerated after World War II.[15–17] The effect has been so profound that fewer than 10% of children under 10 in the United States and in other industrialised countries now are *H pylori*-positive, compared to the historic 70–90% levels.[15–17] As a result of this change, occurring around the developed world to variable extents, risk factors for *H pylori* acquisition can be determined. These include large family size, having parents (especially mothers) carrying *H pylori*, *H pylori*-positive older siblings, and household crowding during childhood.[18 19] Thus, as disappearance begins, the effects compound with each generation, especially as water has become cleaner, family sizes have shrunk, mothers pre-masticate food less, and nutrition has improved.[20]

Another phenomenon that may contribute to *H pylori* disappearance is the widespread use of antibiotics, especially during childhood.[21] To reliably eradicate *H pylori* requires combinations of two to four antimicrobial agents, but early studies with monotherapies, including beta-lactam and macrolide antibiotics, showed eradication rates from 10 to 50%.[22 23] If comparable effects occur every time a child is treated with antibiotics for an upper respiratory or skin infection or for otitis media, then the rapid (and compounding) decline in *H pylori* prevalence in childhood in developed countries in recent decades is not difficult to understand.

CONSEQUENCES OF THE PRESENCE OR ABSENCE OF *H PYLORI*

By comparing persons with and without the organism, medical scientists have studied the costs and benefits of carrying *H pylori*. First came the observation that the presence of *H pylori* in the gastric lumen is associated with the presence in the gastric lamina propria of phagocytic and immune cells.[24] Warren and Marshall recognised the association of *H pylori* with these histological findings, which pathologists call "chronic gastritis";[24 25] the presence of inflammatory cells leads to use of terms implying pathological processes. However, as biologists, we believe that the collection of immune and inflammatory cells in the tissue should be considered as "the physiological response to the indigenous microbiota" (or PRIM). Similarly, the lamina proprias of the mammalian mouth, vagina and colon are populated by phagocytic and immunological cells that respond to the local indigenous microbiota. In contrast, germ-free animals have essentially no phagocytic and immune cells in their lamina propria, but "conventionalising" these animals, by restoring their normal biota restores these cells, which is considered as the normal histopathology.[26]

One difficulty with terming the host response to *H pylori* as "chronic gastritis" is not in the observation, which is correct,

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but in interpreting the finding as pathological, and not as physiological. However, in at least one context PRIM also is pathological, since it is associated with increased risk for development of peptic ulceration,[27 28] and gastric adenocarcinoma and lymphoma.[10 29] Further, the highly interactive CagA-positive strains induce the strongest PRIM and confer the greatest risk of ulceration and carcinoma.[10 28 30] Thus, *H pylori* and the PRIM it induces are clearly associated with risk of disease, and even fatality. The decline in the incidence of these diseases in the 20th century is consistent with the decline in *H pylori* prevalence.

However, it now has become clear that there is an inverse association between *H pylori* and reflux oesophagitis (GORD), and its consequences, including Barrett's oesophagus, and oesophageal adenocarcinoma.[10] Although the gastric PRIM is a risk factor for the development of peptic ulceration and gastric adenocarcinoma, it is inversely associated with the development of these oesophageal diseases, and the more interactive CagA-positive strains are associated with the strongest inverse effects.[10] Thus, a paradigm exists of a host–microbial interaction that in some cases may promote pathological conditions, whereas in other cases may be protective from pathology. This is not a simple concept for most physicians, but in fact fits well with Rosebury's definition of an "amphibiont" as a microbe that could be pathogen or symbiont, depending on context.[31] The phenomenon of "amphibiosis" can be used to characterise our indigenous microbiota,[32] in which, for example, residential oral alpha-haemolytic streptococci protect against oral invaders, but also can cause endocarditis.

EFFECTS OF *H PYLORI* ON HUMAN PHYSIOLOGY

The stomach is an organ with multiple functions; *H pylori* and its induced PRIM affects at least three of these. First, the stomach secretes acid, which is under complex regulatory control, involving autonomic innervation, and the neurendocrine peptides, gastrin and somatostatin. It is evident that *H pylori* status affects this homeostasis.[9] Second, the stomach has adaptive immunological activity in terms of both T and B cell function.[33–37] The *H pylori*-positive and the *H pylori*-free stomachs are immunologically different, not only in terms of *H pylori*-specific responses,[36] but in more general responses as well,[37] and including a far greater population of regulatory T cells.[33–35] Third, the stomach produces leptin, and is the major site for production of ghrelin.[9] These neurendocrine peptides play important roles in mammalian energy homeostasis, and emerging evidence indicates that *H pylori* status is relevant to their regulation.[38 39]

It thus becomes clear that a generation or more of children in developed countries have been growing up without *H pylori* to guide or influence these physiological functions, and others not yet described (fig 1). It is predictable that such altered acid secretion, immunological activation, and neurendocrine regulation have a variety of consequences.

ASSOCIATION WITH ASTHMA AND ALLERGIC CONDITIONS?

In recent years, there has been a rise in the prevalence of asthma, hay fever (allergic rhinitis) and atopy (including eczema) in developed countries.[40] This change, which begins in early childhood, is present across many populations in the world, and is considerable in its extent. A perturbation of such magnitude must be environmentally caused, and some of the leading candidates include exposure to tobacco smoke, air pollution, allergens, exogenous infections and microbial substances in the environment, as well as obesity.[40–42]

In addition to these exogenous causes, an alternative hypothesis could relate to a change in our indigenous microbiota.[1] As such, it is plausible to consider *H pylori*, since its well-documented disappearance is extensive and involves developed country populations.[15–17] Further, the disappearance of *H pylori* has preceded the rise in asthma, but are they related?

Tables 1 and 2 summarise 12 recent cross-sectional and four case–control studies, respectively, in which the relationships of *H pylori* with asthma, atopy, allergic rhinitis, and/or eczema were examined.[43–57] In general, the cross-sectional studies, involving a variety of populations and somewhat differing definitions of atopy and asthma, show significant inverse relationships of these conditions with *H pylori*. The published case–control studies, in general much smaller in scale, do not show any significant direct or inverse relationships (table 2). However, a case–control study we conducted in New York showed an inverse relationship between *H pylori*, especially *cagA*+ strains, with asthma and atopy.[58]

To consider the findings of the cross-sectional analyses, we focus on two other studies that we conducted.[51 54] We first examined a large, publicly available database from the National Health and Nutrition Survey (NHANES) III, conducted between 1988 and 1994.[59] In the mid-1990s, *H pylori* and CagA serology were performed on stored specimens from more than 10 000 NHANES III subjects, with the laboratory workers and statisticians blinded to asthma or atopy status. In 2006, we were able to link 7663 records that contained information on both asthma and *H pylori* status.[51] For all subjects, there was an inverse association of ever having had asthma with having a *cagA*+ *H pylori* strain [OR (95% CI) = 0.79 (0.63 to 0.99)], with a stronger inverse association in those less than the median (43 years) age [0.63 (0.43 to 0.93)], and no association in the older persons. Similarly, the inverse association was strongest in those who had asthma onset before the age of 15 years [0.63 (0.43 to 0.93)], with no association with those with older-onset asthma. Highly similar trends were observed in relation to allergic rhinitis and allergy symptoms, with some inverse relationships also occuring in persons with *cagA*-negative *H pylori* strains. We also linked records for 2386 persons who had skin tests performed for pollens and moulds, and who had *H pylori* status ascertained.[51] For four of the six antigens tested, there were inverse associations in persons with *cagA*+ strains, especially those below the median age. Thus, we found inverse associations between *H pylori*, especially *cagA*+ strains, with asthma and related allergic disorders, especially involving younger individuals, and with early life disease onset.

Because of these findings, we sought independent assessment of the relationships. We then examined the subsequent survey, NHANES 1999–2000.[60] For that study, we found 7412 subjects who had data on asthma and related conditions as well as on *H pylori* status; no testing for *cagA* status had been performed. The median age in this study was 25, and because our prior results highlighted asthma with early age of onset, we focused on patients less than 20 years old. We found significant inverse associations of *H pylori* positivity with early onset of asthma and allergic rhinitis in children and teens under 20, as well as ever having had asthma and current asthma in children 3–13 years old.[54] *H pylori* also was inversely related to having recently had wheezing, allergic rhinitis, and dermatitis, eczema or rash. These two large, cross-sectional, independent studies show highly consistent results across asthma and related allergic disorders, and extend the prior studies which were more limited in sample size, age range of study

Table 1 Cross-sectional studies showing an association between *H pylori* and asthma, allergic rhinitis and atopic disease

Author, year (reference)	Location	Study population	Age (years)	*H pylori* measure	Definition of outcome	Major findings: Condition and OR (95% CI) in relation to *H pylori*+	
Matricardi, 2000 (43)	Caserta, Italy	1659 Italian male military cadets	17–24	IgG ELISA	Total IgE	Atopy For *H pylori, T gondii*, Hep A	
					Atopy: logRU>1.2	1 *v* 0	0.70 (0.52 to 0.94)*
					Non-atopic: logRU <0	2 or 3 *v* 0	0.37 (0.22 to 0.63)*
Kosunen, 2002 (44)	Vammala, Finland	326 and 319 healthy subjects in 1973 and 1994, respectively	15–54	IgA & IgG ELISA	Atopy: any IgE >0.35 IU/ml	Atopy	
						In 1973:	0.97 (0.46 to 2.05)
						In 1994:	0.20 (0.05 to 0.71)*
McCune, 2003 (45)	Bristol, UK	3244 healthy subjects	20–59	^{13}C-urea breath test	Current medications for the disorders: asthma (inhalers), allergic rhinitis (antihistamines), and eczema (topical corticosteroids)	Asthma:	0.78 (0.59 to 1.05)
						Allergic rhinitis:	0.60 (0.36 to 1.00)*
						Eczema:	0.29 (0.06 to 1.26)
						Any of the three:	0.70 (0.54 to 0.91)*
Linneberg, 2003 (46)	Denmark	1101 subjects	15–69	IgG ELISA	Self-reported allergic rhinitis	Atopy	0.78 (0.57 to 1.08)
					Specific IgE to 6 allergens	Allergic rhinitis:	0.74 (0.51 to 1.07)
					Atopy: any IgE >0.35 kU/l		
Jarvis, 2004 (47)	East Anglia, UK	907 randomly invited from 15,000 young adults	20–44	IgG ELISA	Self-reported symptoms in the prior year suggestive of hay fever and asthma	Hay fever/nasal allergies:	1.01 (0.70 to 1.52)
						Wheeze with no cold:	0.80 (0.51 to 1.24)
					Total IgE and specific IgE to house dust mite, cat, grass, *Cladosporium*, and birch	Allergy to grass:	0.65 (0.43 to 0.99)*
						Allergy to >1 allergens:	1.13 (0.81 to 1.59)
Radon, 2004 (48)	Northern Germany	321 with blood samples from 930 randomly selected from 3112 inhabitants	18–44	IgG ELISA, IgG CagA	Specific IgE against a panel of aeroallergens	Atopy:	0.70 (0.39 to 1.28)
					Atopy: any IgE>0.70 kU/l		
von Hertzen, 2006 (49)	Eastern Finland, Western Russia	Healthy adults; 790 from Finland, 387 from Russia	25–54	IgG ELISA	Skin prick testing with a panel of 11 common airborne allergens	Atopy, in Russians:	0.55, p<0.01*†
					Atopy: any wheal diameter ⩾3 mm	In Finns:	0.72, p = 0.53†
Janson, 2007 (50)	Iceland, Sweden, Estonia	1249 healthy adults	Mean 42	IgG ELISA	Detection of specific Atopy:	Atopy:	0.57 (0.43 to 0.77)*
					any IgE >0.35 kU/l	For IgG antibodies to ⩽3 specified infectious Atopy:	0.70 (0.52 to 0.94)*
					Self-reported hay fever, asthma	Allergic asthma:	0.55 (0.34 to 0.89)*
					in the prior year	Allergic rhinitis:	0.59 (0.42 to 0.83)*
Chen, 2007 (51)	USA	7663 adults	20–90; Mean, 43	IgG ELISA, IgG CagA	Self-reported asthma and hay fever (current and lifetime)	OR in relation to CagA+, Ever asthma:	0.79 (0.63 to 0.99)*
					Skin sensitisation tests	Onset age ⩽15:	0.63 (0.43 to 0.93)*
Herbarth, 2007 (52)	Germany	2487 children	Mean 6	^{13}C-urea breath test	Lifetime physician-diagnosed eczema	Eczema:	0.37, p<0.01*†
Shiotani, 2007 (53)	Japan	777 university students	Mean 19	IgG ELISA	Self-reported atopic dermatitis, bronchial asthma, allergic rhinoconjunctivitis, urticaria	Any allergic disease:	0.60 (0.40 to 0.90)*
Chen, 2007 (54)	USA	7412 adults	3–85, Mean 25	IgG ELISA	Self-reported asthma and hay fever (current and lifetime)	Ever asthma: (in ⩽19 years)	0.65 (0.45 to 1.06)
						Current asthma: (in ⩽13 years)	0.41 (0.24 to 0.69)*
						Early childhood: (onset <5 years)	0.58 (0.38 to 0.88)*

*p<0.05.
†CI was not estimated because information on covariates is not available; the study reported a p-value adjusted for covariates only.

populations, as well as data on potential confounders, *H pylori* strains, and age of onset of asthma (table 1).

BIOLOGICAL PLAUSIBILITY FOR *H PYLORI* TO PLAY A PROTECTIVE ROLE AGAINST ASTHMA

H pylori status could be causally related to asthma and its related disorders, with colonised persons having a partial protection. Considering the Bradford Hill criteria[61] provides evidence that supports such a causal role.

First, the secular trend is consistent and reverse causation in not likely; *H pylori* is disappearing while asthma incidence is rising. Importantly, the decline in *H pylori* acquisition, beginning early in the 20th century, precedes the increase in asthma. However, all of the epidemiological studies to date are cross-sectional or case–control studies, and not prospective. Nevertheless, it is not likely that asthma and related disorders could themselves be leading to the disappearance of *H pylori*. Once acquired early in life, if not treated with antibiotics, *H pylori* persists at least for decades, if not for life. The cross-sectional studies could measure an effect of asthma, or of its treatment. For example, if asthmatics receive more antibiotics than non-asthmatics, *H pylori* prevalence could be reduced. However, the specificity of the inverse association with early life asthma and not with long-standing asthma seen in adults is one argument against that proposition.

Second, a dose–response relationship between exposure and disease is present. Studies of differences among *H pylori* strains show the strongest effects for *cagA*+ strains, in terms of risk of disease (ulcers, gastric cancer) or protection from disease (GORD and oesophageal adenocarcinoma). A similar dose–response to that related to GORD is present with asthma, with *cagA*+ strains having the strongest inverse association.[54 58]

Third, as shown in table 1, a variety of cross-sectional studies show protective effects, suggesting consistency of the data. The increasing number of these studies, especially our two large, independent, and population-based studies, point toward a correct association. Nevertheless, that not all studies, especially the case–control studies (table 2), show this inverse association could indicate that there is population-based specificity for the observation, and/or differences in study design.

Fourth, is the role of specificity; asthma is considered as predominantly allergic or not. The strong inverse associations with *H pylori* are present for asthma and other allergic disorders consistent with the allergic (atopic) spectrum. In addition, the inverse association with *H pylori* appears stronger for childhood-onset asthma. There may be aetiological differences between childhood-onset and adulthood-onset asthma. Childhood asthma often remits during adolescence, although many of these patients in remission have relapses during young adulthood.[62] Consistently, the case–control studies of *H pylori* and current asthma in adults did not find any association (table 2). The effect of *H pylori* may be less important in adult-onset asthma, since the risk factors may be much more heterogeneous than in childhood asthma. In addition, asthma in adults may be new onset, persistent from childhood, or exacerbated from childhood asthma. Although commonly associated with atopy, adult asthma is more complex and onset may be complicated by environmental exposures (e.g. tobacco, occupation).[63 64] Finally, the misclassification of current status of asthma and *H pylori* could be more serious in adults. Since the misclassifications of asthma and *H pylori* status do not depend on one another, it is non-differential, which would lead to a bias toward the null.

Fifth, the inverse association is coherent with our knowledge, and there is no evidence of plausible competing theories or rival hypotheses. One possibility is that *H pylori* status, while related to asthma risk, is merely a marker for other phenomena. For example, early life antibiotic use[65 66] that eliminates *H pylori* carriage also could eliminate one or more other microbes that actually are the protective agents. There are insufficient data at present to rule out this possibility. Several studies that have evaluated multiple infections suggest their additive effect in the aetiology of asthma[43 50] (table 1). In addition, the inverse association between *H pylori* and asthma is independent of indicators of socioeconomic status, age, gender, ethnic background, smoking status and hepatitis A infection.[51] An independent phenomenon that makes asthma more likely and *H pylori* carriage less likely could be underlying the inverse association. Such a phenomenon could be due to enhancement of Th-2 immunity induced by another microbe, for example, and a consequent effect on *H pylori* status could provide a maker of risk.

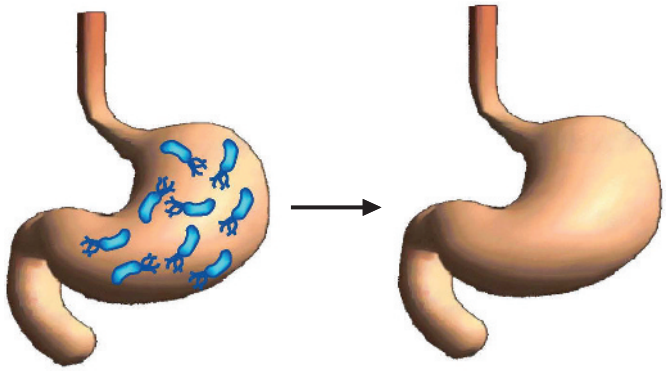
Sixth, mechanisms exist (see below) that could explain a protective effect. In total, there is considerable biological plausibility for a protective role of *H pylori* (especially *cagA*+) strains toward asthma and related disorders.

MECHANISMS BY WHICH GASTRIC *H PYLORI* COLONISATION MIGHT AFFECT ASTHMA RISK

In the simplest statement, it is increasingly clear that the gastric physiology of the *H pylori*-positive and negative subjects differs.[9 20 67] Several non-exclusive mechanisms could be playing a role.

Table 2 Case–control studies showing an association between *H pylori* and asthma, allergic rhinitis and atopic disease

Author, year (reference)	Location	Study population	Age (years)	*H pylori* measure	Definition of outcome	Major findings: Condition and OR (95% CI) in relation to *H pylori*+	
Matricardi, 2000 (43)	Caserta, Italy	240 atopic cases and 240 non-atopic controls	17–24	IgG ELISA	Total IgE Atopy: logRU >1.2 Non-atopic: logRU<0	Atopy:	0.76 (0.47 to 1.24)
Bodner, 2000 (55)	Grampion, Scotland	97 cases and 208 controls	39–45	IgG ELISA	Skin & specific IgE tests Atopy: weal ⩾3 mm, or any IgE >0.35 IU/ml Self-reported adult-onset wheeze and asthma	Wheeze: Wheeze and asthma: Atopy:	1.20 (0.70 to 2.20) 0.50 (0.20 to 1.50) 0.90 (0.60 to 1.60)
Tseng, 2000 (56)	Hong Kong	90 cases with stable asthma and 97 controls	Mean 43	IgG ELISA	Current asthma diagnosed by ATS guidelines	Asthma:	1.55 (0.83 to 2.90)
Jun, 2005 (57)	Japan	46 cases with asthma, and 48 healthy controls	Mean 52	IgG ELISA IgG CagA	Current asthma diagnosed by ATS guidelines	Compared with healthy controls, Asthma: For CagA+, Asthma:	1.10 (0.45 to 2.69) 1.20 (0.39 to 3.69)



Criterion		References
Somatostatin production	↑	74
Gastrin release	↓	75
Gastric acidity	↑	76
Leptin production	?	73
Ghrelin production	↑	38
T-regulatory cell populations	↓	33-36

Figure 1 Changes in gastric physiology as the ancient (*H pylori*-colonised) stomach is becoming the post-modern (*H pylori*-free) stomach. Representative references are cited.

First, if *H pylori* is actually protecting against GORD,[10] it also could protect against asthma, since some proportion of asthma is due to GORD;[68] this component may actually be underestimated.[69] However, this mechanism is unlikely to be sufficient to explain protective *H pylori* effects in hay fever and atopic dermatitis.

Second, the constellation of asthma, atopy, hay fever and skin sensitisation suggests immunological mediation. *H pylori*-positive persons have a gastric population of immunocytes, including regulatory T cells,[33–36] that is largely or completely absent from *H pylori*-negative subjects. Such cells may have systemic immunomodulatory activities. Recent studies indicate an interaction of *H pylori* colonisation with *Mycobacterium tuberculosis*, with colonisation associated with the maintenance of tuberculosis latency,[70] again pointing to a global immunomodulatory role.

A third mechanism may relate to the effects of *H pylori*-induced inflammation on gastric hormonal levels.[9] Both leptin and gastrin have immunomodulatory activities as well as intermediary effects on energy homeostasis.[71 72] There is increasing evidence that *H pylori* gastric colonisation affects both ghrelin and leptin production[38 73] which thus would affect the immunoregulatory environment.

Finally, the effects of *H pylori* on the autonomic nervous system might play a role. Individual differences in the host–microbial interaction could account for differential risk and disease expression. Prospective studies that evaluate the influence of *H pylori* on both indicators of causal intermediates and asthma risk will help delineate the mechanisms.

CONCLUSIONS

For probably the first time in human history, generations of children are growing without *H pylori* in their stomachs, guiding the development of their immunological capabilities, their hormonal regulation of energy homeostasis, and their regulation of gastric acidity (fig 1). The loss of this ancient, dominant and persistent member of the normal biota of humans would be predicted to have consequences, and now there is much information about the beneficial and deleterious aspects of this change on gastrointestinal tract health and disease.[1 10 77 78] However, increasing evidence is pointing to extra-intestinal manifestations of the disappearance of *H pylori*, including disorders of energy homeostasis[38 39] and asthma. An inverse association of *H pylori* and childhood asthma, allergic rhinitis and atopy is becoming increasingly obvious. Although this may represent an epiphenomenon as part of a more general change in human microecology,[1] there is substantial biological plausibility for a role of the disappearance of *H pylori* and the rise of these allergic disorders of children. Nevertheless, if *H pylori*, and especially *cagA* status, only is a marker for asthma risk, it could become useful for clinical and epidemiological studies. These questions are of sufficient importance that confirmatory and prospective studies in different populations should be carried out.

Clearly, the interactions of *H pylori* are complex, somewhat host-specific, and certainly incompletely understood. Ten years ago, one of us predicted that doctors of the future will have the tools to perform relevant phenotyping and genotyping of young children and then take the appropriate stocks of *H pylori* from their pharmacy and deliberately colonise that child with that strain (or combination of strains) most likely to optimise their life-long health.[79] The continuing beneficial associations of *H pylori* with reduction of risk for oesophageal diseases (including malignancy), now with asthma and atopy, and possibly with obesity and diabetes,[9 38 39] should be considered in *H pylori* treatment and intervention plans, and move that earlier prediction closer to reality.

It is possible that for most individuals, *H pylori* is beneficial in childhood and more deleterious later in life. Within such a paradigm, a public health framework for *H pylori* introduction and eradication can be envisioned.

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Editor's quiz: GI snapshot

Robin Spiller, editor

An infrequent cause of acute left lower quadrant abdominal pain

CLINICAL PRESENTATION

A 65-year-old male patient referred with acute abdominal pain in the left lower quadrant and a low grade fever (38°C) was admitted to the surgical emergency department of our institution. He was haemodynamically stable. His bowel movements were completely normal. Physical examination demonstrated localised tenderness in the left iliac fossa, but there was no peritonism. Serological studies revealed no abnormality apart from a white blood cell (WBC) count of 12×10^9/l and C-reactive protein (CRP; 3.0 mg/l). As a first step, abdominal and bowel ultrasound (US) without oral contrast agent was performed. A relevant US finding was the appearance of a well-delineated echogenic mass with a peripheral hypoechoic rim in the left flank; this lesion appeared small, oval and non-compressible, located anteromedial to the left colon with perienteric hypertrophied mesenteric adipose tissue, and absence of vascular flow on colour Doppler sonography (fig 1). Subsequent CT examination allowed the correct diagnosis to be made (fig 2).

QUESTIONS

What is the differential diagnosis? What radiological abnormalities are seen and what is the most likely diagnosis?
See page 622 for answers.

This case is submitted by:

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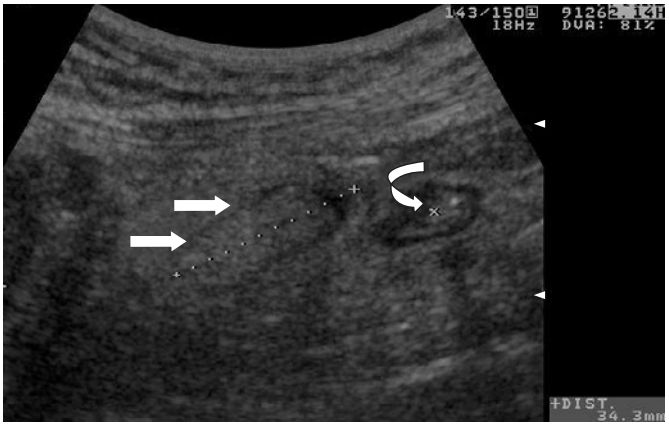

Figure 1 Ultrasound appearance of a non-compressible, oval, well-delineated echogenic mass with a peripheral hypoechoic rim (double arrows), located anteromedial to the left colon (curved arrow) with perienteric mesenteric fat proliferation visualised with a convex probe. Informed consent was obtained for publication of this figure.

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Patient consent: Informed consent was obtained for publication of the person's details in this report.

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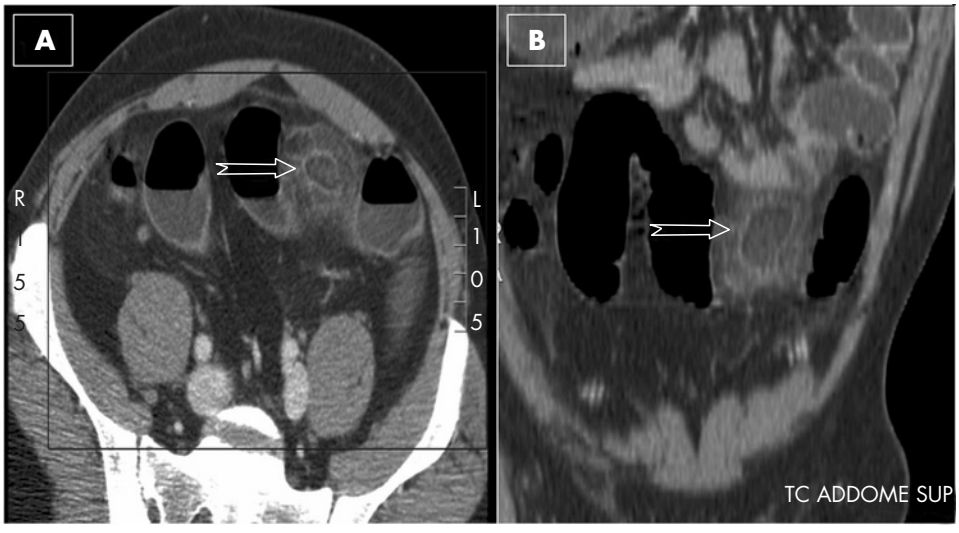

Figure 2 Axial (A) and reconstructed coronal image (B) from a contrast-enhanced CT enteroclysis showing (arrow) a fat density lesion that has a hyperattenuating rim with surrounding inflammation abutting the sigmoid colon–descending colon junction. Informed consent was obtained for publication of this figure.