INTRODUCTION

The principal cause of death in the Western world is cardiovascular diseases, the majority of which are coronary heart disease or cerebrovascular disease with a pathogenic mechanism of atherothrombosis.

In recent years, a theory of «response to the lesion» has been proposed as the inductor mechanism for atherothrombosis; basically this theory states that inflammatory and immunological processes triggered by viral or bacterial infections are the underlying cause of the atherosclerotic process.

2-4 In fact, there is scientific evidence supports this theory with regard to Chlamydia pneumoniae, Chlamydia TWAR, and cytomegalovirus such as, for example, the finding on PCR or immunofluorescence of Chlamydia pneumoniae and Chlamydia TWAR in atheromatous plaques by PCR, immunocytochemistry, and electron microscope.

A relationship has been observed between dental infections and coronary cardiopathy, as has a co-


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Helicobacter Pylori: ¿un nuevo factor de riesgo cardiovascular?

En los últimos años se ha propuesto que podría existir una asociación entre el proceso aterotrombótico y la infección por ciertos microorganismos, entre éstos Helicobacter pylori, agente etiopatógeno de enfermedad gastroduodenal. Esto se ha basado en: a) la mayor prevalencia de infección por Helicobacter pylori detectada en pacientes con cardiopatía coronaria, infarto agudo del miocardio o isquemia cerebrovascular; b) la asociación entre la seroprevalencia de Helicobacter pylori y factores de riesgo cardiovascular, como concentraciones de colesterol, triglicéridos y fibrinógeno plasmático; c) la correlación entre la seroprevalencia de Helicobacter pylori y marcadores de procesos inflamatorios asociados con un mayor riesgo de cardiopatía coronaria o con un peor pronóstico de ella, como la proteína C reactiva, y d) estudios controvertidos que han utilizado PCR sobre la presencia de Helicobacter pylori en placas ateromatosas. El análisis de la evidencia científica existente hasta el momento sugiere que la infección por Helicobacter pylori contribuiría, de forma indirecta al desarrollo y la severidad de la enfermedad cardiovascular.

Regression of low-grade MALT lymphoma. In fact, it has

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11-13 and cerebrovascular disease. 14

Helicobacter pylori

Helicobacter pylori is a gram-negative micro-
aerophilic bacillus; it requires an atmosphere of 5% O2
and 5% to 10% CO2. Its morphology is heterogeneous in
that it can take a helicoidal, spiral, or curved shape,
with 2 to 6 flagella; nevertheless, in aged cultures it
tends to present in coccoid form. It measures 0.5 mm
to 1.0 mm in diameter by 2.5 mm to 5.0 mm long. It is
characterized by the production of a urease that, via
the production of ammonia, creates a microenviron-
ment with a pH greater than that of gastric mucous,
allowing it to survive. Culturing Helicobacter pylori is
somewhat difficult as it requires a longer incubation
period than the majority of bacteria (5 days instead of
24 hours), and enriched culture mediums must be
used. 15-17

H. pylori is a bacterium that occurs worldwide, with
a prevalence that varies according to the socioeconomic
conditions of the population being studied. It is
considered the etiopathogenic agent of both benign
and malignant gastro duodenal disease, based principally
on the fact that eradication of the bacteria is as-
sociated with the scarring of peptic ulcers, disappear-
ance of gastritis, decrease in recidive ulcers, improvement
in dyspeptic symptomatology, and regression of low-grade MALT lymphoma. In fact, it has
been classified as a type 1 carcinogen by the World
Health Organization (WHO). 18-21 H. pylori has also
been isolated in bile and biliary vessicules. 22 In addi-
tion, as mentioned above, in recent years it has been
proposed that H. pylori has a role in the atherothrom-
botic process; the evidence for this is analyzed below.

Association between H. pylori infection
and cardiovascular disease

The study of the association of H. pylori with car-
diovascular disease (coronary cardiopathy and ische-
mic cerebrovascular disease) has been undertaken by
different investigators:

Case-control epidemiological studies

These reveal, by the detection of antibodies, a grea-
ter prevalence of infection by H. pylori in patients
with coronary cardiopathy 12 and in patients with cere-
brovascular ischemia; nevertheless, there are studies
with the opposite results, such as the investigation car-
rried out by Regnström et al. 23 A study by Pasceri et
al 13 revealed a greater prevalence of infection by
strains of H. pylori cagA+ in patients with coronary

cardiopathy vs a control group, while the prevalence
of infection by strains of cagA− did not reveal diffe-
rences between the patients and the control group.
This would explain the contradictory results obtained
by other authors.

Studies of the correlation between the
seroprevalence of H. pylori and cardiovascular
risk factors

There are factors that increase the risk of atheroth-
rombosis, such as an elevation of plasma fibrinogen
and coagulation factor VII, an increase in reactive protein C synthesis, hypercholesterolemia, and hypertriglyceri-
demia. There are also with contradictory results in
this respect. Niemëla et al. 24 found significant diffe-
rences between triglyceride and HDL values among
seropositive and seronegative subjects vs H. pylori.
Rengström et al 23 did not observe significant differen-
ces in plasma fibrinogen, cholesterol, or triglyceride
levels among seropositive and seronegative patients.
Nevertheless, Patel et al 10 found a significant increase
in fibrinogen in seropositive patients, but did not find
differences in the plasma cholesterol or triglyceride
values, parameters that are elevated in some gram-ne-
gative infections. 7 Blood coagulation factor VII has
also been studied, but no significant differences have
been found among patients seropositive for H. pylori
with regard to those who were seronegative. 25,26

Studies of the correlation of the seroprevalence
of H. pylori and markers of inflammatory
processes

There is growing evidence that inflammation plays
an etiopathogenic role in atherosclerosis and that some
markers of inflammation are associated with a greater
risk of coronary cardiopathy or a worse prognosis,
such as reactive protein C, 27 white blood cell count, 28
plasma fibrinogen, 25,28 or the presence of heat shock
proteins (hsp). 29 Upon comparison of patients sero-
positive for H. pylori with seronegative patients, Patel et
al 10,28 found a significant elevation in the white blood
cell count; Birnie et al detected an hsp increase
60/65,30 and the elevation of reactive protein C has
been associated with a worse prognosis in patients
with unstable angina or recent myocardial infarction. 27
There have also been studies of the association of co-
ronary cardiopathy with TNF-α values, another mar-
ker for inflammation, but statistically significant diffe-
rences have not been detected. 23

Presence of H. pylori in atheromatous plaques

Studies have been performed using the polymerase
chain reaction (PCR) to ADN detector of H. pylori in
the tissues analyzed. These studies, in addition to
being few in number (only 2 groups of investigators have presented results) are contradictory. Cunningham et al. found the presence of *H. pylori* in atheromatous plaques (First European Congress of Chemotherapy), while Blasi et al., in a study carried out on surgical samples of aortic aneurysms, could not identify the presence of *H. pylori* in any of the 51 samples, in spite of the fact that 47 of the patients were seropositive for the bacteria. On the other hand, it is known that bacteria that resists serum, or the lytic activity of its serum complement, survive longer in the bloodstream, allowing it to colonize other areas of the organism. In this respect, *H. pylori* is susceptible to the bactericide activity of human serum (principally due to the activation of the alternate pathway of the complement), and there is variation in the union of the different strains to C3, making its survival in the bloodstream unlikely.32

**Pathogenic mechanisms**

Based on the existing scientific evidence, various mechanisms have been proposed to explain the association of infection by *H. pylori* with cardiovascular disease.

**Inflammatory response**

A low-grade chronic inflammatory response is produced, provoking the atherogenic process via changes in some cardiovascular risk factors, such as coagulation and lipid factors, with liberation of fibrinogen, reactive protein C, TNF-α, and interleukine 6 (IL-6), in addition to an increase in the white blood cell count, which would induce a prothrombotic state.33-35 In adults, *H. pylori* induces an active chronic inflammatory process with the presence of neutrophils, T lymphocytes, B lymphocytes, and plasma cells;36 in other words, it produces a response that is as much cellular as it is humeral. The specific cellular response is characterized by being mounted by T helper 1 lymphocytes,37 causing an increase in the liberation of cytokines, especially IL-1, IL-6, IL-8, TNF-α and interferon ɣ.26 The capability of inducing cytokines differs among the strains of *H. pylori*, with the cagA+ strains being observed to produce the most intense liberation and a greater variety of cytokines.38 On the other hand, it has also been observed that soluble extracts of *H. pylori* promote plaque aggregation in the microcirculation of gastric mucous.39

**Modification of blood lipids**

Infection by *H. pylori* induces an elevation of cholesterol and triglyceride levels with a decrease in HDL cholesterol,24 contributing to the development of dyslipidemia, a known cardiovascular risk factor.

**Formation of oxidants**

Some authors propose that the formation of oxidants is also important, as it has been observed that antioxidants decrease in patients with *H. pylori*, which may cause lipid peroxidation and thus atherogenesis, as oxidation of low density lipoproteins (LDL) is 1 of the fundamental steps in the atherogenic process.7

**Crossed reactivity with anti heat shock protein (hsp) antibodies**

Another theory is that of anti-hsp antibodies with crossed reactivity, as *H. pylori* produces hsp of 60 kDa with a high degree of sequence homology with the human 60 kDa hsp expressed by the endothelium.30

**Hyperhomocysteinemia**

Hyperhomocysteinemia is a new cardiovascular risk factor, as it has been observed that an elevation in homocysteine values is associated with an increase in cardiovascular risk.40,41 In this respect, in patients with chronic gastritis (generally caused by *H. pylori* infection) it can produce a decrease in the absorption of vitamin B12 and folate, causing secondary hyperhomocysteinemia.42

**Socioeconomic level**

There are studies that demonstrate a greater prevalence of coronary cardiopathy and cardiovascular events in people at lower socioeconomic levels.43 However, it has been proposed that infection by *H. pylori* would only be a marker of socioeconomic level, as it is lower in infected patients than in non-infected patients, similar to what is observed in a comparison of cardiopaths vs non-cardiopaths.44

In summary, an etiopathogenic relationship between various chronic diseases and microorganism infections has been found, whether it occurs via direct pathogenic mechanisms or the immune response of the host against the microorganism. *H. pylori*, give its widespread distribution in the world population and the high incidence of gastro duodenal disease, is 1 of the most important microorganisms associated with illness that were previously considered to have a non-infectious etiology. With respect to the association of this bacterium with coronary cardiopathy, the existing scientific evidence suggests that infection by *H. pylori* contributes to the genesis, progression, and severity of cardiovascular disease, although it is unlikely that it triggers cardiovascular disease on its own. Ultimately, it is the balance between the factors that favor cardiovascular disease and the host’s protective factors that will determine the course of each individual, but perhaps in the future we should carry out treatment to eradicate...
H. pylori in those patients at greater cardiovascular risk, as we now do with weight reduction, a decrease in the consumption of fat, and smoking cessation, among others.

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REFERENCES


