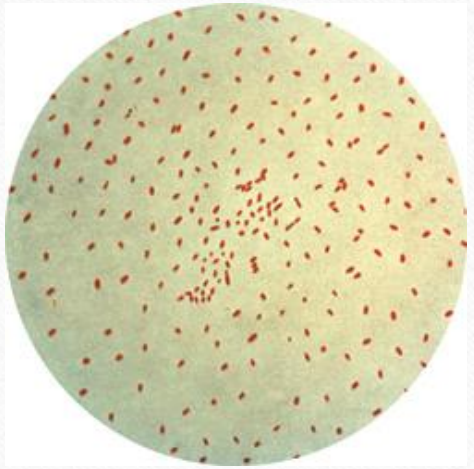
Bordetella



- Bordetella is an extremely small, strictly aerobic, gram negative very thin ovoid or rod-shaped bacillus.
- Three species responsible for human disease;
- *Bordetella pertusis* : the agent responsible for pertussis or whooping cough

Bordetella parapertussis: responsible for a milder form of pertussis

Bordetella bronchiseptica: responsible for respiratory disease in dogs, swine, lab animals and occasionally, pertussis-like symptoms in humans.

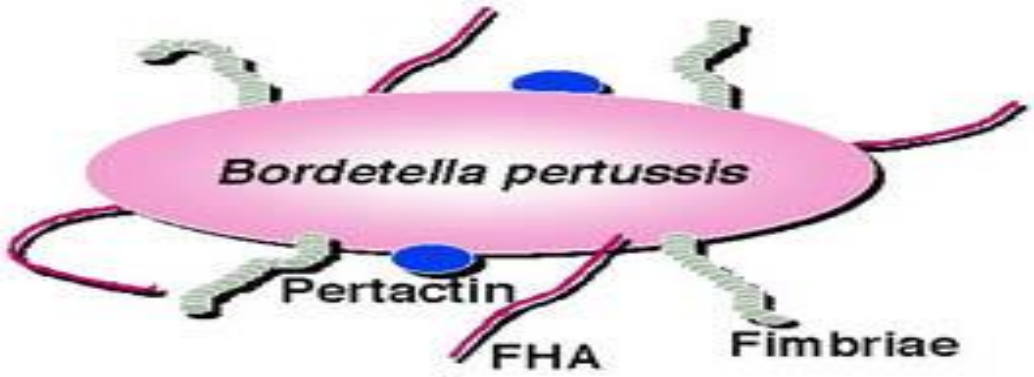
- *Bordetella* species have simple nutritional requirements but *B. pertussis* require media supplemented with charcoal, starch, blood, or albumin. (because of their toxic substances that must be absorbed by the supplemented material of medium)
- The organisms are non-motile, oxidise amino acids but do not ferment carbohydrates.
- It grows in 3 days for first isolation.

- human is only natural host ; obligate parasites of human
- Disease is highly communicable (highly infectious)
- Person-to-person spread via inhalation of infectious aerosols
- Children under one year at highest risk , but prevalence increasing in older children and adults

Virulence Factors Associated with Bordetella pertussis

Virulence Factor	Biologic Effect
Adhesins	
Filamentous hemagglutinin	Binds to sulfated glycolipids on ciliated cell membranes; binds to CR3 on surface of polymorphonuclear leukocytes and initiates phagocytosis.
Pertussis toxin	S2 subunit binds to glycolipid on surface of ciliated respiratory cells; S3 subunit binds to ganglioside on surface of phagocytic cells.
Pili	Binds to mammalian cells. Role in disease is unknown.
Pertactin	Binds to mammalian cells. Role in disease is unknown.
Toxins	
Pertussis toxin	S1 subunit adenosine diphosphate–ribosylates host cell G protein, causing deregulation of host cell adenylate cyclase; toxin inhibits phagocytic killing and monocyte migration.
Adenylate cyclase/hemolysin toxin	Increases intracellular level of adenylate cyclase and inhibits phagocytic killing and monocyte migration.
Dermonecrotic toxin	Causes dose-dependent skin lesions or fatal reactions in experimental animal model. Role in disease is unknown.
Tracheal cytotoxin	A peptidoglycan fragment that kills ciliated respiratory cells and stimulates the release of interleukin-1 (fever).
Lipopolysaccharide	Two distinct lipopolysaccharide molecules with either lipid A or lipid X; activates alternate complement pathway and stimulates cytokine release. Role in disease is unknown.

Pathogenesis of *Bordetella pertussis*



Adherence to ciliated respiratory epithelial cells, and multiplication

Systemic intoxication
- Pertussis toxin
- Adenylate cyclase toxin
- Tracheal cytotoxin
- Dermonecrotic toxin

Local mucosal damage; paroxysmal cough

Entry

Persistence ?

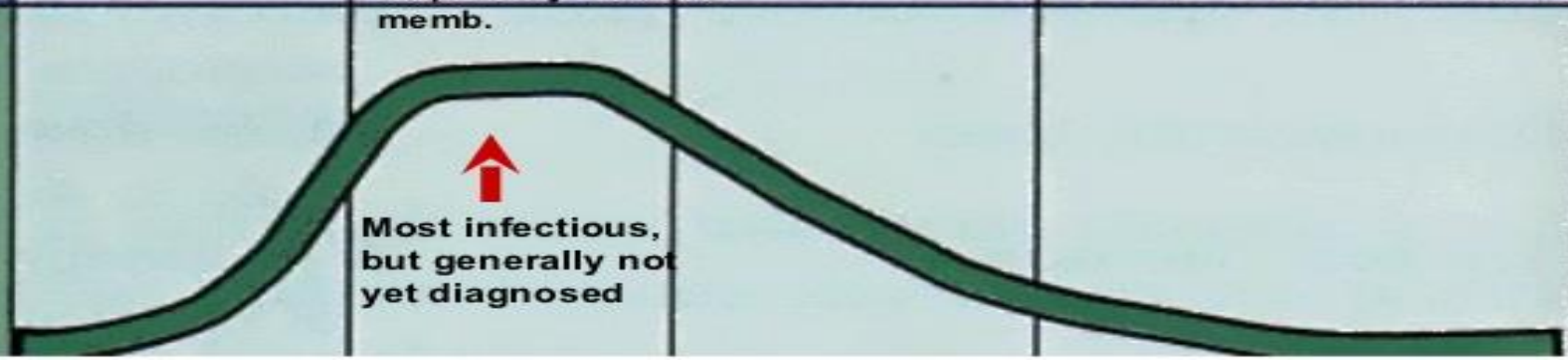
Transmission

Interaction with immune effector cells

Entry, survival within macrophages

- Pertussis is primarily a toxin-mediated disease. The bacteria attach to the respiratory cilia, produce toxins that paralyze the cilia, and cause inflammation of the respiratory tract, which interferes with the clearing of pulmonary secretions. Pertussis antigens appear to allow the organism to evade host defenses. Despite remarkable lymphocytosis, chemotaxis is impaired.

Clinical Progression of Pertussis

	Incubation	Catarrhal	Paroxysmal	Convalescent
Duration	7–10 days	1–2 weeks	2–4 weeks	3–4 weeks (or longer)
Symptoms	None	Rhinorrhea, malaise, fever, sneezing, anorexia, Inflammation of respiratory mucosal memb.	Repetitive cough with whoops, vomiting, leukocytosis	Diminished paroxysmal cough, development of secondary complications (pneumonia, seizures, encephalopathy) or death
Bacterial culture				

https://www.slideshare.net/MMASSY/bordetella-class-notes

Diagnosis

- Fastidious- slow growing
- Requires supplementary substances in media
- Isolated on modified Bordet-Gengou agar (glycerin, potato, blood)+ penicillin to inhibit growth of other organisms
- After isolation confirmation with PCR
- Direct Fluorescent antibody test (low sensitivity)

Differential Characteristics of Bordetella Species

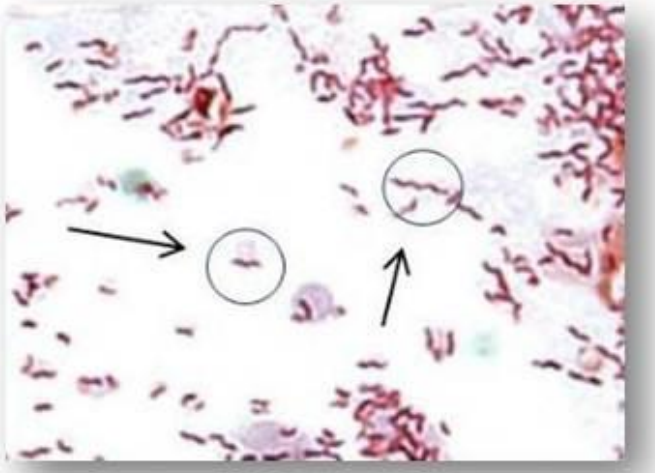
Characteristics	*B. pertussis*	*B. parapertussis*	*B. bronchiseptica*
Oxidase	+	−	+
Urease	−	+	+
Motility	−	−	+
Growth on			
Sheep blood agar	−	+	+
MacConkey agar	−	+/−	+

Prevention- Control and Treatment

- Active immunization is quite effective
- Inactivated whole bacterial cells and toxoid are prepared in formalin for **DPT vaccine**
- **Subunit (acellular) vaccine** also available (DTaP)
- In most developing countries, the whole cell pertussis vaccine is still in use whereas in the developed country the acellular pertussis vaccine is widely used.
- Treatment with erythromycin

Campylobacter

- Small, microaerophilic gram negative rods, helical (spiral or curved) morphology
- Tendency to form coccoid & elongated forms on prolonged culture or when exposed to O_2
- Motile with polar flagellum
- Unable to oxidize or ferment carbohydrates.



- Characteristics that facilitate penetration and colonization of mucosal environments.
- Campylobacter could be isolated from the normal flora of farm animals and fowl and caused periodically diarrheal diseases.

- They are often called “thermophilic campylobacter because they grow best at 37-42 ^{o}C (for the selective isolation in stool specimens)
- Most of the early illnesses attributed to Campylobacter was caused by *C. fetus*.
- The enteritis of Campylobacter, caused by *C. jejuni* and *C. coli*,

- Today, enteritis caused by *C. jejuni /coli* is as common as that caused by Salmonella and Shigella combined.
- Infections acquired by ingestion of contaminated food, unpasteurized milk or contaminated water.

- Campylobacters were first isolated in 1906 from aborting sheep in the UK. They were later called as *C. fetus*.
- The ***C. jejuni*** and ***C. coli*** commonly cause **enteritis** in man were discovered in the late of 1970s.
- Several other species, such as ***C. upsaliensis***, ***C. lari*** are occasionally associated with **diarrhea**, mainly in children in developing countries.

- ***C. fetus*** is a major cause of **abortion** in sheep and cattle worldwide. It is a rare cause of human fetal infection and abortion and occasionally causes **bacteremia in patients** with immune deficiency.
- *C. fetus* is associated with **septicemia** and is disseminated to multiple organs.

- *C. jejuni* gastrointestinal disease characteristically produces **histologic damage** to the mucosal surface of the jejunum, ileum and colon.
- **Acute enteritis** with diarrhea, malaise, fever and abdominal pain (*C. jejuni, C. coli, C. upsaliensis*)
- Most infections self limited but can persist for a week or more

Campylobacter Species Associated with Human Disease

Species	Reservoir Host	Human Disease	Frequency
C. jejuni	Poultry, pigs, bulls, dogs, cats, birds, minks, rabbits, insects	Gastroenteritis, septicemia, meningitis, spontaneous abortion, proctitis, Guillain-Barré syndrome	Common
C. jejuni subsp. *doylei*	Humans	Gastroenteritis, gastritis, septicemia	Uncommon
C. coli	Pigs, poultry, bulls, sheep, birds	Gastroenteritis, septicemia, gastroenteritis, spontaneous abortion, meningitis	Uncommon
C. upsaliensis	Dogs, cats	Gastroenteritis, septicemia, abscesses	Uncommon
C. fetus	Cattle, sheep	Septicemia, gastroenteritis, spontaneous abortion, meningitis	Uncommon
C. fetus subsp. *venerealis*	Cattle	Septicemia	Uncommon
C. hyointestinalis	Pigs, cattle, hamsters, deer	Gastroenteritis	Rare
C. concisus	Humans	Periodontal disease, gastroenteritis	Rare
C. sputorum subsp. *sputorum*	Humans, cattle, pigs	Abscesses, gastroenteritis	Rare
C. curvus	Humans	Periodontal disease, gastroenteritis	Rare
C. rectus	Humans	Periodontal disease	Rare
C. showae	Humans	Periodontal disease	Rare
C. lari	Poultry, birds, dogs, cats, monkeys, horses, seals	Gastroenteritis, septicemia	Rare

Virulence factors

Cellular components:

- Endotoxin
- Flagellum
- Motility
- Adhesins
- Invasins

- Guillain-Barré syndrome (GBS) is associated with *C. jejuni* serogroup O19
- S-layer protein "microcapsule" in *C. fetus*:
- **Extracellular components:** Enterotoxins and Cytopathic toxin

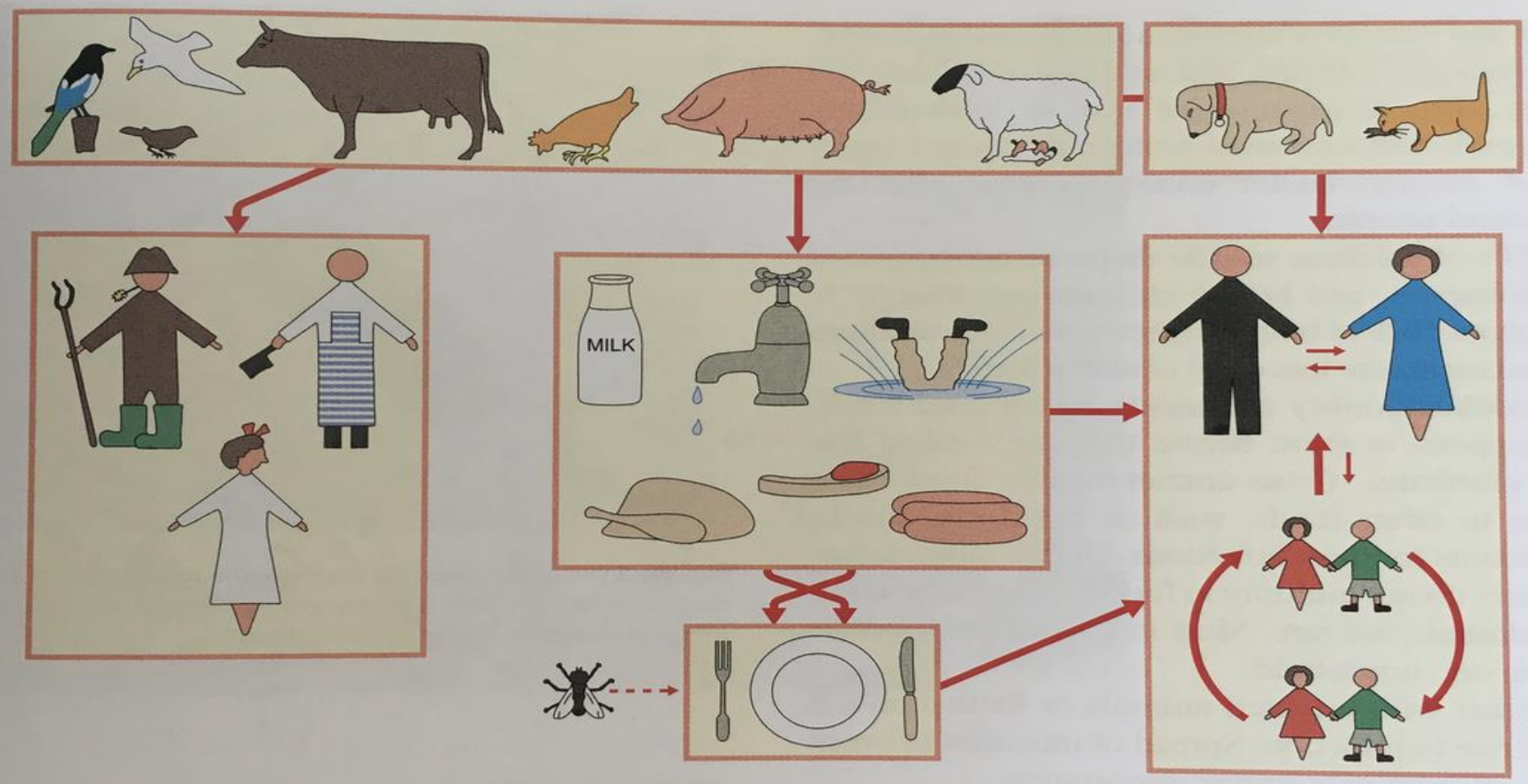


Fig. 29.4 Sources and transmission of *C. jejuni* and *C. coli*. Top boxes: animal reservoirs and sources of infection (the sheep has just given birth to a dead campylobacter-infected lamb). Left-hand box: transmission by direct occupational contact (farmer, butcher, poultry processor). Right-hand box: transmission by direct domestic contact (puppy or kitten with campylobacter diarrhoea; intra-familial spread, mainly from children). Central box: indirect transmission through consumption of untreated water, raw milk, raw or undercooked meat and poultry, food cross-contaminated from raw meats and poultry; possible transmission from flies. (From document VPH/CDD/FOS/84.1 by permission of the World Health Organization, which retains the copyright.)

Diagnosis

- Microscopy
- Culture: isolation from stool; Charcoal based blood free agar containing cefaperazone or other selective antimicrobial agents to inhibit competing fecal flora.
- Serology (ELISA)

Characteristics	*C. jejuni*	*C. coli*	*C. upsaliensis*	*C. fetus*
Oxidase	+	+	+	+
Catalase	+	+	−/W	+
Nitrate reduction	+	+	+	+
Urease	−	−	−	−
Hydrolysis of:				
Hippurate	+	−	−	−
Indoxyl acetate	+	+	+	−
Growth at:				
25°C	−	−	−	+
37°C	+	+	+	+
42°C	+	+	+	−
Growth in 1% glycine	+	+	V	+
Susceptibility to:				
Nalidixic acid	S	S	S	V
Cephalothin	R	R	S	S

Treatment- Control

- *Campylobacter* enteritis is usually self limited and patients require fluid and electrolyte replacement.
- For severe and complicated infections, antibiotic is required.
- Erythromycin, ciprofloxacin
- The purification of water and pasteurization of milk are obvious and basic measures.

KEY POINTS FOR CAMPYLOBACTER

- *Campylobacter jejuni*, a food-borne pathogen generally associated with fecal contamination of food or water, is the most frequently recognized cause of bacterial enteritis.
- The generally self limiting clinical presentation includes acute abdominal pain followed by diarrhea with blood and leucocytes and antibiotic treatment is required in only severe cases.

Helicobacter pylori

- In 1983, spiral gram negative rods resembling campylobacters were found in patients with type B gastritis (chronic inflammation of stomach antrum) and classified as campylobacter, then recalssified as a new genus Helicobacter.
- *H. pylori* has been associated with gastritis, peptic ulcers, gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue B cell lymphomas.

- Urease production at very high levels is typical of gastric helicobacter (e.g; *H. pylori*) and uncommon in intestinal helicobacter: important test for the identification of *H. pylori*)

Virulence factors of *H. pylori*

- Motility
- Adhesion to gastric epithelium
- Endotoxin-like activity of lipopolysaccharide
- Urease enzyme activity
- Proteolytic enzymes
- Phospholipase A

Virulence Factors of Helicobacter

Virulence Factors	Function
Urease	Neutralizes gastric acids; stimulates monocytes and neutrophil chemotaxis; stimulates production of inflammatory cytokines
Heat shock protein (HspB)	Enhances expression of urease
Acid-inhibitory protein	Induces hypochlorhydria during acute infection by blocking acid secretion from parietal cells
Flagella	Allow penetration into gastric mucous layer and protection from acid environment
Adhesins	Mediate binding to host cells; examples of adhesins are hemagglutinins, sialic acid–binding adhesin, Lewis blood group adhesin
Mucinase	Disrupts gastric mucus
Phospholipases	Disrupt gastric mucus
Superoxide dismutase	Prevents phagocytic killing by neutralizing oxygen metabolites
Catalase	Prevents phagocytic killing by neutralizing peroxides
Vacuolating cytotoxin	Induces vacuolation in epithelial cells; stimulates neutrophil migration into mucosa
Poorly defined factors	*H. pylori:* Stimulates interleukin-8 secretion by gastric epithelial cells, which recruits and activates neutrophils Stimulates gastric mucosal cells to produce platelet-activating factor (PAF), which stimulates gastric acid secretion Induces nitric oxide synthase in gastric epithelial cells, which mediates tissue injury Induces death of gastric epithelial cells

Helicobacter Species Associated with Human Disease

Species	Reservoir Host	Human Disease	Frequency
H. pylori	Humans, primates, pigs	Gastritis, peptic ulcers, gastric adenocarcinoma	Common
H. cinaedi	Humans, hamsters	Gastroenteritis, septicemia, proctocolitis, cellulitis	Uncommon
H. fennelliae	Humans	Gastroenteritis, septicemia, proctocolitis	Uncommon
H. canis	Dogs	Gastroenteritis	Rare
H. pullorum	Poultry	Gastroenteritis	Rare
H. rappini	Humans, sheep, mice	Gastroenteritis	Rare
H. canadensis	Humans	Gastroenteritis	Rare

- Infections are common, particularly in people in a low socioeconomic class or in developing nations.
- Humans are the primary reservoir
- Person- to person spread is important

Diagnosis

- Microscopy
- Urease test, **urea breath test**
- *H. pylori* antigen test
- Culture
- Serology

Urea breath test: During the **test** you will swallow a capsule containing **urea**, which is made from an isotope of carbon. (Isotopes of carbon occur in minuscule amounts in nature, and can be measured with special **testing** machines.) If *H. pylori* is present in the stomach, the **urea** is broken up and turned into carbon dioxide.

Treatment-Prevention and Control

- Use of single antibiotic is ineffective
- The greatest success in curing gastritis or peptic ulcer disease has been accomplished with the combination of a proton pump inhibitor and one or more antibiotics (Clarithromycin, amoxicillin, metronidazole, tetracycline).

KEY POINTS FOR HELICOBACTER

- *Helicobacter pylori* is a flagellated spiral micro-aerobe causing peptic ulcer and gastritis. Infection is a risk factor for gastric cancer.
- It produces a cell-damaging toxin and a system that alters host cell signal transduction pathways.
- Treatment is by eradication of *H. pylori* using a combination of antibiotics and proton pump inhibitors.

KEY POINTS FOR OTHER GRAM NEGATIVE BACTERIA

- ***Pasteurella multocida*** sometimes infects human, usually through animal bites. It's infection responds penicillin and other antibiotics.
- ***F. tularensis*** is the cause of **tularemia**, a febrile illness that can be severe and life threatening. It is usually acquired from infected animals. There are six clinical forms of the disease.

- **Legionella** species are water borne bacilli and include *L. pneumophila* which is responsible for a form of pneumonia known as legionnaires' disease, and less serious influenza-like illness called Pontiac fever. Suppression of the organism in air-conditioning system and water supplies in public buildings is central to control of disease.

- ***Campylobacter jejuni,*** a food borne pathogen generally associated with fecal contamination of food and water , is the most frequently recognized cause of bacterial enteritis.
- ***Helicobacter pylori*** is a flagellated spiral micro-aerobe causing peptic ulcer and gastritis. Infection is a risk factor of gastric cancer. Treatment is by eradication of *H. pylori* using a combination of antibiotics and proton pump inhibitors.

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