

Person-to-person transmission

Nov 29, 2006

Ch. 26

Tuberculosis (TB)

- Someone in the world is newly infected with TB bacilli every second
- Overall, one-third of the world's population is currently infected with the TB bacillus
- 5-10% of people who are infected with TB bacilli (but who are not infected with HIV) become sick or infectious at some time during their life



World Health Organization

Areas of Concern

- TB cases continue to be reported in every state
- Drug-resistant cases reported in almost every state
- Estimated 10-15 million persons in U.S. infected with *M. tuberculosis*
 - Without intervention, about 10% will develop TB disease at some point in life



Department of Health and Human Services

Centers for Disease Control and Prevention

Transmission of *M. tuberculosis*

- Spread by droplet nuclei
- Expelled when person with infectious TB coughs, sneezes, speaks, or sings
- Close contacts at highest risk of becoming infected
- Transmission occurs from person with infectious TB disease (not latent TB infection)

Pathogenesis

- 10% of infected persons with normal immune systems develop TB at some point in life
- HIV strongest risk factor for development of TB if infected
 - Risk of developing TB disease 7% to 10% each year
- Certain medical conditions increase risk that TB infection will progress to TB disease

Conditions That Increase the Risk of Progression to TB Disease

- HIV infection
- Substance abuse
- Recent infection
- Diabetes mellitus
- Silicosis
- Prolonged corticosteroid therapy
- Other immunosuppressive therapy

TB Morbidity Trends in the United States

- From 1953 to 1984, reported cases decreased by an average of 5.6% per year
- From 1985 to 1992, reported TB cases increased by 20%
- Since 1993, reported TB cases have been declining again
- 18,361 cases reported in 1998

Factors Contributing to the Increase in TB Morbidity: 1985-1992

- Deterioration of the TB public health infrastructure
- HIV/AIDS epidemic
- Immigration from countries where TB is common
- Transmission of TB in congregate settings

Factors Contributing to the Decrease in TB Morbidity Since 1993

Increased efforts to strengthen TB control programs that

- Promptly identify persons with TB
- Initiate appropriate treatment
- Ensure completion of therapy

Persons at Higher Risk for Exposure to or Infection with TB

- Close contacts of person known or suspected to have TB
- Foreign-born persons from areas where TB is common
- Residents and employees of high-risk congregate settings
- Health care workers (HCWs) who serve high risk clients

Testing for TB Disease and Infection



Purpose of Targeted Testing

- Find persons with LTBI who would benefit from treatment
- Find persons with TB disease who would benefit from treatment
- Groups that are not high risk for TB should not be tested routinely

Groups That Should Be Tested for LTBI

Persons at higher risk for exposure to or infection with TB

- Close contacts of a person known or suspected to have TB
- Foreign-born persons from areas where TB is common
- Residents and employees of high-risk congregate settings
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Administering the Tuberculin Skin Test

- Inject intradermally 0.1 ml of 5 TU PPD tuberculin
- Produce wheal 6 mm to 10 mm in diameter
- Read reaction 48-72 hours after injection

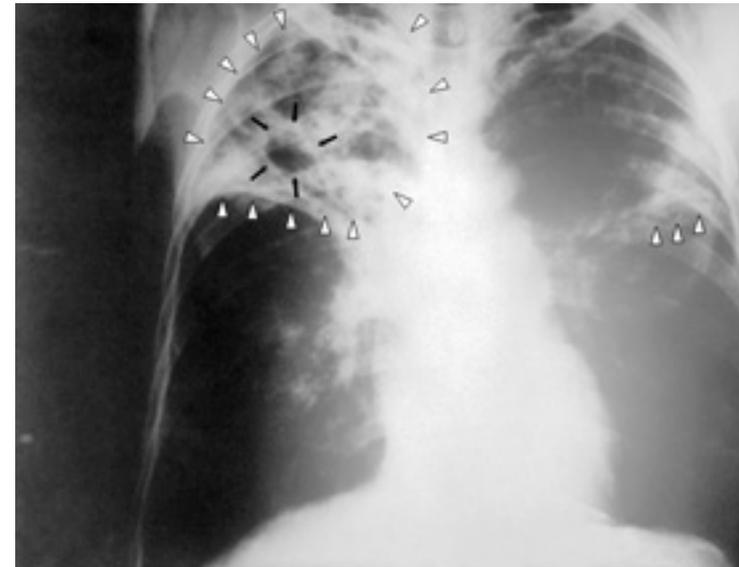


Symptoms of Pulmonary TB

- Productive, prolonged cough (duration of \gt 3 weeks)
- Chest pain
- Hemoptysis

Chest Radiograph

- Abnormalities often seen in apical or posterior segments of upper lobe or superior segments of lower lobe
- May have unusual appearance in HIV-positive persons
- Cannot confirm diagnosis of TB



Specimen Collection

- Obtain 3 sputum specimens for smear examination and culture
- Persons unable to cough up sputum, induce sputum, bronchoscopy or gastric aspiration
- Follow infection control precautions during specimen collection

Smear Examination

- Strongly consider TB in patients with smears containing acid-fast bacilli (AFB)
- Results should be available within 24 hours of specimen collection
- Presumptive diagnosis of TB

AFB smear

Image removed due to copyright restrictions.

AFB (shown in red) are tubercle bacilli

Cultures

- Use to confirm diagnosis of TB
- Culture all specimens, even if smear negative
- Results in 4 to 14 days when liquid medium systems used

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Colonies of *M. tuberculosis* growing on media

Treatment of TB Disease

Photograph of a patient taking medication for tuberculosis removed due to copyright restrictions.

Basic Principles of Treatment

- Provide safest, most effective therapy in shortest time
- Multiple drugs to which the organisms are susceptible
- Never add single drug to failing regimen
- Ensure adherence to therapy

Adherence

- Nonadherence is a major problem in TB control
- Use case management and directly observed therapy (DOT) to ensure patients complete treatment

Treatment of TB for HIV-Negative Persons

- Include four drugs in initial regimen
 - Isoniazid (INH)
 - Rifampin (RIF)
 - Pyrazinamide (PZA)
 - Ethambutol (EMB) or streptomycin (SM)
- Adjust regimen when drug susceptibility results are known

Preventing and Controlling TB

Three priority strategies:

- Identify and treat all persons with TB disease
- Identify contacts to persons with infectious TB; evaluate and offer therapy
- Test high-risk groups for LTBI; offer therapy as appropriate

Influenza

- The flu is a contagious respiratory illness caused by influenza viruses. It can cause mild to severe illness, and at times can lead to death
- The best way to prevent this illness is by getting a flu **vaccination** each fall
- Every year in the United States, on average:
 - 5% to 20% of the population gets the flu
 - more than 200,000 people are hospitalized from flu complications, and
 - about 36,000 people die from flu

<http://www.cdc.gov/flu/keyfacts.htm>

Avian Influenza (Bird Flu)

- These influenza viruses occur naturally among birds
 - Wild birds worldwide carry the viruses in their intestines, but usually do not get sick from them
 - However, avian influenza is very contagious among birds and can make some domesticated birds, including chickens, ducks, and turkeys, very sick and kill them
- The risk from avian influenza is generally low to most people because the viruses occur mainly among birds and do not usually infect humans
 - However, more than 100 human cases of avian influenza infection have been reported since 1997
 - Most cases of avian influenza infection in humans have resulted from contact with infected poultry (e.g., domesticated chicken, ducks, and turkeys)

<http://www.cdc.gov/flu/avian/gen-info/facts.htm>

Influenza A (H5N1) virus

- An influenza A virus subtype that occurs mainly in birds & is highly contagious
 - Outbreaks of avian influenza H5N1 occurred among poultry in eight countries in Asia (Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam) during late 2003 and early 2004
 - At that time, more than 100 million birds in the affected countries either died from the disease or were killed in order to try to control the outbreaks
 - By March 2004, the outbreak was reported to be under control
 - Since late June 2004, however, new outbreaks of influenza H5N1 among poultry were reported by several countries in Asia
- To date, human infections with avian influenza A viruses detected since 1997 have not resulted in sustained human-to-human transmission

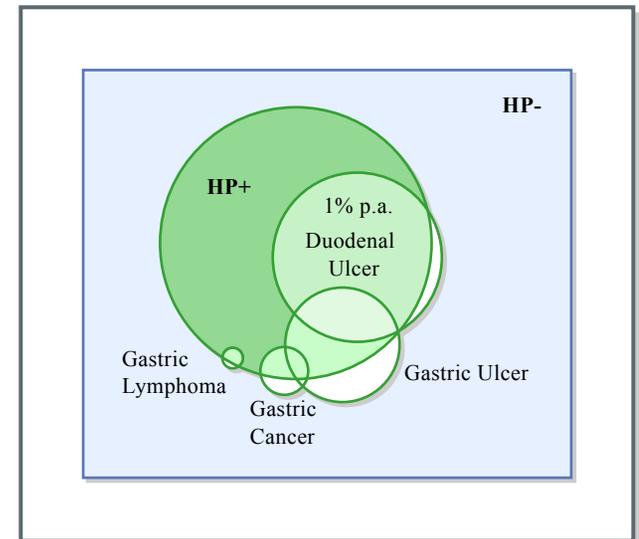
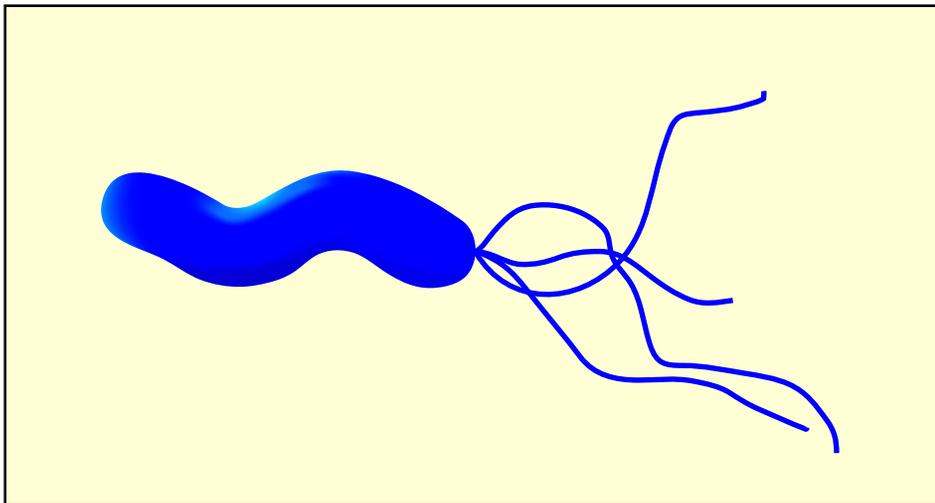
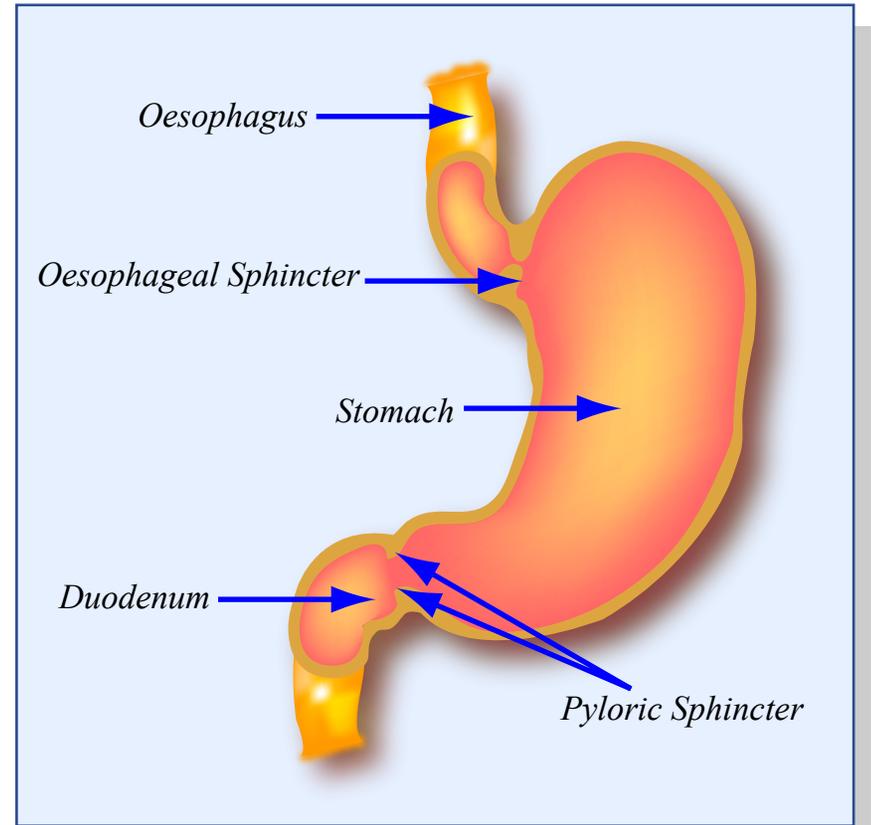
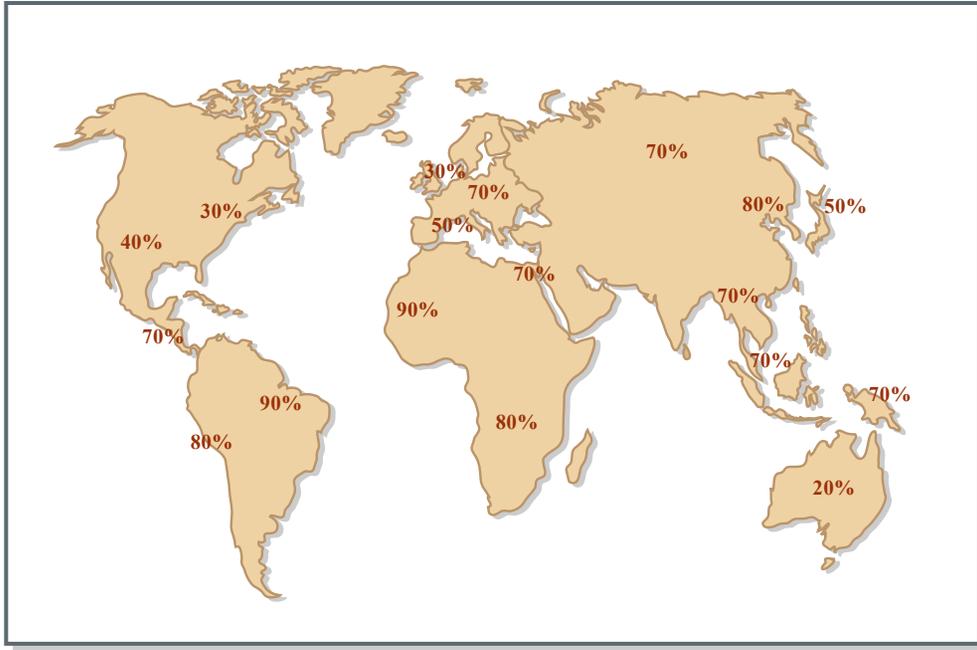
Influenza A (H1N1) virus

1918 “Spanish flu” pandemic

- The influenza pandemic of 1918-19 killed an estimated 20 to 50 million people worldwide, many more than the subsequent pandemics of the 20th century
- Many experts believe that the next pandemic strain will be related to emergence of an avian influenza strain
- The 1918 virus gene sequences are related more closely to avian H1N1 viruses than are any of the other known mammalian influenza H1N1 strains

<http://www.cdc.gov/flu/about/qa/1918flupandemic.htm>

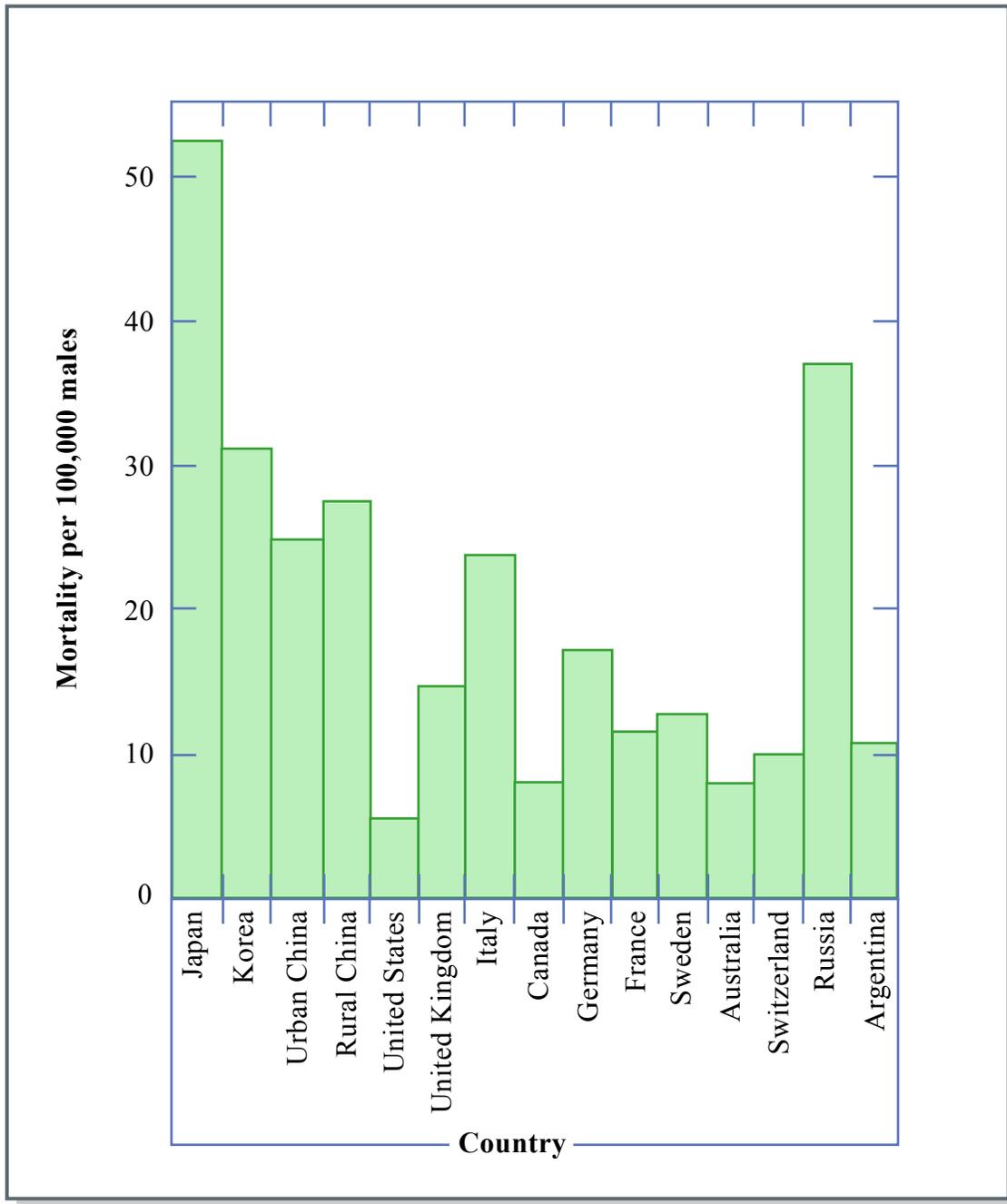
Helicobacter pylori



Helicobacter pylori epidemiology

- Prevalence varies greatly among countries and among population groups
- The infection is acquired by oral ingestion of the bacterium and is mainly transmitted within families in early childhood
- In industrialized countries, the rate of acquisition of *H. pylori* has decreased substantially over recent decades
- Therefore, the continuous increase in the prevalence of *H. pylori* with age is due mostly to a cohort effect

Geographic distribution of gastric carcinoma



- Almost 40% of gastric carcinomas occur in China, where it is the most common malignancy
- The age-adjusted incidence rates are highest in Japan and Korea
- Gastric carcinoma occurs in almost epidemic proportions in Japan, with an incidence of 70 cases per 100,000 men
- The incidence of gastric carcinoma in the United States is only 10 per 100,000 males

Figure by MIT OCW.

Helicobacter pylori pathogenesis

- *H. pylori* is highly adapted for the gastric mucosa
- *H. pylori* genome (1.65 million bp) codes for about 1500 proteins
- The majority of *H. pylori* strains express the 95-kD vacuolating cytotoxin VacA
 - Secreted exotoxin
- Most strains of *H. pylori* possess the cag pathogenicity island (cag-PAI)
 - 37-kb genomic fragment containing 29 genes
 - Encode components of a predicted type IV secretion apparatus that translocates the 120-kD protein CagA into the host cell

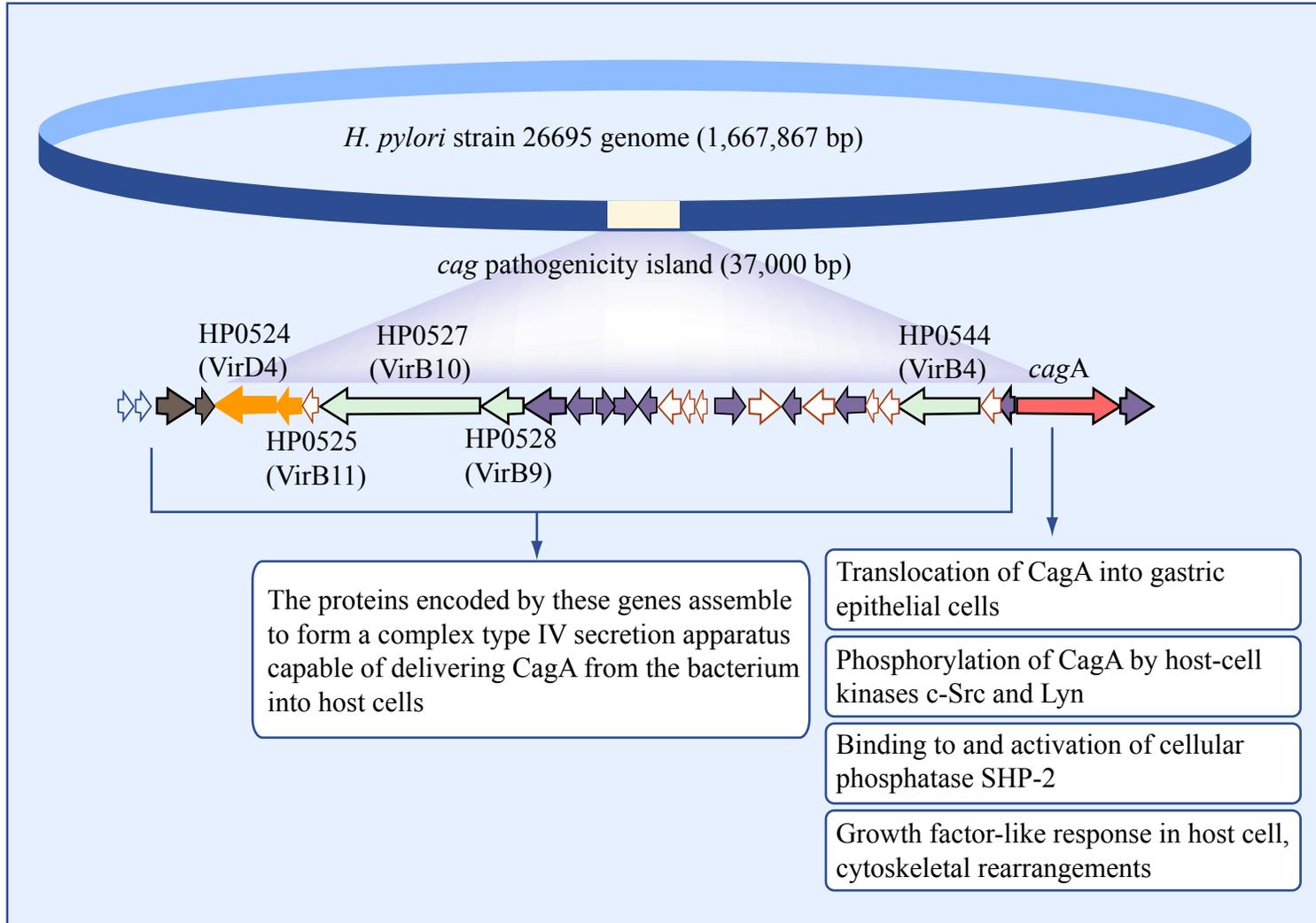


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Bourzac KM, Guillemin K. *Cell Microbiol* 7:911, 2005

Innate and acquired immune responses during *H. pylori* infection

- Intimate attachment via BabA and other adhesins
- Secertion of vacuolating cytotoxin (VacA)
- Type IV secretion system delivers CagA
- Induction of chemokine secretion by gastric epithelial cells
- Recruitment of leukocytes (PMN and macrophages)
- Little to no TLR activation by LPS, flagella
- Preferential induction of a Th1 immune response
- Immunomodulatory effects of VacA on T cells, macrophages

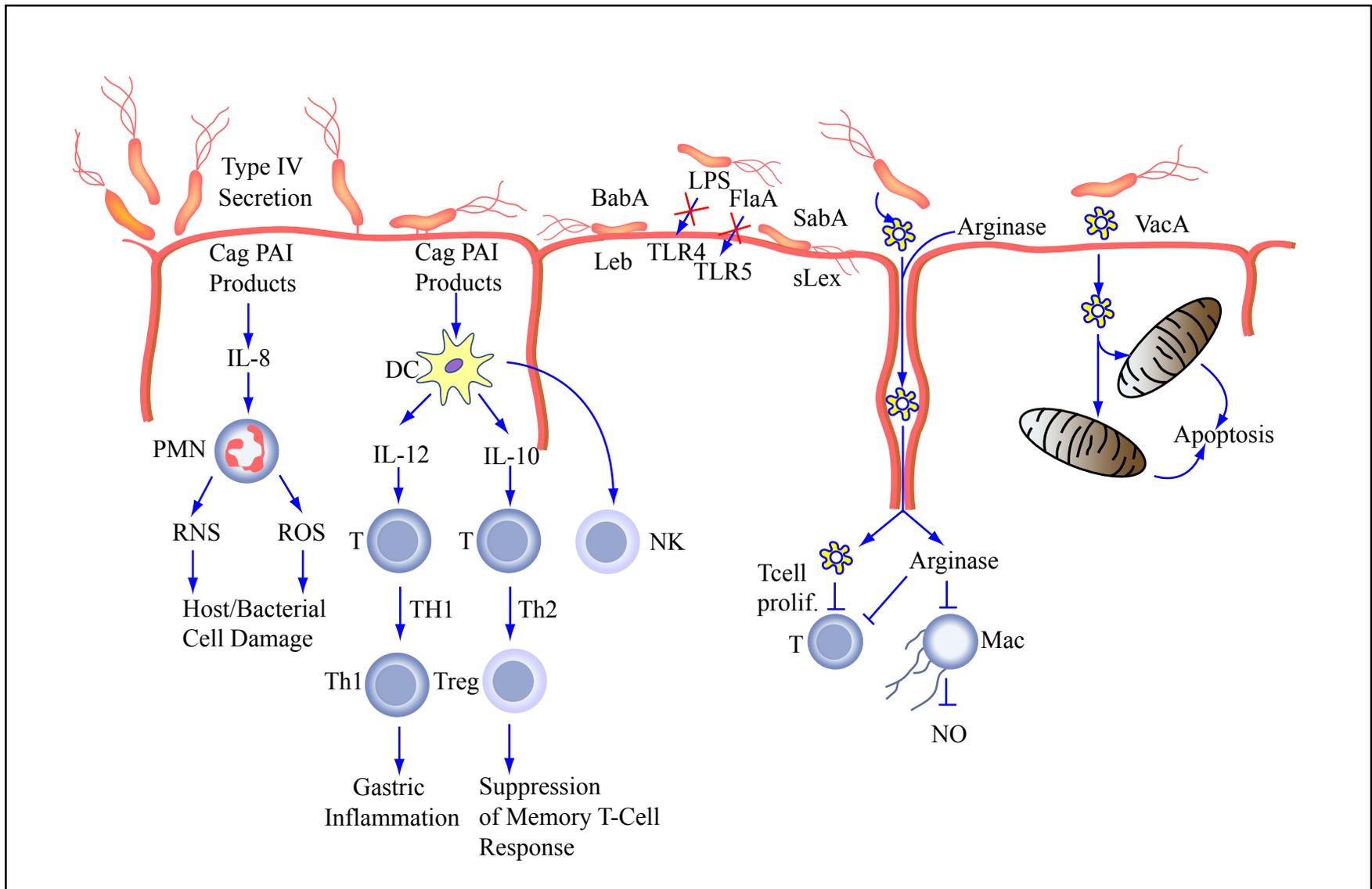


Figure by MIT OCW.

Cellular activities of CagA

1. CagA is delivered into host cells via a type IV secretion system
2. Associates with the tight junction proteins JAM and ZO-1
3. c-Src tyrosine phosphorylates CagA at EPIYA sites
4. In a negative feedback loop, CagAP-Tyr inhibits c-Src directly and by activation of Csk
5. Inhibition of c-Src leads to dephosphorylation of cortactin and ezrin which may contribute to cell morphology changes and motility
6. CagAP-Tyr associates with and activates SHP-2 via interaction with SH2 domains
7. CagA associates with the c-Met receptor located on the basolateral cell surface and with PLC γ surface
8. SHP-2 stimulates prolonged ERK kinase activity

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