

out as a factor that causes effusion–constriction with relative frequency, whereas cardiac surgery may cause this condition relatively less frequently. Cases of pericarditis caused by tuberculosis or another infectious disease have been relatively infrequent in reports from the United States and Europe, but such cases have been reported more frequently in other countries. Infective pericarditis is often observed to evolve over a period of days or weeks, from a stage of acute pericarditis with effusion and tamponade, through a stage of organizing exudates, and eventually to a stage of constrictive pericarditis without effusion. The effusive–constrictive condition appears to be a middle stage in this evolution. Such an evolution probably also follows other causes in which there may be a less flagrant, or even a clinically silent, initial stage of active pericarditis. Thus, the monitoring of intracardiac and intrapericardial pressures as part of a pericardiocentesis procedure is most relevant in patients who present with a subacute course of pericardial tamponade, particularly those in whom the condition is idiopathic or is related to infection, neoplasm, or rheumatologic disease.

Studies of effusive–constrictive pericarditis have provided insight into the pathophysiology of pericardial diseases. Cardiac tamponade and constrictive pericarditis are basically similar in restricting the filling of the heart and raising the systemic and pulmonary venous pressures. The venous-pressure

waveforms differ, however, reflecting a single wave of forward flow (during systole) in tamponade, as compared with a biphasic pattern (a lesser wave in systole and a greater wave in early diastole) in constrictive conditions. Removing the pericardial fluid from a patient with effusive–constrictive pericarditis tends to change the pattern from one more like that found in tamponade to one more like that associated with constriction.

The recognition of effusive–constrictive pericarditis should attract the attention of physicians in many specialties. The treatment options for the management of pericardial effusion range from conservative medical management, through less invasive procedures such as pericardiocentesis or balloon pericardiostomy, to more invasive procedures such as subxiphoid surgical pericardiostomy or thoracoscopic parietal pericardiectomy, to full-scale pericardiectomy by means of thoracotomy. Varying clinical circumstances, such as the presence of metastatic neoplasm, previous radiation therapy, previous cardiac surgery, and the presence of end-stage renal disease or rheumatologic disease, will affect treatment decisions. The timely recognition of the effusive–constrictive condition enables physicians to choose the most appropriate therapy.

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1. Case Records of the Massachusetts General Hospital (Case 19-1997). *N Engl J Med* 1997;336:1812-9.

## Preventing Foodborne Disease — What Clinicians Can Do

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The food in the United States is among the safest in the world, but recent outbreaks of hepatitis A remind us that foodborne illness remains an important public health concern. Between September and November 2003, outbreaks of hepatitis A were identified in Tennessee, North Carolina, Georgia, and Pennsylvania. In total, these outbreaks included nearly 1000 cases. The Pennsylvania outbreak among patrons of a single restaurant was the largest outbreak of foodborne hepatitis A ever reported in the United States, with more than 600 infected persons identified to date, including 3 who died. Epidemiologic field investigations of restaurant-asso-

ciated outbreaks in the four states implicated green onions, rather than infected restaurant workers, as the source of transmission. Trace-back investigations indicate that the green onions served in the restaurants were grown in Mexico. Pending further investigation into the cause of contamination, the Food and Drug Administration (FDA) has advised consumers about the need to cook green onions thoroughly and to ask about the use of green onions in foods prepared outside the home.

Outbreaks of foodborne hepatitis A often attract intense media coverage, but such outbreaks are not common in the United States, where most cases of

hepatitis A are acquired through person-to-person transmission in households and extended-family settings or by adults with specific risk factors for infection. On the basis of the epidemiology of hepatitis A, the Advisory Committee on Immunization Practices has made recommendations for the use of hepatitis A vaccine in the United States, which are summarized by Craig and Schaffner in this issue of the *Journal* (pages 476–481). The national incidence of hepatitis A has declined precipitously with the use of hepatitis A vaccine, from approximately 25,000 to 35,000 reported cases per year in the 1980s and early 1990s to fewer than 10,000 cases in 2002. Despite the recent large outbreaks associated with green onions, the overall rate for 2003 remains very low. However, the full implementation of the current recommendations would result in the vaccination of many millions more people — including people, such as those with chronic liver disease, who are at increased risk for severe hepatitis A. Persons for whom routine vaccination is not currently recommended but who wish to reduce to nearly zero the small risk of transmission of hepatitis A through food or close contact can also be vaccinated. Employers who want to ensure that their workers are protected from hepatitis A and health care plans that want to reduce hepatitis A–related claims can also take advantage of the availability of this safe and effective prevention measure, just as some employers and plans choose to reduce influenza-related illness and costs by providing vaccination against influenza.

Hepatitis A virus is only one of many foodborne pathogens (see Table), and hepatitis A vaccination would prevent a small fraction of the more than 76 million foodborne illnesses and 5000 related deaths that occur annually in the United States. Many of these illnesses are unrecognized or unreported, or their source is never identified, because they are never linked to an outbreak that would prompt an epidemiologic investigation. Laboratory-based surveillance and molecular epidemiology are improving our understanding of the scope and source of foodborne outbreaks by permitting more rapid identification of clusters of cases of illness and links among “sporadic” infections that are not geographically or temporally clustered.

However, the identification of outbreaks still depends on alert clinicians who make accurate and timely diagnoses and report cases of foodborne illness immediately to the appropriate public health agency. For some foodborne pathogens, such as *Es-*

*cherichia coli* O157:H7, salmonella, and *Listeria monocytogenes*, subtyping in public health laboratories is critical for the rapid detection and investigation of large outbreaks. Clinical laboratories should rapidly send isolates from patients affected by such outbreaks to the appropriate public health laboratories. The spectrum of agents and clinical presentations is broad and includes diseases that have long incubation periods, such as hepatitis A and listeriosis, and diseases in which gastrointestinal symptoms are not a prominent part of the clinical presentation, such as botulism and ciguatera. Self-limited gastrointestinal infection with *E. coli* O157:H7 or *Campylobacter jejuni* may be followed (and obscured) by life-threatening sequelae, such as the hemolytic-uremic syndrome or Guillain-Barré syndrome, respectively. Early diagnosis is also important if the risk of severe complications is to be kept at a minimum. For example, the use of antibiotics should be avoided in patients infected with *E. coli* O157:H7, and patients who might have hepatitis A should be cautioned to avoid medications that are potentially hepatotoxic, including nonprescription medications such as acetaminophen.

For some persons, certain pathogens confer a greater risk than others of adverse outcomes or death. Patients who are at increased risk for severe hepatitis A can be protected by vaccination. Patients at increased risk for severe infections with other foodborne pathogens should seek advice from health care professionals about how to avoid infection. For example, specific guidelines have been issued by public health agencies and professional associations to help pregnant women reduce their risk of contracting listeriosis by properly cooking or avoiding certain foods. Health care providers should also follow federal, state, and local advisories about other foods that may put their most vulnerable patients at risk.

The year-round availability and increased variety of fresh produce can help to improve the typical U.S. diet, and physicians should continue to promote the health benefits of fresh fruits and vegetables. However, the centralization of food production and widespread distribution also provide opportunities for the broader dissemination of foodborne pathogens. As the per capita consumption of produce has increased, outbreaks associated with contaminated produce have accounted for an increasing proportion of reported outbreaks of foodborne illness. For example, fresh produce has replaced raw shellfish as the most commonly identified source of

**Table. Selected Clinical and Epidemiologic Characteristics of Typical Illnesses Caused by Common Foodborne Pathogens.\***

Pathogen	Typical Incubation Period†	Duration	Typical Clinical Presentation‡	Associated Foods§
<b>Bacterial</b>				
<i>Salmonella</i> species	1–3 Days	4–7 Days	Gastroenteritis	Undercooked eggs or poultry, produce
<i>Campylobacter jejuni</i>	2–5 Days	2–10 Days	Gastroenteritis	Undercooked poultry, unpasteurized dairy products
<i>Escherichia coli</i> O157:H7	1–8 Days	5–10 Days	Gastroenteritis	Undercooked beef, produce, unpasteurized dairy products
<i>E. coli</i> , enterotoxigenic	1–3 Days	3–7 Days	Gastroenteritis	Many foods
<i>Shigella</i> species	1–2 Days	4–7 Days	Gastroenteritis	Produce, egg salad
<i>Listeria monocytogenes</i>	2–6 Wk	Variable	Gastroenteritis, meningitis, abortion¶	Deli meat, hot dogs, unpasteurized dairy products
<i>Bacillus cereus</i>	1–6 Hr	<24 Hr	Vomiting, gastroenteritis	Fried rice, meats
<i>Clostridium botulinum</i>	12–72 Hr	Days–months	Blurred vision, paralysis	Home-canned foods, fermented fish
<i>Staphylococcus aureus</i>	1–6 Hr	1–2 Days	Gastroenteritis, particularly nausea	Meats, potato and egg salads, cream pastries
<i>Yersinia enterocolitica</i>	1–2 Days	1–3 Wk	Gastroenteritis, appendicitis-like syndrome	Undercooked pork, unpasteurized dairy products
<b>Viral</b>				
Norovirus	1–2 Days	12–60 Hr	Gastroenteritis	Undercooked shellfish
Hepatitis A virus	15–50 Days	Weeks–months	Hepatitis	Produce, undercooked shellfish
<b>Parasitic</b>				
<i>Cryptosporidium parvum</i>	2–10 Days	Weeks	Gastroenteritis	Produce, water
<i>Cyclospora cayentanensis</i>	1–11 Days	Weeks	Gastroenteritis	Produce, water
<i>Toxoplasma gondii</i>	5–23 Days	Months	Influenza-like illness, lymphadenopathy	Food contaminated by cat feces, undercooked meat
<i>Giardia lamblia</i>	1–4 Wk	Weeks	Gastroenteritis	Water
<i>Taenia solium</i>	Variable	Variable	Asymptomatic, cysticercosis	Raw pork

\* Adapted from “Diagnosis and Management of Foodborne Illnesses: A Primer for Physicians” (available at <http://www.ama-assn.org/ama/pub/category/3629.html>).

† Incubation periods may vary; the average periods are given, but wider ranges have been reported.

‡ Gastroenteritis typically includes nausea, vomiting, diarrhea (which may be bloody), fever, and abdominal pain.

§ These foods are among those most commonly implicated in epidemiologic investigations. For some pathogens, person-to-person transmission or transmission through foods prepared by an infected person is more common.

¶ *L. monocytogenes* may also cause gastroenteritis with a short (two-to-three-day) incubation period.

hepatitis A outbreaks caused by foods that become contaminated before distribution.

The events of September 11, 2001, led Congress to enact the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, which required the FDA to develop four regulations. The first regulation requires domestic and foreign facilities that manufacture, process, pack, or hold food

that will be consumed by humans or animals in the United States to register with the FDA. The second regulation requires that the FDA receive prior notification of all food imported or offered for import into the country. The FDA published both of these regulations as interim final rules on October 10, 2003, and it plans to issue the other two regulations by March 2004. One would require persons who

manufacture, process, pack, hold, transport, distribute, receive, or import food to keep records that would assist the FDA in identifying the immediate previous sources and immediate subsequent recipients of the food if the FDA had a reasonable belief that an article of food presented a threat of serious adverse health consequences or death to humans or animals. The final regulation will outline the procedures whereby the FDA could detain any article of food for which there is credible evidence of such a threat. The authority to detain food under these criteria became effective with the enactment of the Bioterrorism Act. These regulations will improve our ability to investigate outbreaks that are caused by intentional or unintentional acts or that result from naturally occurring agents.

The identification of steps in the food-production process that can result in contamination and the implementation of measures or protocols that reduce the risk of contamination can reduce the rate of foodborne illness. For example, improving sanitation in the communities where food is grown, harvested, processed, or prepared can reduce the opportunities for food contamination. Outbreaks such

as the hepatitis A outbreaks of 2003 highlight gaps in our knowledge about why food contamination occurs and how it can be prevented or minimized. Some foods, such as green onions, seem more prone than others to contamination with certain pathogens, perhaps because they must be handled extensively during harvesting or because of certain characteristics of the plant surfaces. In addition, protocols for the detection of pathogens — especially nonbacterial pathogens — that can be effectively integrated into food-production systems require further development and evaluation.

From farm to table, further improvements in food handling at every stage are critical for ensuring food safety. Health professionals can play an important part in preventing foodborne illness by educating their patients about the risks of foodborne illness, making rapid and appropriate diagnoses, and reporting cases promptly to public health authorities.

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## Hypogonadism in Elderly Men — What to Do Until the Evidence Comes

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Testosterone treatment for elderly men made the news again recently, when the Institute of Medicine Committee on Assessing the Need for Clinical Trials of Testosterone Replacement Therapy issued its long-awaited report,<sup>1</sup> which concluded that there is insufficient evidence that testosterone treatment benefits elderly men. What is the background behind this report, and what are its implications?

Many studies document that serum testosterone concentrations in men decrease as they age. In contrast to the precipitous and profound decrease in estradiol concentrations that occur when women enter menopause, the decrease in testosterone in men occurs moderately and gradually over a period of several decades. The serum total testosterone concentration decreases from a mean of about 600 ng per deciliter (20.8 nmol per liter) at 30 years of age to a mean of about 400 ng per deciliter (13.9 nmol

per liter) at 80 years, although the range is wide at all ages. In one study, approximately 20 percent of men older than 60 years of age had total serum testosterone concentrations that were below the normal range for young men.

An essential but still unanswered question is whether this decrease in the testosterone concentration is physiologic, perhaps conveying a benefit, or pathologic, causing harm. Testosterone normally has many different effects on many different tissues, which can be explained in part by its ability to act directly through the androgen receptor, through conversion to dihydrotestosterone, which also acts through the androgen receptor, or through conversion to estradiol, which acts through the estrogen receptor (see Figure). The decrease in testosterone with aging, therefore, could affect many different tissues.