# What illnesses contraindicate immunization?

**Marcus Plescia, MD, MPH**
North Carolina Division of Public Health, Raleigh;
Department of Family Medicine, University of North Carolina, Chapel Hill

**Laura Leach, MLIS**
Carolinas Healthcare System, Charlotte, NC

## EVIDENCE-BASED ANSWER

The Advisory Council on Immunization Practices (ACIP) reports that the only contraindication for all vaccines is a history of severe allergic reaction to a previous vaccine or vaccine constituent (strength of recommendations: **C**, based predominantly on case series, case reports, and expert opinion).

Vaccination is safe and efficacious in the following situations: during a mild illness (eg, diarrhea, otitis media or other mild upper respiratory infection whether or not the patient has a fever), during antimicrobial therapy, during the convalescent phase of an acute illness, when breastfeeding, and after mild to moderate reactions to a previous dose of vaccine.

Live vaccines (varicella, MMR) should not be used for pregnant women or significantly immunocompromised patients, and may not be effective for patients receiving immunoglobulin therapy. They can be administered to HIV-positive patients who are asymptomatic or not severely immunosuppressed, as determined by age-specific CD4 counts.

## CLINICAL COMMENTARY

### Know true contraindications; provide clear, factual information to concerned parents

Immunizations are among the safest and most cost-effective interventions available in modern medicine. Offices should be organized to assist in assuring delivery of immunizations during preventive, sick, and follow-up visits, and to follow recommended and catch-up schedules to reduce the time patients are susceptible to preventable infectious diseases. Failure to vaccinate due to inappropriate contraindications, particularly mild illness, is a missed opportunity and significant contributor to under-immunization. Know and observe true contraindications and provide clear, factual information to parents concerned about vaccine risks. When temporarily delaying vaccination is prudent—eg, with evolving neurologic conditions and moderate to severe illness—scheduling a return visit for immunizations and documenting the intention to vaccinate at the next visit are strategies to reduce the risk that catch-up immunization will be forgotten.

**Rebecca Meriwether, MD**
Tulane University, New Orleans, La

## Evidence summary

Public misperceptions and provider uncertainty about contraindications create missed opportunities for immunization.[1–3] The Centers for Disease Control and Prevention (CDC) defines contraindications as conditions that increase the risk of a serious reaction to vaccination. Precautions are conditions that might increase the risk of a serious reaction, or that diminish vaccine

**FAST** TRACK

**The only contraindication for all vaccines is a history of severe allergic reaction to a previous vaccine**

**TABLE**

**Contraindications and precautions for vaccine administration**

| SITUATION | COMMENTS |
|---|---|
| Mild acute illness (with or without fever) (otitis media, diarrhea, etc) | No contraindication |
| Breastfeeding | No contraindication |
| Serious allergic reaction to vaccine or component (anaphylaxis) | Absolute contraindication |
| Pregnancy | Tetanus and influenza should be kept current<br>No contraindication to give indicated inactivated immunizations<br>Live vaccines are contraindicated, although no reports of adverse reactions reported |
| Moderate to severe illness | Temporary precaution—hold until patient improved |
| Encephalopathy <1 week after DTP or DtaP | Pertussis immunization contraindicated |
| Fever >40.5° C<br>*or* Hypotonic, hyporesponsive episode<br>*or* Persistent, inconsolable crying >3 hours <48 hours after DTP or DTaP<br>*or* seizure <3 days after DTP or DTaP | Avoid pertussis, but vaccination may be appropriate during an outbreak |
| Recipients of blood, IVIG, and other antibody-containing products | Hold live vaccines for variable timing depending on dose (see CDC Recommendations)<br>Oral typhoid and yellow fever OK |
| Chemotherapy or radiotherapy | Give influenza<br>Avoid others (decreased immune response) |
| Antibacterials | Should not be taken with oral (live) typhoid vaccine (decreased effectiveness) |
| Antivirals against herpes spp | Should not be taken with live varicella vaccine (decreased effectiveness) |
| Postpartum anti-Rho(D) | Simultaneous rubella vaccination effective |
| Hematopoietic Stem Cell transplant recipients | See separate CDC Recommendations* |
| Altered immune status (HIV, solid organ transplant recipients, etc) | See separate CDC Recommendations†<br>Inactivated immunizations are safe, may be less effective |

Table based on general recommendations on immunization, *MMWR Recomm Rep* 2002.[4]
* Available at: www.cdc.gov/mmwr/preview/mmwrhtml/rr4910a1.htm
† For HIV, www.cdc.gov/mmwr/preview/mmwrhtml/rr5108a1.htm; for others, www.cdc.gov/mmwr/preview/mmwrhtml/00023141.htm.

efficiency.[4] Recommendations about contraindications and precautions for vaccine administration are partially based on studies of adverse effects (see the **TABLE** for common situations). Complete information on the contraindications and precautions for all common vaccinations can be accessed at www.cdc.gov/mmwr/preview/mmwrhtml/rr5102a1.htm#tab5.[4]

Data on vaccination risks are limited by a relative lack of experimental studies. Initial recommendations of the Advisory Council on Immunization Practices have been based on the findings of a 14-member Institute of Medicine (IOM) expert committee and are updated regularly.[5–7] The IOM committee reported that because vaccine-related adverse events occur infrequently,

available randomized controlled trials were too small to detect differences in incidence.[6] Much of the data come from adverse effect surveillance systems, such as the Vaccine Adverse Event Reporting System (VAERS), to which health care providers report possible adverse effects of vaccinations.

Updated contraindications by ACIP to the initial IOM recommendations have also been based on observational reports and studies.[4] A recent Cochrane review on acellular pertussis vaccines concluded that the acellular vaccine had fewer adverse effects than the whole-cell version, but did not support any changes in contraindications or precautions.[8]

## Recommendations from others

The ACIP recommendations serve as national standards and have been adopted by American Academy of Pediatrics and the American Academy of Family Physicians and are included in most standard reference texts.[4,9]

### REFERENCES


1. Wald ER, Dashefsky B, Byers C, Guerra N, Taylor F. Frequency and severity of infections in day care. *J Pediatr* 1988; 112:540–546.
2. Szilagyi PG, Rodewald LE. Missed opportunities for immunizations: a review of the evidence. *J Public Health Manag Pract* 1996; 2:18–25.
3. Farizo KM, Stehr-Green PA, Markowitz LE, Patriarca PA. Vaccination levels and missed opportunities for measles vaccination: a record audit in a public pediatric clinic. *Pediatrics* 1992; 89:589–592.
4. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices and the American Academy of Family Physicians. *MMWR Recomm Rep* 2002; 51(RR-2):1–35.
5. Howson CP, Howe CJ, Fineberg HV, eds. *Adverse Effects of Pertussis and Rubella Vaccines.* Washington, DC: National Academy Press, last updated 1991. Available at: www.nap.edu/books/0309044995/html/index.html. Accessed on June 10, 2005.
6. Stratton KR, Howe CJ, Johnston RB, eds. *Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality.* Washington, DC: National Academy Press, Last updated 1994. Available at: www.nap.edu/catalog/2138.html. Accessed on June 10, 2005.
7. Update: vaccine side effects, adverse reactions, contraindications, and precautions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 1996; 45(RR-12):1–35.
8. Tinnion ON, Hanlon M. Acellular vaccines for preventing whooping cough in children. *Cochrane Database Syst Rev* 2000(2): CD001478.
9. American Academy of Pediatrics. Active and Passive Immunization. In: Pickering LK, ed. *Red Book: 2003 Report of the Committee on Infectious Diseases.* 26th ed. Elk Grove Village, Ill: American Academy of Pediatrics; 2003:46–49.





EARN FREE CME CREDITS ONLINE!

Explore a range of free CME and educational opportunities at www.hormonecme.org:

- Courses include CME Slide Libraries, Symposiums, Newsletters & more
- Receive your CME certificate & credits award instantly
- Additional features include *Ask the Expert & Expert Commentary*
- Completely redesigned & updated website is better organized and easier to use
- Registration & courses are free to all qualified physicians

LOG ON TODAY!
www.hormonecme.org

COUNCIL ON HORMONE

Putting Research into Practice.
www.hormonecme.org

Jointly sponsored by the University of Wisconsin Medical School and DesignWrite, Inc., in cooperation with the Council on Hormone Education.

SUPPORTED BY AN UNRESTRICTED EDUCATIONAL GRANT FROM WYETH PHARMACEUTICALS.

# Who should get hepatitis A vaccination?

**Rhett Brown, MD**
Medical Director, Eastland Family Practice, Charlotte, NC

**Kathy Cable, MLS**
East Carolina University Health Sciences Library, Greenville, NC

## EVIDENCE-BASED ANSWER

The following groups are at increased risk of contracting or having severe outcomes from hepatitis A and should receive vaccination.

- Persons traveling to or working in countries that have high or intermediate rates of infection. Specific country recommendations are available at www.cdc.gov/travel/destinat.htm (strength of recommendation [SOR]: **B**)
- Men who have sex with men (SOR: **B**)
- Illegal-drug users (whether drug is injected or not) (SOR: **B**)
- Persons who have occupational risk for infection (eg, research settings working with nonhuman primates) (SOR: **C**)
- Persons with clotting-factor disorders (SOR: **C**)
- Persons with chronic liver disease (SOR: **B**)
- Children (age 2 to 18) living in states, counties, and communities where rates of hepatitis A are at least twice the national average. These states include: Alaska, Arizona, California, Idaho, Nevada, New Mexico, Oklahoma, Oregon, South Dakota, Utah, and Washington. The rates of hepatitis A for individual counties can be found at the Centers for Disease Control and Prevention (CDC) web site (www.cdc.gov/ncidod/diseases/hepatitis/a/vax/index.htm). Consider giving hepatitis A vaccine to children (age 2 to 18) in areas with rates greater than the national average but less than twice the national average. These states include Arkansas, Colorado, Missouri, Montana, Texas, and Wyoming (SOR: **B**).

## CLINICAL COMMENTARY

### Anyone who does not want to get hepatitis A should receive the vaccine

A good information master needs to know his resources. The question posed in this clinical inquiry is a good example. Questions about who should receive which vaccine are determined by the Advisory Committee on Immunization Practices, and their recommendations are available on the CDC's web site (www.cdc.gov/nip/publications/acip-list.htm).

With that said, anyone who does not want to get hepatitis A should receive the vaccine. Hepatitis A is the most common vaccine preventable disease, which on occasion can be severe, especially in adults. The vaccine has no serious side effects, is highly effective and, if widely adopted, would dramatically decrease the incidence of hepatitis A in the population.

**Richard Sams II, MD**
Camp Pendleton Naval Hospital

## Evidence summary

Infection with hepatitis A virus (HAV) is a reportable illness in all 50 states, and it continues to be one of the most reported vaccine-preventable illnesses. The persistence of extensive community-wide outbreaks indicates that hepatitis A remains a major public health problem.

The costs associated with HAV are substantial: 11% to 22% of individuals with HAV are hospitalized, and adults who become ill lose an average of 27 days of work. The average cost of hepatitis A ranges from $1817 to $2459 per case for adults and $433 to $1492 for children. In 1989, the estimated annual direct and indirect costs of HAV in the United States were more then $300 million (in 1997 dollars).[1]

Hepatitis A can produce either asymptomatic or symptomatic infection in humans after an average incubation period of 28 days. The illness is usually marked by a sudden onset of symptoms including fever, malaise, nausea, anorexia, abdominal

discomfort, jaundice, and dark urine. The illness usually lasts less than 2 months. Though not usually life threatening, an estimated 100 deaths annually are attributed to acute liver failure due to hepatitis A. Patients with chronic liver disease may be at higher risk of developing fulminant hepatitis A.[2,3] The likelihood of symptomatic disease is directly related to age, with 70% of adults developing jaundice and most infections in children aged <6 years having no symptoms.

HAV is transmitted primarily from fecal-oral route by either person-to-person contact or ingestion of fecally contaminated food or water. Although rare, it is possible for transmission by blood or blood products collected from donors during the viremic phase of their infection. Although HAV has been detected in saliva, transmission by saliva has not been demonstrated. Under the right conditions HAV can be stable in the environment for months. Heating foods to >185° F for 1 minute or disinfecting surfaces with 1:100 dilution of bleach in tap water is necessary to inactivate HAV.[1]

Vaccination against HAV is recommended for those at high risk for contracting the illness or for any person wishing to obtain immunity. Prospective studies indicate that persons traveling in areas with high rates of HAV are themselves at 44 times increased risk.[4] Among men who have sex with men, numerous cohort studies reveal increased rates of infection due to anal-oral sexual practices and higher number of sexual partners.[5–7] Intravenous drug users and non-IV illicit drug users are both at increased risk of HAV infection.[8–10] In the United States, children living in states with increased HAV incidence rates are also considered to be at high risk.[1] Less strong evidence exists for vaccinating those with occupational hazards (for example, working in a research setting with nonhuman primates) or persons with clotting factor disorders.[11,12]

A corollary question is who does not routinely need hepatitis A vaccine. In general, food service workers, sewerage workers, healthcare workers, children aged <2 years, day-care attendees, and residents of institutions for the developmentally disabled do not need routine immunization

The currently licensed inactivated hepatitis A vaccines are highly immunogenic and clinically effective in children 2 to 18 years and in adults. In a double-blind, controlled, randomized study of 1000 children in New York revealed clinical efficacy of 100%.[13] A second study of 40,000 children in Thailand had a clinical efficacy of 94%.[13] Numerous other studies have supported findings of near 100% immunogenicity in all age groups and clinical efficacy in all age groups.[1]

**REFERENCES**


1. Prevention of hepatitis A through active or passive immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 1999; 48(RR-12):1–37.
2. Vento S, Garofano T, Renzini C, et al. Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. *N Engl J Med* 1998; 338:286–290.
3. Keeffe EB. Is hepatitis A more severe in patients with chronic hepatitis B and other chronic liver diseases? *Am J Gastroenterol* 1995; 90:201–205.
4. Steffen R, Rickenbach M, Wilhelm U, Helminger A, Schar M. Health problems after travel to developing countries. *J Infect Dis* 1987; 156:84–91.
5. Villano SA, Nelson KE, Vlahov D, Purcell RH, Saah AJ, Thomas DL. Hepatitis A among homosexual men and injection drug users: more evidence for vaccination. *Clin Infect Dis* 1997; 25:726–728.
6. Henning KJ, Bell E, Braun J, Barker ND. A community-wide outbreak of hepatitis A: risk factors for infection among homosexual and bisexual men. *Am J Med* 1995; 99:132–136.
7. Corey L, Holmes KK. Sexual transmission of hepatitis A in homosexual men: incidence and mechanism. *N Engl J Med* 1980; 302:435–438.
8. Bell BP, Shapiro CN, Alter MJ, et al. The diverse patterns of hepatitis A epidemiology in the United States—implication for vaccination strategies. *J Infect Dis* 1998; 178:1579–1584.
9. Schade CP, Komorwska D. Continuing outbreak of hepatitis A linked with intravenous drug abuse in Multnomah County. *Public Health Rep* 1988; 103:452–459.
10. Harkess J, Gildon B, Istre GR. Outbreaks of hepatitis A among illicit drug users, Oklahoma, 1984–87. *Am J Public Health* 1989; 79:463–466.
11. Hinthorn DR, Foster MT Jr., Bruce HL, Aach RD. An outbreak of chimpanzee associated hepatitis. *J Occup Med* 1974; 16:388–391.
12. Mannucci PM, Gdovin S, Gringeri A, et al. Transmission of hepatitis A to patients with hemophilia by factor VIII concentrates treated with organic solvent and detergent to inactivate viruses. The Italian Collaborative Group. *Ann Intern Med* 1994; 120:1–7.
13. Innis BL, Snitbhan R, Kunasol P, Laorakpongse T, Poopatanakool W, Kozik CA et al. Protection against hepatitis A by an inactivated vaccine. *JAMA* 1994; 271:1328–1334.


**FAST** TRACK

**Hepatitis A vaccine is highly effective, and, if widely adopted, would dramatically decrease the incidence of the disease**

# Do statins delay onset or slow progression of Alzheimer's dementia?

**Slade A. Suchecki, DO, Paul V. Aitken, Jr, MD, MPH, Rick Potts, MD**
University of North Carolina, Chapel Hill;
New Hanover Regional Medical Center, Wilmington, NC

**Linda J. Collins, MSLS**
University of North Carolina, Chapel Hill

## EVIDENCE-BASED ANSWER

Statins (coenzyme-A reductase inhibitors) should not be used with the single intent to delay the onset or slow the progression of dementia. Large randomized control trials (RCTs) found that the administration of a statin had no significant effect on preventing or slowing all-cause cognitive decline (strength of recommendation [SOR]: **A**, based on large RCTs with narrow confidence interval).[1,2] Specifically, there is insufficient evidence that statins delay the onset or slow the progression of Alzheimer's dementia (SOR: **B**, based on systematic review with heterogeneity).[3]

While 3 epidemiologic studies[4–6] have found a decreased incidence of dementia among those taking statins, these studies have significant methodological shortcomings and do not show a causal relationship (SOR: **C**, based on poor-quality studies).

## CLINICAL COMMENTARY

### We are obligated to protect patients from potential risks of unnecessary medications

Alzheimer's disease is a difficult and emotionally charged topic. Many patients who have watched a family member suffer from Alzheimer's disease would go to great lengths to delay or prevent developing Alzheimer's disease themselves. As a result of direct drug marketing to consumers, plus increased lay media coverage of health issues, our patients are now better informed than ever and make more direct requests for certain medications by name.

Imagine talking with a well-read patient who has learned from a newspaper article or morning news show about 1 of the 3 epidemiological studies that show decreased incidence of dementia among statin users. The patient now stands before you, requesting a prescription for a statin. Though this patient is otherwise healthy and has a desirable cholesterol level, you will still find it difficult to explain to the patient why you will not write the prescription. As physicians, we are obligated to protect our patients from the potential risks of unnecessary medications. We are also obligated to protect our healthcare system from escalation of already high healthcare costs. Evidence from rigorous clinical trials is the tool that can help us provide this protection.

**Seema Modi, MD**
East Carolina University, Greenville, NC

## Evidence summary

Approximately 4 million people in the United States suffer with Alzheimer's disease. The prevalence rises with age and is approximately 47% among those aged 85 years and older.[7]

Amyloid plaques are thought to be responsible for clinical changes associated with Alzheimer's dementia. Research has indicated that amyloid precursors may be more prevalent in a cholesterol-rich environment. This led to the theory that treating hypercholesterolemia may decrease the prevalence of Alzheimer's disease.[8]

The PROSPER trial, which was designed to test the effect of pravastatin (Pravachol) on coronary heart disease and stroke, randomized 5804 study participants into 1 group assigned to take pravastatin and another group assigned to take

placebo. An additional study endpoint was pravastatin's effect on cognitive function as measured by 4 different tests, including the Mini-Mental Status Exam (MMSE). Overall cognitive function declined at the same rate in treatment and placebo groups. There was no significant difference between the 2 groups over 3 years using 4 different methods of assessment. In particular, the MMSE scores differed by only 0.06 points (95% confidence interval [CI], 0.04–0.16; *P*=.26).

The largest RCT of a statin agent, the Heart Protection Study, enrolled more than 20,000 people and randomized them to simvastatin (Zocor) or placebo. After a median of 5 years of follow-up, there was no difference in cognitive scores or the rate of diagnosis of dementia between the 2 groups.[2]

A systematic review concluded that no good evidence recommended statins for reducing the risk of Alzheimer's dementia.[3] Notably, the review did find a body of inconclusive evidence that lowering serum cholesterol may retard disease pathogenesis. An observational study of 56,790 charts included in the computer databases of 3 hospitals found that the prevalence of probable Alzheimer's dementia in the cohort taking statins was 60% to 73% (*P*<.001) lower than in the total patient population or in patients taking antihypertensive or cardiovascular medications.[4]

Also included in the review was a nested case-control study of 1364 patients that found an adjusted relative risk for dementia of 0.29 (95% CI, 0.013–0.063; *P*=.002) among those taking statins.[5] This study did not distinguish between Alzheimer's dementia and other forms of dementia. These studies do not demonstrate a causal relationship between statins and Alzheimer's dementia.

The best way to determine if there is a true effect of statins on Alzheimer's dementia is to conduct a clinical trial. Two ongoing clinical trials are designed specifically to determine if the use of statins delay the onset or slow the progression of Alzheimer's dementia.[9,10] To date, these trials have not published interim findings.

## Recommendations from others

No organization has issued recommendations for the use of statins to delay the onset or slow the progression of Alzheimer's dementia.

### REFERENCES


1. Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet* 2002; 360:1623–1630.
2. Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20,536 people with cerebrovascular disears or other high-risk conditions. *Lancet* 2004; 363:757–767.
3. Scott HD, Laake K. Statins for the prevention of Alzheimer's disease. *Cochrane Database Syst Rev* 2001; (3):CD003160.
4. Wolozin B, Kellman W, Rousseau P, Celesia GG, Siegel G. Decreased prevalence of Alzheimer disease associated with 3-hydroxy-3-methyglutaryl coenzyme A reductase inhibitors. *Arch Neurol* 2000; 57:1439–1443.
5. Jick H, Zornberg GL, Jick SS, Seshadri S, Drachman DA. Statins and the risk of dementia. *Lancet* 2000; 356:1627–1631.
6. Zamrini E, McGwin G, Roseman JM. Association between statin use and Alzheimer's disease. *Neuroepidemiology* 2004; 23:94–98.
7. Evans DA, Funkenstein HH, Albert MS, et al. Prevalence of Alzheimer's disease in a community population of older persons. Higher than previously reported. *JAMA* 1989; 262:2551–2556.
8. Selkoe DJ. Physiological production of the beta-amyloid protein and the mechanism of Alzheimers-Disease. *Trends Neurosci* 1993; 16:403–409.
9. Sano, M, Thal, LJ. Cholesterol Lowering Agent to Slow Progression (CLASP) of Alzheimer's Disease Study. February 3, 2003 (Last reviewed December, 2004). Available at: www.clinicaltrials.gov/ct/show/NCT00053599?order=4. Accessed on June 8, 2005.
10. Lipitor as a Treatment of Alzheimer's Disease. September 19, 2001 (Last reviewed November, 2004). Available at: www.clinicaltrials.gov/ct/show/NCT00024531?order=1. Accessed on June 8, 2005.


**FAST** TRACK

**While 3 studies have found lower incidence of dementia in those taking statins, these studies have significant methodological shortcomings**

# Do preparticipation clinical exams reduce morbidity and mortality for athletes?

**Stephen Hulkower, MD, Blake Fagan, MD, Jana Watts, MD**
MAHEC Family Practice Residency Program, Asheville, NC

**Elizabeth Ketterman, MLS**
East Carolina University, Greenville, NC

## EVIDENCE-BASED ANSWER

Though clinical preparticipation exams (PPE) are recommended by experts and required in most states, we found no medium- or better-quality evidence that demonstrates they reduce mortality or morbidity. PPEs detect only a very small percentage of cardiac abnormalities among athletes who subsequently die suddenly (strength of recommendation [SOR]: **C**, case series study). PPEs are also unable to accurately identify athletes with exercise-induced bronchospasm (SOR: **C**, small cross-sectional study) and are poorly predictive of which athletes are at increased risk of orthopedic injuries (SOR: **C**, cross-sectional study).

## CLINICAL COMMENTARY

### The PPE provides us an opportunity to address preventive health issues

Most physicians involved in screening athletes recognize the limitations of PPEs in detecting those at risk for sports-related morbidity and mortality. The history is the most important part of the examination for identifying athletes who might be at risk and should be thorough. Prepared PPE forms such as those endorsed by the AAFP and ACSM can assist in obtaining this history. Because this may be the only occasion for the athlete to see a physician, the examination is best performed by a primary care provider who can use the opportunity to address preventive health issues such as tobacco, alcohol, and drug use, depression and suicidality, sexuality, nutrition, and accident prevention. This kind of counseling is difficult to do in a group format.

**Beth Anne Fox, MD, MPH**
East Tennessee State University, Kingsport Family Medicine Residency, Kingsport, Tennessee

## Evidence summary

A systematic review of the literature on PPE identified 310 studies of athletes age <36 years. The authors searched multiple electronic databases and reviewed the bibliographies of retrieved articles but did not perform hand searches of journals or contact authors directly. The review did not find any prospective cohort or randomized trials addressing the effectiveness of clinical PPE. The 5 studies that assessed the format of the PPE concluded that it is not adequately standardized, does not consistently address the American Heart Association (AHA) recommendations for cardiovascular screening and exam, and is administered by a variety of health care professionals, some without proper training.[1]

Sudden cardiac death is defined as a nontraumatic, nonviolent, unexpected event resulting from sudden cardiac arrest within 6 hours of a previously witnessed state of normal health.[2] Such events occur in about 1 in 200,000 high school athletes per academic year (about 16 deaths in the US annually). Detection of cardiovascular abnormalities that may cause morbidity or mortality is difficult. A case series reviewed 158 sudden deaths that occurred in trained athletes in the US from 1985 to 1995. The athletes were identified from news accounts, the National Center for Catastrophic Sports Injury Registry, and informal communications and reports. The authors interviewed families, witnesses, and coaches, and they analyzed postmortem information. Of the 115 athletes who had a standard preparticipation medical evaluation, only 4 (3%)

CONTINUED

were suspected of having cardiovascular disease. The cardiovascular abnormality responsible for sudden death was prospectively identified in only 1 athlete.[3]

PPE does not accurately identify student athletes with exercise-induced bronchospasm (EIB). Of the studies on EIB, the best was a prospective cross-sectional study of 352 adolescents from 3 suburban Washington state schools. The students completed a 14-item EIB questionnaire, had a physical exam, and underwent a 7-minute exercise challenge spirometry. Complete data were available for 256 of the students. EIB was diagnosed by spirometry in 9.4% of the athletes. No student had EIB detected solely by physical exam. Using a cutoff of 2 positive questions, the questionnaire had a sensitivity of 71% and a specificity of 47%, with a negative and positive predictive value of 6% and 12%, respectively. This study concluded that EIB occurs frequently in adolescent athletes, but screening by physical exam and medical history does not accurately detect it.[4]

PPEs are not able to predict which student athletes will experience an orthopedic injury, and no controlled studies have been done to determine whether PPE prevents or reduces the severity of orthopedic injuries. A study surveyed 1204 student athletes (aged 13–20 years) from Richmond County, Georgia, who had a standardized PPE before participating in sports. The questionnaire was administered via mail or telephone and inquired about injuries sustained after the PPE. The response rate to the survey was 56%. The study found that a history of knee or ankle injury and abnormal findings on exam in male athletes slightly increased the likelihood of repeated injury of the same joint. However, the sensitivities of history or physical exam for ankle or knee injuries were all <25%.[5]

**TABLE**

### AHA recommendations for preparticipation exams

**CARDIOVASCULAR SCREENING QUESTIONS**

1. Have you ever become dizzy or passed out during or after exercise?
2. Have you ever had chest pain during or after exercise?
3. Do you get tired more quickly than your friends do during exercise?
4. Have you ever had racing of your heart or skipped heartbeats?
5. Have you ever had high blood pressure or high cholesterol?
6. Have you ever been told that you have a heart murmur?
7. Has any family member or relative died of heart problems or sudden death before age 50?
8. Have you had a severe viral infection such as mononucleosis or myocarditis within the last month?
9. Has a physician ever denied or restricted your participation in sports for any heart problems?
10. Have any of your relatives ever had any of the following conditions:
    a. Hypertrophic cardiomyopathy
    b. Dilated cardiomyopathy
    c. Marfan's syndrome
    d. Long QT syndrome
    e. Significant heart arrhythmia

**CARDIOVASCULAR SCREENING EXAM**

1. Recognition of the physical manifestations of Marfan's Syndrome
2. Blood pressure, seated position
3. Palpation of radial and femoral pulses
4. Cardiac exam to include rate, rhythm and characterization of murmurs and abnormal heart sounds.
    a. Precordial auscultation supine
    b. Precordial auscultation standing
    c. Maneuvers to clarify murmurs such as squat-to-stand, deep inspiration, or Valsalva

**CARDIAC FINDINGS REQUIRING FURTHER EVALUATION**

1. Murmur grade 3/6 or greater
2. Diastolic murmur
3. Murmur that increases with Valsalva or other maneuver

## Recommendations from others

The AHA recommends a national standard for PPE and that screening should be mandatory for all high school and college athletes before participation in organized sports, with screening repeated every 2 years, and an interim history obtained during the intervening years. Specific items are given in the **TABLE**.[6]

In 2004, the American Academy of Family Physicians, along with the American Academy of Pediatrics, American College of

CONTINUED ON PAGE 632

# What is the best way to distinguish type 1 and 2 diabetes?

**Brian K. Crownover, MD, FAAFP**
Eglin AFB Family Medicine Residency, 96th Medical Group, Headquarters Air Armament Center, Eglin Air Force Base, Fla

**Joan Nashelsky, MLS**
Family Physicians Inquiries Network, Inc, Iowa City

## EVIDENCE-BASED ANSWER

No clinical characteristic or diagnostic test is available to readily distinguish type 1 from type 2 diabetes mellitus. Although C-peptide levels, autoantibodies, and adiponectin-to-leptin ratios show some utility, they do not yet have a standard diagnostic role; research on the pathophysiology of diabetes suggests that the classic type 1 and type 2 distinctions may not be appropriate for all patients1 (strength of recommendation: **C**, based on expert opinion).

## CLINICAL COMMENTARY

### Focus on attaining optimal diabetes control goals as recommended by the ADA

Not long ago, clinicians were advised to avoid the terms *type 1* and *type 2* diabetes, because they were not very helpful in clinical management of our patients. Instead, it was suggested that we use *insulin-dependent* or *non-insulin-dependent*. The rationale is that for patients with diabetes, there is an absolute insulin deficiency due to premature beta-cell failure in type 1 diabetes, as well as a relative insulin deficiency due to insulin resistance in type 2. In addition, studies also suggest that a majority of patients with type 2 diabetes would require some form of exogenous insulin therapy after a duration of 8 to 10 years of their disease. Therefore, distinguishing between types 1 and 2 is neither clinically helpful nor cost-effective, as suggested by current review of the literature. Instead, clinicians should focus on attaining optimal diabetic control goals as recommended by the practice guidelines of management of diabetes mellitus from the ADA. Furthermore, it was also recognized that one of the hurdles of failure to reach the target goal of $HbA_{1C}$ <7.0, among patients with type 2 diabetes is the delayed use of exogenous insulin therapy. Therefore, it is imperative for clinicians to discuss with each patient with a new diagnosis of diabetes, the natural progression of its disease process and its potential need and benefit of exogenous insulin therapy in the near future.

**Vincent Lo, MD**
St. Elizabeth Family Medicine Residency Program/
SUNY Upstate Medical University, Utica, New York

## Evidence summary

Onset of diabetes in childhood with ketoacidosis and insulin dependency has traditionally been sufficient to diagnose type 1 diabetes, while onset in older, obese patients with primary insulin resistance suggested type 2 diabetes. Unfortunately, features of type 1 and type 2 diabetes may be present in the same patient, making differentiation difficult. No diagnostic studies in the literature were identified that definitively demonstrate how to separate type 1 from type 2 diabetes.

A patient's age may suggest, but does not reliably distinguish, diabetes types. A study of 569 new-onset type 1 and type 2 diabetic children and adolescents showed that older age was only weakly associated with type 2 diagnosis (odds ratio [OR]= 1.4 for each 1-year increment in age; 95% confidence interval [CI], 1.3–1.6).[2] In fact, newly diagnosed 12-year-old children have an equal incidence of type 1 as type 2 diabetes. Likewise, adults with type 2 phenotype (no initial insulin requirement) can present with positive autoantibodies typically found in younger type 1 patients. Older patients who fit this profile have

been classified as type 1.5 diabetes or latent autoimmune disease in adults (LADA).[3]

A history of diabetic ketoacidosis (DKA) also does not reliably distinguish between types 1 and 2. A retrospective chart review gathered data on adults over 18 years of age who were admitted for DKA in a urban US hospital. Many patients with DKA were subsequently diagnosed with type 2 diabetes. Rates of type 2 diabetes in patients with DKA varied by race: 47% of Hispanics, 44% of African Americans, and 17% of Caucasians had type 2 diabetes.[4]

The overlapping presence of autoantibodies in both types of diabetes limits their use (**TABLE**). Autoantibodies do predict an earlier need for insulin. One prevalence study of 101 type 2 adult patients found 20% were positive for glutamic acid decarboxylase autoantibody (GADAb), which was positively associated with insulin dependence at 4 years postdiagnosis (OR=5.8; 95% CI, 1.8–18.9).[5] Eighty percent of patients with autoantibodies required insulin compared with 41% of patients without autoantibodies. Another study in young adults with type 2 or unclassified diabetes from Sweden found 93% of patients who were GADAb+ required insulin at 3 years, compared with 51% who were GADAb– (OR=18.8; 95% CI, 1.8–191).[6]

One motivation to study autoantibody testing is a potential benefit in preserving pancreatic function. Kobayashi proposed treating those with autoantibody-positive diabetes (presumed type 1 or type 1.5) with insulin immediately, while initiating oral medications in those who test negative (presumed type 2 diabetes). This approach lacks significant patient-oriented outcome data, but his small RCT of 55 patients was encouraging. With a 3-year follow-up rate of 89%, early insulin use in GADAb+ patients preserved C-peptide levels and possibly prolonged pancreatic beta cell survival.[7] Insulin dependency, defined as needing insulin for survival, occurred in 47% of controls (who received oral sulfonylureas) and only 13% of patients receiving insulin (number needed to treat [NNT]= 4; $P$=.043).[7] The theoretical benefit is that if beta cell exhaustion can be delayed, endogenous insulin production could be maintained to assist prevention of damaging postprandial glucose spikes.

**TABLE 1**

**Antibody markers and diabetes type**

| PREVALENCE OF ANY AUTOANTIBODY MARKER | PERCENT |
|---|---|
| Newly diagnosed type 1 (Caucasian) | 73–90 |
| Newly diagnosed type 1 (African or Asian) | 50 |
| Newly diagnosed type 2 (Caucasian) | 3–22 |
| Healthy individuals | 1–2 |

*Source:* Wingfield et al 2004[1] and Maron et al 1996.[3]

Although daily variation in serum insulin levels limits its use, C-peptide levels show more promise. Random C-peptide levels were superior to fasting or glucagon stimulated levels in 1093 patients, who were followed for 3 years to confirm insulin requirements. Using a receiver operating characteristic (ROC) curve, the area under the curve for random C-peptide levels to distinguish diabetes types was 0.98 (95% CI, 0.97–0.99).[8] For patients under the optimal cutoff of 0.5 nmol/L, the positive predictive value was 96% for diagnosing type 1 and the likelihood ratio was 22.5.

Finally, the ratio of adiponectin to leptin hormone may show diagnostic merit. Adipocytes secrete adiponectin which acts as an insulin sensitizer, antiatherogenic and anti-inflammatory agent. Obesity and type 2 phenotype correlate with lower levels of adiponectin, but are associated with higher levels of leptin hormone, another molecule secreted by adipocytes. A recent case-control study of children aged 6 to 21 years analyzed adiponectin and leptin hormone levels in patients with classical type 1 and 2 diabetes, as determined by 2 pediatric endocrinologists; interestingly, 29% of the type 1 patients were autoantibody negative.[9] After plotting a ROC curve, they found the area under the curve was 0.97 (95% CI, 0.93–1.00). At an adiponectin-to-leptin ratio cutoff less than 0.7, they

**FAST** TRACK

**The classic type 1 and type 2 distinctions may not be appropriate for all patients**

found the sensitivity to diagnose type 2 was 88% (95% CI, 64–99%), the specificity was 90% (95% CI, 77–97), and the likelihood ratio for a positive test was 8.8.[9]

## Recommendations from others

The National Academy of Clinical Biochemistry and the American Association of Clinical Endocrinologists recommend against routine testing of insulin, C-peptide, autoantibodies and genetic markers.[1,10] Guidelines from the American Diabetes Association admit that many diabetic individuals do not easily fit into a distinct diagnostic category; however, they only provide criteria for the general diagnosis of diabetes, not specific criteria to distinguish type 1 from type 2.[11]

**ACKNOWLEDGMENTS**

The opinions and assertions contained herein are the private views of the author and are not to be construed as official, or as reflecting the views of the US Air Force medical department or the US Air Force at large.

**REFERENCES**

1. Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 2002; 48:436–472.
2. Macaluso CJ, Bauer UE, Deeb LC, et al. Type 2 diabetes mellitus among Florida children and adolescents, 1994 through 1998. *Public Health Rep* 2002; 117:373–379.
3. Pozzilli P, Di Mario U. Autoimmune diabetes not requiring insulin at diagnosis (latent autoimmune diabetes of the adult): definition, characterization, and potential prevention. *Diabetes Care* 2001; 24:1460–1467.
4. Balasubramanyam A, Zern JW, Hyman DJ, Pavlik V. New profiles of diabetic ketoacidosis: type 1 vs type 2 diabetics and the effect of ethnicity. *Arch Int Med* 1999; 159:2317–2322.
5. Grasso YZ, Reddy SK, Rosenfeld CR, et al. Autoantibodies to IA-2 and GAD65 in patients with type 2 diabetes mellitus of varied duration: prevalence and correlation with clinical features. *Endocr Pract* 2001; 7:339–345.
6. Torn C, Landin-Olsson M, Ostman J, et al. Glutamic acid decarboxylase antibodies (GADA) is the most important factor for prediction of insulin therapy within 3 years in young adult diabetic patients not classified as Type 1 diabetes on clinical grounds. *Diabetes Metab Res Rev* 2000; 16:442–447.
7. Kobayashi T, Maruyama T, Shimada A, et al. Insulin intervention to preserve beta cells in slowly progressive insulin-dependent (type 1) diabetes mellitus. *Ann NY Acad Sci* 2002; 958:117–130.
8. Berger B, Stenstrom G, Sundkvist G. Random C-peptide in the classification of diabetes. *Scand J Clin Lab* Invest 2000; 60: 687-693.
9. Morales A, Wasserfall C, Brusko T, et al. Adiponectin and leptin concentrations may aid in discriminating disease forms in children and adolescents with type 1 and type 2 diabetes. *Diabetes Care* 2004; 27:2010–2014.
10. The American Association of Clinical Endocrinologists. The American Association of Clinical Endocrinologists Medical Guidelines for the Management of Diabetes Mellitus: the AACE system of intensive diabetes self-management—2000 Update. *Endocr Pract* 2000; 6:43–84.
11. Genuth S, Alberti KG, Bennett P, et al. Follow-up report on the diagnosis of diabetes mellitus. *Diabetes Care* 2003; 26:3160–3167.

CONTINUED FROM PAGE 629

Sports Medicine, American Medical Society for Sports Medicine, American Orthopedic Society for Sports Medicine, and the American Osteopathic Academy of Sports Medicine, published recommendations for PPEs. They suggested a detailed history (consisting of a 16-point questionnaire incorporating AHA recommendations for cardiovascular screening), limited medical exam, and a detailed musculoskeletal exam evaluating strength, flexibility, and stability of major joints.[7]

**REFERENCES**

1. Wingfield K, Matheson GO, Meeuwisse WH. Preparticipation evaluation: an evidence-based review. *Clin J Sport Med* 2004; 14:109–122.
2. Lyznicki JM, Nielsen NH, Schneider JF. Cardiovascular screening of athletes. *Am Fam Physician* 2000; 62:765–774. Erratum in: *Am Fam Physician* 2001; 63:2332.
3. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes. Clinical, demographic, and pathological profiles. *JAMA* 1996; 276:199–204.
4. Hallstrand TS, Curtis JR, Koepsell TD, et al. Effectiveness of screening examinations to detect unrecognized exercise-induced bronchoconstriction. *J Pediatr* 2002; 141:343–348.
5. DuRant RH, Pendergrast RA, Seymore C, Gaillard G, Donner J. Findings from the preparticipation athletic examination and athletic injuries. *Am J Dis Child* 1992; 146:85.
6. Maron BJ, Thompson PD, Puffer JC, et al. Cardiovascular preparticipation screening of competitive athletes. A statement for health professionals from the Sudden Death Committee (clinical cardiology) and Congenital Cardiac Defects Committee (cardiovascular disease in the young), American Heart Association. *Circulation* 1996; 94:850–856.
7. Smith DM, American Academy of Family Physicians, Preparticipation Physical Evaluation Task Force. *Preparticipation Physical Evaluation.* 3rd ed. Minneapolis: McGraw-Hill Healthcare; 2004.

# What are the indications for bariatric surgery?

**Pamela L. Pentin, JD, MD**
Puget Sound Family Medicine Residency, Bremerton, Wash

**Joan Nashelsky, MLS**
Family Physicians Inquiries Network, Inc, Iowa City

## EVIDENCE-BASED ANSWER

No studies evaluate the commonly used indications for bariatric surgery. Consensus guidelines suggest that the surgical treatment of obesity should be reserved for patients with a body-mass index (BMI) >40 kg/m$^2$ or with BMI >35 kg/m$^2$ and 1 or more significant comorbid conditions, when less invasive methods of weight loss have failed and the patient is at high risk for obesity-associated morbidity and mortality (strength of recommendation: **C**, based on consensus guidelines).

## CLINICAL COMMENTARY

### Assessing perioperative risk and long-term complications is critical

National data indicate that more than 5 million Americans have a BMI >35. Thus the implications of recommending bariatric surgery are enormous. Patients who have undergone surgical treatment for obesity require lifelong monitoring and often nutritional supplementation, and the lifelong severe dietary restriction that follows bariatric surgery can be psychologically devastating. Psychological and behavioral factors must be carefully considered in presurgical evaluation. No standardized protocol exists for this assessment and few empiric data specify which factors predict successful surgical outcomes.

Great progress has been made in developing safer and more effective surgical procedures for promoting weight loss, yet the possibility of significant adverse effects remain. Assessing both perioperative risk and long-term complications is critical and requires a risk/benefit analysis in each case.

## Evidence summary

Because of the nature of major surgery, there are practical and ethical barriers to true randomized controlled trials (RCTs) comparing bariatric surgery with placebo or to no intervention. However, multiple RCTs have compared the weight-reducing effects of different bariatric surgical techniques against each other.[1] All studies included patients who had a BMI >40 kg/m$^2$, or a BMI >35 kg/m$^2$ with at least 1 comorbidity, such as cardiovascular disease, sleep apnea, uncontrolled type 2 diabetes, or weight-induced physical problems interfering with performance of daily life activities. It is these study inclusion criteria that, by default, have become widely accepted indications for bariatric surgery. Weight loss in all RCTs was substantial, ranging from 50 to 100 kg over 6 months to 1 year. Comorbid factors associated with obesity showed either resolution or improvement after surgery in 91% of patients.

Patients with a BMI >40 have substantially more serious health consequences and a reduced life expectancy. Obesity significantly impairs quality of life, and the risk of morbidity and mortality increases with the degree of obesity.[2] Those who are extremely obese often do not have sustained benefit from more conservative treatment. The benefits of nonsurgical treatment are significantly limited by the failure to maintain reduced body weight.

A large literature of controlled and uncontrolled cohort studies show that surgery has produced the longest period of sustained weight loss.[3] A recent meta-analysis proved bariatric surgery not only

**FAST** TRACK

**Psychological and behavioral factors as well as an assessment of perioperative risk and complications must be considered before bariatric surgery**

efficacious for weight loss, but showed that a substantial majority of patients with diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea experienced complete resolution or significant improvement of their comorbid condition after surgery.[4]

The possibility of significant adverse effects remains. The postoperative mortality rate for bariatric surgery is approximately 0.2%. Reoperation is required for up to 25% of patients within 5 years. Other complications are wound infection, staple failure, vitamin deficiency, diarrhea, and hemorrhage.[3] The long-term health effects of bariatric surgery are not well known.

### Recommendations from others

The NIH statement "Gastrointestinal Surgery for Severe Obesity" concluded that the benefits outweigh the risks and that surgical treatment is reasonable in those who strongly desire substantial weight loss and have life-threatening comorbid conditions.[2]

Clinical guidelines developed by the National Heart, Lung, and Blood Institute Expert Panel on the identification, evaluation, and treatment of obesity for adults recommend that bariatric surgery be an option for carefully selected patients with clinically severe obesity (BMI >40 or >35 with comorbid conditions) when less invasive methods of weight loss have failed and the patient is at high risk for obesity-associated morbidity and mortality.[1]

The American Gastroenterological Association (AGA) medical position statement on obesity finds surgical therapy to be the most effective approach for achieving long-term weight loss. The AGA recommends surgery for patients with a BMI >40, or those with BMI >35 and 1 or more severe obesity-related medical complication (eg, hypertension, heart failure, or sleep apnea) if they have been unable to achieve or maintain weight loss with conventional therapy, have acceptable operative risks, and are able to comply with long-term treatment and follow-up.[5]

The American College of Preventive Medicine, in its policy statement on weight management counseling, recommends limiting surgical therapy for obesity to severely obese patients, defined as BMI >40.[6] ■


**REFERENCES**

1. NHLBI Obesity Education Initiative. *Clinical Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults: The Evidence Report.* NIH Publication No. 98-4083. Bethesda, Md: National Heart, Lung, and Blood Institute; 1998.
2. NIH conference. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. *Ann Int Med* 1991; 115:956–961.
3. US Preventive Services Task Force. *Screening for Obesity in Adults: Recommendations and Rationale.* Rockville, Md: Agency for Healthcare Research and Quality, 2003.
4. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA* 2004; 292:1724–1737.
5. American Gastroenterological Association. American Gastroenterology Association medical position statement on Obesity. *Gastroenterology* 2002; 123:879–881.
6. Nawaz H, Katz D. ACPM Practice Policy Statement. Weight management counseling of overweight adults. *Am J Prev Med* 2001; 21:73–78.


## What are Clinical Inquiries?

**Clinical Inquiries** answer recent questions from the practices of family physicians. Practicing family physicians choose the most relevant questions submitted through a web-based voting system operated by the Family Physicians Inquiries Network (FPIN; online at www.fpin.org).

FPIN is national, not-for-profit consortium of family medicine departments, community residency programs, academic health sciences libraries, primary care practice-based research networks, and other specialists. Once questions are selected, FPIN editors then organize teams of clinicians and librarians to answer them based on systematic review of the world literature. Answers are developed through an explicit, systematic method:

- FPIN librarians and editors identify questions recently answered in best evidence sources (e.g. Cochrane Reviews, Clinical Evidence, the US Preventive Services Task Force, Evidence Based Guidelines, a published systematic review).
- FPIN librarians then conduct systematic and standardized literature searches of best evidence sources, Medline, and other databases in collaboration with an FPIN clinician or clinicians. If a best evidence source has been identified, the search begins from the date of the search conducted for that source. Otherwise, the searches are comprehensive.
- FPIN clinician authors then choose the highest quality original research sources, and critically appraise the research and integrate the findings in the Evidence Based Answer and Evidence Summary section of Clinical Inquiries. Authoritative sources are also quoted in the "Recommendations from Others" section of the Clinical Inquiry.
- Each Clinical Inquiry is reviewed by 4 or more peers or editors before publication in *JFP*.
- FPIN medical librarians are accountable for the thoroughness of the literature search, for recording the databases searched, search hedges used and the search terms. The details of each search is available to any interested reader (contact managingeditor@fpin.org).
- Finally, a practicing family physician or other clinician writes an accompanying commentary to provide a clinical perspective.