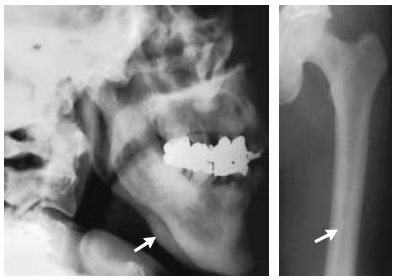
This Week in the Journal

May 16, 2002



High Bone Density Due to an *LRP5* Mutation

Osteoporosis can be caused by a loss-of-function mutation in the gene for low-density lipoprotein receptor–related protein 5 (*LRP5*). In this study, the authors, reasoning that a gain-of-function mutation in the same gene might be associated with high bone density, performed biochemical and genetic analyses of a kindred with high bone density, a prominent mandible, and torus palatinus. Genetic analysis revealed an *LRP5* mutation, the substitution of valine for glycine at codon 171, that segregated with the clinical findings. In vitro studies demonstrated that the defect in LRP5 resulted in changes in signaling events with other molecules that normally interact with this receptor-related protein, resulting in increased bone density.

The findings suggest that molecules that interact with LRP5 *may provide targets for the treatment of osteoporosis.*

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"Our results suggest that a t-PA infusion offers no significant benefit to patients with cardiac arrest and pulseless electrical activity."

Tissue Plasminogen Activator in Cardiac Arrest

Coronary thrombosis and pulmonary embolism are common causes of cardiac arrest, providing a rationale for the use of thrombolytic therapy in cases of cardiac arrest. In this study, patients with cardiac arrest and pulseless electrical activity were randomly assigned to receive tissue plasminogen activator (t-PA) or placebo in a double-blind fashion. Treatment with t-PA did not increase either the rate of survival to hospital discharge or the rate of return of spontaneous circulation.

The study was relatively small and therefore does not exclude the possibility of a small beneficial effect of t-PA or an effect in selected subgroups of patients. However, on the basis of the findings, there is little reason for optimism regarding this therapeutic approach in cases of cardiac arrest.

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PERSPECTIVE

Physicians and Addiction

A report in this issue of the *Journal* (see pages 1529–1537), describes an outbreak of bloodstream infections in an intensive care unit that was traced to an employee who was suspected of tapping into fentanyl infusions that were being administered to critically ill patients. A sample of the employee's hair showed traces of the narcotic, but he denied wrongdoing. He left the hospital, and the outbreak ceased. What is unusual is that the health care worker in question was a respiratory therapist and not a physician. When narcotics are misappropriated, the person implicated is usually a physician. But substance abuse can affect any health care worker. If the stories of such workers intrigue us, it is because of the paradox of the occurrence of addiction in people who we think should know better.

One of my medical students —a former professional tennis player — struggled with a powerful addiction, a disease that relapsed during his internship and led to his death. In an effort to understand that tragedy, I have tried to learn about the experience of addiction. I visited one of the premier centers in the United States where doctors with addiction are treated and was there on a night when all 70 or so residents gathered for their weekly "Caduceus Club" meeting. But for the fact that we were seated in a large circle, the gathering could have been grand rounds somewhere. Nothing about the appearance of these men and women differentiated them from other physicians. But when the proceedings began, I heard incredible stories of drug use, of preoccupation with a drug, of efforts at concealment — the doctor who loaded her windshield-wiper reservoir with bourbon and routed it into the cab so she could take hits between hospitals; the doctor who would catheterize himself to fill his bladder with artificial urine solution to void when he had to give a urine sample for testing; the doctor who used the pretext of a home visit to steal back the narcotics he had prescribed; the emergency medicine physician who, after a shift, would embark on a 400-mile round trip to score his drug and be back in time for the next shift. A few of the physicians had committed criminal acts in pursuit of their drugs. As varied as the tales were, the doctors had one common feature — namely, exquisite denial that allowed them to believe they could still care for patients perfectly well (including patients with addictions).

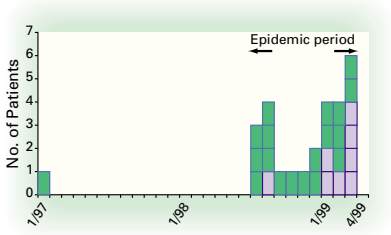
That evening, I viscerally understood something about addiction that I had only thought I understood before: addiction is truly a disease. The addicts were in its clutches and could only watch as they lost everything they had previously valued. When the physicians' secrets were discovered, they experienced great shame — but also relief, because they knew they could not help themselves.

At first glance, access to drugs would seem to explain the phenomenon of doctors' becoming addicts. Anesthesiologists, for example, are overrepresented in substance-abuse treatment programs for physicians. However, the drug most abused by all kinds of doctors is alcohol, just as it is in society at large. And other associations between particular specialties and the use of particular drugs reflect not access, but temperament. For example, cocaine abuse is more common among emergency-medicine physicians, whereas psychiatrists are more likely to abuse mood-altering drugs.

No tidy unifying theory can explain addiction in any group of people. But in my conversations with recovering physicians, I was struck by how often stress — the dysphoria brought on by residency training, a busy practice, time pressures, the threat of litigation, debt — had led to somatic symptoms. The same symptoms that, in a patient, might lead us to delve more deeply into the patient's marriage, job, drinking habits, and levels of stress and depression, instead led these physicians to engage in self-medication. (We physicians are notorious for denying the need to become a patient.) Knowledge of pharmacology gave these doctors the sense of being protected somehow from the addictive effects of a drug. But the drugs they ingested or injected rarely produced the advertised euphoria. Instead, the drug relieved the dysphoria of their existence. "I felt as if a black weight that I had carried in my chest for years suddenly melted away," a physician said to me, "and I was hooked."

The clues that might suggest drug use include mood swings, unexplained absences, repeated health problems, marital discord, bizarre working hours, medical errors, and arrests for driving under the influence. Fellow physicians often hesitate to confront a colleague who is in trouble with drugs or alcohol. We fear taking away his or her livelihood, and we fear litigation. We, too, find it difficult to see addiction as an illness. Coworkers get caught up in an addict's denial and unwittingly "enable" their drug use.

A carefully planned or even rehearsed intervention will protect patients and can save the life of an impaired physician. The intervention team should include recovering physicians as well as peers and family members. Most county and state medical societies and many hospitals have committees for helping impaired physicians. A good time for intervention is in the morning, when the physician is least likely to be under the influence of drugs. The purpose of such an intervention is not punishment but



Bacteremia Due to Tampering with Narcotic Infusions

An outbreak of *Serratia marcescens* bacteremia among patients in a surgical intensive care unit was extensively investigated. A total of 26 infected patients were identified. In a case–control study, the main risk factors were receipt of continuous fentanyl infusions and exposure to two specific respiratory therapists. Isolates from the patients were similar to isolates from the infused medication.

This large nosocomial outbreak appears to be the result of the actions of a single health care worker, whom a nurse reported for tampering with a needle and a narcotic infusion. Analysis of the worker's hair documented fentanyl exposure. With his removal from the unit, the outbreak ended.

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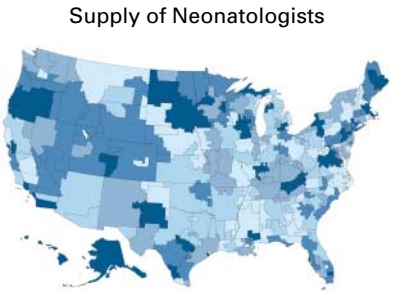

Relation between the Availability of Neonatal Intensive Care and Neonatal Mortality

Despite marked regional variation in the availability of neonatal intensive care, it is not known whether the supply of neonatologists or neonatal intensive care beds is associated with neonatal mortality. This retrospective cohort study involved almost 3.9 million U.S. infants with a birth weight of 500 g or greater who were born in 1995. As compared with infants born in regions with a very low supply of neonatologists (2.7 per 10,000 births), those from regions with a low supply of neonatologists (4.3 per 10,000 births) were less likely to die in the first 27 days of life. However, further increases in the supply of neonatologists were not associated with greater reductions in risk.

Although a few regions in the United States may have an inadequate supply of neonatologists, when judged on the basis of neonatal mortality, many other regions may have more than they need. Whether the availability of neonatologists affects other health outcomes is not known.

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advocacy. The aim is to get the physician to decide voluntarily to enter a residential treatment facility where detoxification and medical evaluation is followed by residential outpatient treatment, typically for several months. Breaking down a doctor's formidable denial requires skilled efforts. Most programs use the 12-step method, along with intense personal and family therapy. Eventually, the physician may return to work under close supervision, with random drug testing and after signing a contingency contract. In some cases, return to the doctor's original specialty may present an unacceptable risk of relapse. The good news is that physicians who go through the rehabilitation process maintain sobriety at a much higher rate than do other persons with addiction. The incentive is great: physicians cannot pursue their livelihood without a license, and any drug use will put that license in jeopardy.

In Alcoholics Anonymous circles, addiction is said to be a disease of secrecy and loneliness. Such groups work precisely because they force addicts to change their world and give up their secrets. Despite our many medical societies and fellowships, individual physicians often lead lonely lives; they carry secrets, both personal and professional, for which they have no ready outlet. We need a better understanding of the types of stress involved in medical training and practice and the nature of the dangerous dysphoria it can produce. We must be willing to teach and talk openly about the disease of addiction. Many suicides of physicians are related to drug abuse. The measure of the health of our profession is not only how well we care for our patients, but also how well we care for ourselves.

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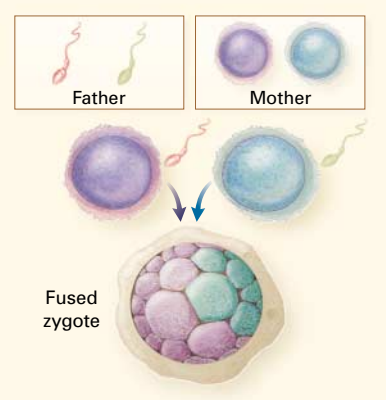

Brief Report: **Tetragametic Chimerism**

Chimerism is the presence of two genetically distinct cell lines in an organism. This report describes a phenotypically normal woman who was found to have tetragametic chimerism after histocompatibility testing of family members suggested that she was not the biologic mother of two of her three children. She had only one cell line in peripheral blood but had more than one in other tissues. Her T lymphocytes showed full tolerance of cells from family members with any combination of four familial HLA haplotypes.

Chimerism is rare but is likely to be underdiagnosed. Molecular studies to detect chimerism should be considered in cases in which the results of histocompatibility testing suggest unexpectedly that family members are not related.

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"Management of radiation exposure is difficult, in part, because of misinformation about the effects of exposure."

Current Concepts: **Major Radiation Exposure**

This article reviews possible sources of major exposure to radiation, summarizes the physical and biologic principles of radiation exposure, and describes the main syndromes. The authors explain the medical management of radiation exposure, as well as the components of preparation for crisis management.

The acute clinical effects of large doses of radiation are well known and can be assessed with simple laboratory tests.

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"If a compromise cannot be reached, no law will pass, and unscrupulous persons will continue efforts to create a cloned child."

The Stem-Cell Debate

Legislation is pending in the Congress that could affect research using embryonic stem cells. In a Legal Issues in Medicine article, Annas outlines the bill passed by the House of Representatives, the bills pending in the Senate, and the position of the current administration on these issues. In his opinion, the issue of reproductive cloning must be considered separately from issues related to therapeutic cloning if any real progress is to be made. The controversy surrounding the scientific and medical use of stem cells is further explored in two Sounding Board articles by Weissman and Evers. Weissman discusses the situation in the United States, and Evers presents the European perspective.

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