

**From the Editor**

- The Complexities of Everyday Illness** 721  
Kelly A. Carroll

**Clinical Cases**

- Controlling Diabetes** 723  
Commentary by Robert P. Hoffman

- Treating Short Stature with Growth Hormone** 727  
Commentary by Melissa D. Colman,  
David E. Sandberg, David B. Allen and Wilma C. Rossi

- Partial Androgen Insensitivity Syndrome** 739  
Commentary by William G. Reiner, David A. Diamond,  
Tammy Camp and Surendra K. Varma

**Journal Discussion**

- In the Left Corner: The Starving Endocrinologist** 748  
Christina Fradelos

**Clinical Pearl**

- After the Women's Health Initiative—  
Menopausal Women and Hormone Therapy** 751  
JoAnn V. Pinkerton

**Health Law**

- The Importance of Standard of Care and  
Documentation** 756  
Allison Grady

**Policy Forum**

- Implications of Viewing Obesity as a Disease** 759  
Joylene John-Sowa

**Op-Ed**

**Medical Ethics and Performance-Enhancing Drugs** 764  
Carlos R. Hamilton

**Steroid Hysteria: Unpacking the Claims** 767  
Norman Fost

**Upcoming Issues of *Virtual Mentor***

December: Physicians in Public Roles

January: Ethical Issues in Screening

February: Expertise in Medicine

# Virtual Mentor

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## From the Editor

Ethical discussions in medicine often take place at the fragile margins of life and death. Hospital ethics committees predominantly deal with end-of-life cases; bioethicists ponder when life begins vis-à-vis the stem cell or cloning debates. Certainly, the temporality of the human condition has fascinated men and women for thousands of years. Yet, as we focus our attention on examples such as the Terri Schiavo case, I cannot help but feel we are neglecting the more mundane medical conditions that affect a much broader group of individuals. This quest to recognize the ethical significance of everyday illness on overall health led me to devote November's *Virtual Mentor* to endocrinology, a medical subspecialty that frequently manages chronic illnesses and whose expertise resides in controlling that which often seems to control us—our hormones. But this issue of *VM* isn't just for a relatively small group of subspecialists—we all know someone who struggles with diabetes or obesity. Indeed, this is an issue we can all relate to.

Through your reading of this month's *VM*, I hope you will come to the same surprising conclusion as I: the everyday ethical dilemmas faced by endocrinologists and of concern to most of us are, in truth, anything *but* mundane. They range from the theoretical (whether or not obesity is a “disease”) to the practical (a patient's nonadherence to a diabetes management plan). As the authors lead us to discover, these questions and concerns should not be categorized so simply. The “diseasification” of obesity (and one could replace obesity with other endocrine conditions like menopause or premenstrual dysphoric disorder) has substantial practical implications for Medicare, insurance, and prescription drug coverage decisions. On the flip side, there remains a significant theoretical semantic divide between patient “compliance” and patient “adherence,” the implications thereof delineating the obligations of the physician in the patient-physician relationship.

Endocrinologists also find themselves on the front lines of certain “sexier” issues that have found play in the bioethics literature of late (and, for that matter, on episodes of “Oprah”). In clinical case 3, the authors contemplate a case of intersexuality in a newborn about which no clear consensus exists regarding assignment of sex. This case illustrates the important differences between sex and gender, theoretical questions about gender identity and patient autonomy, and pragmatic concerns regarding the timing and necessity of surgical interventions. The op-ed discusses a “hot topic” resonating in the medical literature, on ESPN, and on Capitol Hill: use of performance-enhancing hormones by athletes. Do physicians have specific obligations beyond those ascribed by law? Finally, clinical case 2 provides enough fodder for debate that *The New York Times Magazine* scooped us in mid-October. Thus, I will not describe it in detail here, but will say

only that, whether you are of short stature like me, or fairly tall like most US Presidents, you will find it of interest.

I hope that this month's *VM* provides you with insight into the complex ethical quandaries facing endocrinologists today. The field of endocrinology encompasses such a broad array of conditions that it was impossible to address them all here; notably absent are problems confronting reproductive endocrinologists, in part because the ethics of assisted reproductive technologies have been the topic of debate in prior issues of *VM*. It strikes me that while endocrinology stands as a subspecialty in medicine, its practitioners treat a large and diverse group of patients, many with well-known "general" conditions. As this month's authors indicate, endocrinologists often serve their patients as part of a team of health care professionals; I would argue that they are uniquely well-suited and well-trained to do so, considering their vast expertise in the management of chronic illnesses. Moreover, these articles demonstrate both that chronic conditions are by no means static and often not routine (for the patients or the physicians). Clinical ethicists know well that some of the most interesting ethical issues arise in daily practice, not just in what we see as acute decision points at the fringes of life; but it is difficult to gain first-hand insight into these instances which rarely warrant a consult. I am grateful to the authors for providing valuable insight into the difficult ethical matters they encounter across their patients' lifespans, which are pertinent to more than endocrinologists, and are anything *but* ordinary.

Kelly A. Carroll

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# Virtual Mentor

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## Clinical Case

### Controlling Diabetes

Commentary by Robert P. Hoffman, MD

Sharon Smith was diagnosed with type 1 diabetes at age 11. Under the watchful eye of her parents, Sharon was an active teenager, participating in high school sports and extracurricular activities. In college, she continued with soccer and diligently controlled her blood sugar, following the same insulin regimen she had begun in her mid-teens. After college, Sharon moved across the country to pursue graduate studies. To help pay her living expenses, she began working 4 days a week as a waitress. One night as her shift was ending she noticed that her hands were shaking as she was replacing glassware, and she later passed out. The restaurant staff, unaware that she was diabetic, called 911 for assistance.

Sharon was admitted to the hospital, and Dr Stone—an endocrinologist—was called. Dr Stone had seen Sharon quite a few times since her move to the city about 6 years earlier, usually after emergency episodes. When he first met Sharon, she was moderately overweight and had elevated cholesterol levels. Examining Sharon's medical records at that time, Dr Stone noted that these developments were recent. Since their initial clinical encounter, Dr Stone had encouraged Sharon to lose weight and had explained the possible complications for someone who had had type 1 diabetes for more than 5 years. Sharon claimed that she had tried to lose weight, but found it impossible to balance glycemic control with weight loss. Adding to her frustration were a bum ankle, intense graduate coursework, and her waitressing job, all of which prevented her from exercising as regularly as she had in college.

Dr Stone has attempted—numerous times—to modify Sharon's insulin regimen and provide her with a clearly laid-out dietary plan to help her lose weight and control her blood sugar. He believes some of Sharon's noncompliance might be due to depression or other psychological factors and referred her to a counselor who had worked successfully with many of his patients with diabetes. Sharon saw the counselor once but refused to continue, stating that she had neither the time nor the money to attend regular sessions. Despite Dr Stone's continued efforts, Sharon has been admitted to the hospital a number of times with recurrent diabetic ketoacidosis.

Sharon repeatedly tells Dr Stone that she understands the consequences of ignoring his advice, and she constantly expresses her annoyance with this disease, especially in relation to her living situation. Dr Stone is sympathetic to Sharon's plight—she is young, busy, and burdened with a disease that will be with her for the rest of her life. But he is frustrated by her lack of responsibility; she doesn't adhere to the diet, she sometimes cancels appointments at the last minute, and, he suspects, she has begun drinking alcohol. When he confronted Sharon about her behavior during her latest

hospital stay, she shrugged and responded, “C'mon, Dr Stone. It's not that bad. You always pull me through.”

### **Commentary**

Study after study has demonstrated that many patients—adults and adolescents, alike—with type 1 diabetes do not follow through with the numerous aspects of their diabetes care [1]. Sharon's failure to appropriately follow diabetes management recommendations may be due to a variety of problems including subclinical eating disorders, depression, fear of hypoglycemia, feelings of failure due to recurrent hospitalization, or dislike of injections and glucose monitoring.

How Dr Stone reacts to Sharon's situation will be reflected by the terminology he uses when discussing his concerns and by who he thinks is in charge of managing Sharon's diabetes. According to the American Heritage Dictionary, to adhere means to “to carry out a plan, scheme, or operation without deviation” and to comply means “to act in accordance with another's command, request, rule, or wish.” Thus, if Dr Stone believes the patient should follow his rules, and she does not, he will consider her to be noncompliant; if he believes she must help develop her own treatment plan, and she is unsuccessful, he will then view her as being nonadherent. This difference between compliance and adherence plays a critical role in answering several questions regarding Sharon's care.

#### **Is Dr Stone obligated to continue to serve as Sharon's endocrinologist?**

If Dr Stone uses the language of compliance to describe Sharon's actions, then he is not obligated to continue to care for her. Simply stated, she has not followed his prescribed medical plan and recommendations, and thus he is wasting his time caring for a patient who doesn't follow through. In this situation he is only obligated to take care of her in an emergency if he is the best available physician to do so. Once the crisis is over he can give her names of other health care professionals in the area who can care for her diabetes, as her health care coverage allows.

This course of action puts Dr Stone in a position of power over Sharon, and its ultimate purpose may be to feed Dr Stone's ego. He would do well to consider that he is most likely noncompliant in some area or areas of his own health care [2] and to remember the Golden Rule: “Do to others what you would have them do to you.”

If, instead, Dr Stone uses the language of adherence, his obligation to Sharon is different. He will have to help her develop a treatment plan for controlling her diabetes that is compatible with her lifestyle. The goal of diabetes management should always be to train and encourage the person who has the condition to assume control and responsibility for his or her treatment [3]. In this situation Dr Stone must provide Sharon with the best possible evidence-based medical advice and the basis for this advice. This approach reduces his paternalism while allowing Sharon to make choices based on his recommendations.

In this scenario Dr Stone's decision to continue or discontinue his care of Sharon is based on whether he believes he is the best person available to help her manage her

diabetes. If he feels that his frustrations with Sharon or her emotional dependence on him interferes with helping her to develop and follow an effective diabetes treatment plan, then he must tell her why this is the case and offer to assist her in finding a professional who will help her. This future care may or may not be under Dr Stone's supervision, depending on the availability of allied health care professionals such as diabetes nurse educators, dietitians, and psychologists.

### **What responsibilities does Sharon have to manage her diabetes?**

Ultimate responsibility for Sharon's diabetes care clearly falls on her. She appears to be mentally competent; she is attending graduate school and holding a job. This is not a situation in which Dr Stone has the right, responsibility, or ability to carry out medical care independent of Sharon's wishes [4].

Sharon's obligations when she was under the pediatric care team would have been much different. The responsibility for managing her diabetes would legally have fallen to her parents until Sharon reached her eighteenth birthday. Prior to her turning 18 the physician would have been required by the state to report Sharon's parents' failure to assure that she got proper diabetes care. In part due to Sharon's minor status, the patient-physician relationship would have been much more paternalistic when Sharon was first diagnosed with diabetes, although one hopes that, even at age 11, there was an attempt to involve her in some of the decisions regarding her treatment plan. If this did not happen, particularly as Sharon became an older adolescent, her current nonadherence may be traced back to her overdependence on others to keep her safe. At the other end of the spectrum, adolescents given *excessive* autonomy by their parents also have poor metabolic control [5].

Unfortunately, patient transition from the more paternalistic pediatric care model to the more autonomous adult model is not always well handled, due to factors both within and beyond the control of the physician or patient. These include insurance company and hospital regulations that govern the age of patients allowed to be seen by pediatric and internal medicine subspecialists, decisions regarding employment, advanced education, and changes in location. Because of these factors many young adult patients with diabetes are in a medical "limbo" when it comes to getting their diabetes care. It was thus critical for those managing Sharon's diabetes during her adolescence to ensure that she had the skills to take over that responsibility independently by the time she left pediatric care and to assure that she was aware of the importance of regular close followup and where this could be obtained.

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*Robert P. Hoffman, MD, is an associate professor in the Division of Pediatric Endocrinology at the Ohio State University College of Medicine and Public Health and Columbus Children's Hospital. The viewpoints expressed on this site are those of the authors and do not necessarily reflect the views and policies of the AMA.*

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# Virtual Mentor

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## Clinical Case

### Treating Short Stature with Growth Hormone

Commentaries by Melissa D. Colman, MA, and David E. Sandberg, PhD;  
by David B. Allen, MD; and by Wilma C. Rossi, MD, MBe

Mr and Mrs Malcolm are worried about the growth of their 5-year-old son, David. David was the shortest child in his preschool classes, and his parents worry that, as he enters kindergarten, he may be teased for his shortness. Looking ahead, they fear all kinds of other consequences; competitive sports could be closed to him, and dating and job finding could be more difficult than for his taller contemporaries. Mrs Malcolm is 5 ft tall, and Mr Malcolm is 5 ft 4 in. They have expressed their concerns over the course of David's last few pediatrician visits. The pediatrician, noting in David's chart that he has been approximately 3 standard deviations below the mean for height since 18 months of age, refers the Malcolms to Dr Tyson, a pediatric endocrinologist.

Dr Tyson orders several tests to determine whether David's short stature is due to an underlying pathology (eg, Turner's syndrome, renal insufficiency) or growth hormone deficiency. All tests come back negative. After a radiological evaluation, Dr Tyson concludes that David has idiopathic short stature (ISS), specifically, familial short stature; he is short because his parents are short. The Malcolms are relieved that David does not have a serious illness, but their fears and concerns are not abated by Dr Tyson's diagnosis. Mr Malcolm recalls the pain of being a short teen and still feels that people look at him awkwardly when they first meet him. A lawyer, he prefers to do most of his initial client interviews by telephone. Mrs Malcolm doesn't want her son to be shorter than girls his own age, and she fears that he could be psychologically scarred as he gets closer to puberty.

The Malcolms tell Dr Tyson that they have read on the Internet that human growth hormone therapy (hGH) is safe and effective for children like their son. They are eager to get David's therapy started as soon as possible and ask Dr Tyson to prescribe the treatment for him. When Dr Tyson begins to tell them that most insurance companies do not cover GH therapy for ISS cases, Mr Malcolm declares that they have decided to look at the therapy as an investment in David's future, as important as private school education, if not more so.

### Commentary 1

by Melissa D. Colman, MA, and David E. Sandberg, PhD

The Malcolms' worries about David's future are understandable in view of the stereotypes about negative experiences of individuals with short stature [1]. The Malcolms believe their son can be spared these problems if he receives growth

hormone (GH) therapy. With the possible exceptions of growth hormone deficiency (GHD) and Prader-Willi syndrome, for which metabolic benefits of GH therapy have been documented, the primary rationale for GH treatment has been that extreme short stature constitutes a physical disability and creates a significant psychosocial burden [2-5]. Thus treatment is predicated on the belief that GH-induced increases in height will improve the short individual's quality of life. The abundance of synthetic GH and uncertainty regarding the diagnosis of GHD [6], contribute to the controversy over who should receive treatment. Allen and Fost infer from the growing number of conditions for which GH is prescribed that "the cause of short stature is not morally relevant in deciding who is entitled to treatment" [7]. Instead, they argue that GH therapy is indicated not by virtue of a medical diagnosis but whenever a *disability* in adaptation can be attributable to short stature. Therapy should be aimed, they say, at correcting this disability through treatment up to the point that an adult height within the "normal range," ie, the 5th percentile, is attained.

### **Benefits versus Risks**

It is assumed that GH-induced increases in stature will improve child and adolescent psychosocial adaptation and adult quality of life. Growth benefits of GH treatment for idiopathic short stature, although reliable, are modest, with an average of 4 to 6 cm gained in adult height [8]. Accordingly, many individuals with ISS remain shorter than average even with treatment. Although clinic-based studies corroborate impressions that short stature is associated with psychosocial stresses like teasing and juvenilization (ie, the tendency to misperceive the individual's age and to treat that person as younger than his or her chronological age) these same studies fail to demonstrate that the experiences are associated with psychological dysfunction [9-11]. Moreover, the relationship between negative social experiences and psychosocial adaptation was weaker than the influence of demographic variables such as parental education and marital status [9].

If youths who are shorter than average, even markedly so, are psychologically as well-adjusted as those of average height, detecting psychological benefits of GH-induced increases in growth becomes a dubious pursuit. In fact, no rigorously designed studies provide evidence demonstrating that GH treatment leads to improved psychosocial adaptation in individuals with ISS [12, 13].

With regard to safety of GH, only short-term data are available for individuals receiving the doses approved by the FDA for ISS. The possibility of unforeseen risks in treating children with pharmacologic doses of recombinant human growth hormone (rhGH) [14] is particularly important to parents who report that their main concern about rhGH treatment pertains to its risks [15]. As recently noted in an editorial following the publication of 2 industry-sponsored GH safety studies in ISS [16, 17], Cuttler stated that because ISS, by definition, occurs in otherwise healthy children, decision making must consider the morbidity of the untreated state and the anticipated treatment benefits [18]. If the goal of GH therapy is to maintain positive psychosocial adaptation, then evidence must first be provided that short stature is associated with significant problems for the individual and, secondly, that hormone-

induced increases in growth ameliorate this situation. As already noted, evidence in support of these assumptions is nonexistent.

### **Age as a Factor in Clinical Decision Making**

At 5 years of age, David lacks the ability to give informed assent to GH therapy; rather, his parents' decisions and their informed consent to medical care are substitutes [19]. To be effective at increasing rate of growth or final adult height, GH administration is typically recommended during childhood before bone epiphyses have fused and growth is no longer possible. Hence treatment would need to begin before David is old enough to give either informed consent or assent.

It has been argued that GH treatment of ISS is largely a cosmetic procedure aimed at augmenting or enhancing health or beauty [20, 21]. This claim prompts us to ask whether parents—who have great influence in shaping their child's values, beliefs, and education—should be given the right to extend their decision-making role to physical manipulation of their child's appearance via a lengthy and burdensome medical intervention?

### **Information to Provide to Parents**

Good ethics are predicated on good facts, and, in this instance, it is necessary to provide David's parents with those facts. This can be accomplished by addressing Mr and Mrs Malcolm's specific concerns.

*Teasing.* Some children with short stature do report being teased, but few report difficult psychosocial adaptation as a result of that teasing. Teasing is a normal childhood phenomenon [22] and should not, by itself, be considered a predictor of undesirable outcomes. Also, because growth-promoting benefits of GH treatment are modest and variable, it would be a mistake to assume that height-related teasing will cease with treatment. David's predicted height, based on his parents' average height, is below the mean for adult males, and, even with treatment, David is likely to remain one of the shorter children in his class.

*Competitive sports will be closed to him.* Indeed, David's size may limit his participation and success in some sports. However, we do not know how important sports are to him now, or if they will be in the future. In the event that he comes to value sports, a variety of sports exist where size is not necessarily a predictor of success (eg, swimming, diving, golf, soccer) and there are some where short stature may even be an advantage (eg, gymnastics, equestrianism).

*Job finding will be difficult.* Laboratory studies suggest that people hold stereotypic beliefs that shorter people earn less or are afforded less respect; however, when research is brought out of the lab and into the "real world," the effect is diminished and open to other, nonsocial interpretations [1, 23]. In this case, Mr Malcolm appears to have a successful law practice and has found a way to cope with his perceived difficulties.

*David will be shorter than girls his age and dating will be difficult.* Throughout childhood girls are normally taller than boys because girls enter puberty and achieve their "growth

spurt” earlier than boys. The adult sex dimorphism in height (of approximately 5 inches) is related to the later onset of male puberty [24].

With regard to heterosexual dating and partner selection, although a taller male preference exists, this does not preclude shorter men from dating or marriage. Again, there is a laboratory versus real-world difference. For example, Hensley found evidence that, when asked what about the height of an “ideal partner,” women preferred taller men and men preferred shorter women; however, the magnitude of this preference was reduced when men and women were asked to report their own heights and that of their current partners [25]. Hensley concluded that shorter men are not necessarily disadvantaged; David’s parents are another case in point. Moreover, given that, in the general population, men are taller than women by an average of 5 inches, David, with a mid-parental target height of 5 ft 5 in, would be taller than about half of adult women.

### **Enhancement Medicine**

It can be argued that short stature, unless proven otherwise in the individual case, is a matter of normal variation. The FDA-approved indication of GH treatment for ISS qualifies individuals more than 2.25 standard deviations below the mean for age and sex, or the shortest 1.2 percent of children. If all children under the first percentile received GH therapy, this would shift the mean height and create a new population of those below the first percentile, who would then be eligible to receive treatment and would create a new population below the first percentile, and so on and so on.

One factor that might prevent this “creeping norm” from occurring is cost. Cost does not appear to be an issue for the Malcolm family, so it will not be addressed here other than to say that, given the expense of this treatment regimen (the annual cost for 1 child weighing 30 kg is approximately \$15 000 to \$20 000 [7] with higher pubertal doses that can exceed \$50 000 per year [26]), it is largely inaccessible to any family for whom it is not covered by health insurance. On the societal level, this would have the effect of selectively distributing short stature to the less wealthy or uninsured [19, 27].

### **Role for the Pediatric Endocrinologist**

David’s parents came in with a diagnosis, prognosis, and treatment plan in mind: that their son (1) has short stature, (2) will suffer from psychosocial problems similar to those of his father who attributes his problems to his own short stature, and (3) needs GH injections so that he is no longer “short” and will, therefore, not experience the associated psychosocial problems. This declaration places the physician in an uncomfortable situation—the parents are asking the physician to rely entirely on their report and treat a psychosocial problem (that is not currently in evidence) with a lengthy pharmacological treatment for which informed assent from the child cannot be obtained.

Pediatric endocrinologists and other health care professionals can be instrumental in countering negative stereotypes attributed to short stature as well as allaying parental concerns which are unfounded and which may be interpreted by a child as evidence that there is something “wrong” with him or her. The physician might recommend

counseling for the Malcolms to discuss their unrealistic expectations about the auxologic benefits of GH treatment in GH-sufficient youth [8]. They would also be reassured that, based on the empirical literature, short stature need not limit David's range of interests, experiences, or accomplishments. Should problems emerge, discussions of ways to cope with those problems, possibly with the assistance of a pediatric psychologist, can be helpful. Recommending that the family seek counseling may make the Malcolms feel as though they have not been heard; that the pediatric endocrinologist is recommending a psychosocial treatment for a problem they define as physical/medical. However, the converse is also true: focusing solely on the physical, medical, and pharmacological aspects limits treatment options for addressing the psychosocial adaptation problems, if, in fact, they occur.

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*Melissa D. Colman, MA, is a research associate in the Department of Psychiatry at the School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York.*

*David E. Sandberg, PhD, is associate professor of psychiatry and pediatrics in the School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York. His clinical service and research programs focus on the psychological aspects of short stature and disorders of sexual differentiation and their clinical management.*

## **Commentary 2**

by David B. Allen, MD

Ten years ago in the US, growth hormone (GH) therapy was approved only for GH deficiency, and its scarcity provided a barrier to expanding its use beyond children who were unequivocally GH deficient. Today, human growth hormone (hGH) is approved by the FDA for treatment of short stature due to Turner's syndrome, chronic renal insufficiency, intrauterine growth retardation, Prader-Willi syndrome, and severe familial or idiopathic short stature. GH is now synthesized in unlimited amounts, and the increased supply has been matched by growing demand. The consensus in the medical community is that the etiology of short stature is no longer morally relevant in deciding who is entitled to treatment. More than 40 000 US children are currently receiving treatment at a cost of between \$5000–\$40 000 per year to “correct” their short stature. Prescribing decisions therefore require balancing responsible use of costly medical resources with an obligation to do what is best for each patient.

This case highlights key ethical conundrums involved in access to GH therapy: (1) Does severe short stature in this child constitute a disability that is deserving of medical intervention? (2) What information should be provided regarding benefits, risks, and costs? (3) Is it advisable to wait until David is old enough to give assent or informed consent? (4) Should public funds or private insurance support such treatment, and, if so, how do we decide the height at which David is no longer “disabled” and further treatment would be enhancement?

As illustrated by this vignette, concerns about psychological harm during childhood and adulthood are invoked as the primary rationale for treating short stature. Based on the assumption that there is a link between stature and disability, the normal, short child's valid concern is identical to that of the growth hormone-deficient (GHD) child; namely, “I am short and I would like to be taller.” To child and parent, it is irrelevant whether the condition is a well-characterized “disease” caused by GHD, or a less understood process, as is the case in Turner's syndrome and idiopathic short stature. If “enhancement” refers to a desire for a child to be taller than he would be if left alone, then all children involved in this debate about access to GH are seeking enhancement.

But is short stature really the disability it has been made out to be? If the ultimate goal of GH therapy is improved quality of life by virtue of greater height, documentation of psychosocial impairment due to stature ought to play an important role in the initiation of GH therapy and evaluation of its efficacy. Data confirming this long-held assumption, however, are actually scarce. For instance, a recent community-based study of middle school children (many of whom were in the <5th percentile for height) failed to show a relationship between childhood short stature and psychological morbidity or reputation among peers [1]. In other words, short stature was not shown to be a predictable disability for most children.

Clearly, however, there are situations where treatment can be justified. In the case described here, a likely convergence of familial short stature and constitutional growth delay patterns can result in particularly extreme childhood short stature. The Malcolms can be told with confidence that GH therapy would likely accelerate David's growth and, within a few years, allow him to return to a normal childhood growth curve, though still at the lower height percentiles. Studies suggest that as much as 1 cm of

height per year of treatment can be added to final adult height, particularly if bone age is delayed at initiation, if treatment occurs primarily before puberty, and higher doses are used. In cases like this, where the short stature is primarily genetic and the ability to delay bone age is minimal, prediction about additions to adult height should be more conservative.

Since duration of treatment is a key predictor in ultimate increment in height, the option of waiting until the child gives assent to daily injections would diminish the response. In fact, shifting treatment years from pre-puberty (~\$10 000/year) to puberty (~\$20–40 000/year) could also add to eventual costs. Nevertheless, thoughtful pediatricians raise concerns about the potential harm of labeling an otherwise healthy child as somehow unacceptable in society's and his parents' eyes. The potential adverse effect of being labeled "sick" or "disabled" and receiving daily medical treatment remains unproved in general but merits consideration for each individual child. Other risks of GH therapy appear very low—and thus seem to be balanced favorably by the perceived benefits [2]. However, families should know that: (1) this risk assessment needs to be constantly re-evaluated as dosages used in GH therapy are increased and, (2) safety surveillance represents 20 years of experience, but not 40-60 years.

Aside from responsibly allocating health care resources, those prescribing GH must address what is truly known about the hoped-for benefit—an improved psychosocial outlook resulting from increased height. No one doubts the basic premise that there are measurable benefits in social and economic success associated with taller stature in our society. But the assumption that GH therapy can achieve these same results for short children has not been demonstrated. For example, in a recent study of patients with Turner's syndrome (TS), height at the conclusion of GH therapy did not contribute substantively to quality of life [3]. Given the other health problems confronting women with TS, these findings may not apply to other groups with short stature. On the other hand, one could argue that demonstration of a measurable benefit in quality of life should be required to justify subsidized, expensive, invasive, and long-term GH therapy for children who are otherwise healthy. To date, however, growth rate and final adult height remain the primary measures by which therapeutic success is judged by physicians and insurance providers alike.

### **When to Stop Treatment**

Determining an appropriate end-point for GH therapy remains a challenging ethical issue. The recent FDA approval for GH treatment of children with idiopathic short stature (ISS) includes a threshold for initiation (<first percentile), but provides no guidelines for termination of treatment. Attainment of an individual's predicted maximum potential for height (wherever that may fall in the adult range of height) remains a goal for many. On the other hand, if the rationale for GH therapy is alleviation of "disabling" short stature, the logical definition of therapeutic success would be an adult height no longer considered a disability. Children with extreme short stature of any cause have a rightful claim to effective treatment to become taller, but they cannot make a strong claim to be taller than others who are within the normal range and therefore are not entitled to treatment. This is not changed if parents decide

that an appropriate height for their children is taller than normal. It is difficult to justify use of private or public insurance funds to make some people taller than those in the lower range of the normal distribution. Parental expectations should not determine what treatments are subsidized, but, as implied in this case, if parents want to purchase more GH on their own to buy additional height for their son, there isn't a strong argument for preventing them from doing so.

Until evidence supports that GH treatment for short stature has some value in improving quality of life, access will be guided by predicted adult height as a surrogate outcome. Clearly, however, pressure from payers to provide quality-of-life evidence will increase. While no policy for GH therapy will eliminate those in the first percentile, a coherent policy framework would focus on bringing children into the height that confers a *range of normal opportunity* without further enhancing those who will achieve or have achieved a height within the normal adult distribution. By adhering to *treatment* of disabling short stature and resisting the *enhancement* of normal stature, physicians treating children with GH would minimize their contribution to society's perception that to be taller is to be better.

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*David B. Allen, MD, is a professor of pediatrics, director of pediatric endocrinology, and director of the Pediatric Residency Program at the University of Wisconsin in Madison.*

### Commentary 3

by Wilma C. Rossi, MD, MBe

FDA approval for growth hormone (GH) therapy for individuals with idiopathic short stature (ISS) has made cases like this one commonplace for pediatric endocrinologists.

GH treatment has received much media attention, and parents are exploring it as an option to increase stature in their short children with no medically recognized growth deficiency. In considering GH treatment of a normal child, Dr Tyson faces some ethical dilemmas. The first is efficacy. Pediatric endocrinologists disagree as to whether or not GH treatment actually increases growth in ISS and results in taller adult stature. Dr Tyson is obligated to evaluate the literature critically to determine whether GH will be an effective treatment for this patient. If not, he should not prescribe it. A frequently quoted study funded by the pharmaceutical industry demonstrated that short-statured normal children on GH ultimately achieve adult heights that are an average of 5 cm taller for boys and 5.9 cm taller for girls than their predicted adult height without the hormone [1]. This represents a minimal increase in height; these children were still short as adults. Of note, a group of children in this study did not increase their adult height at all after having been subjected to daily GH injections for an average of 5.5-6 years [1]. Critical review of this study shows that the group of children with low insulin growth factor-1 (IGF-1) levels grew better on GH than those with normal levels whose adult height did not increase. In this instance it is likely that GH was effectively treating a biochemical abnormality.

Assuming that Dr Tyson thinks that David is likely to be taller if he is treated with GH, the second ethical point to consider is the risk/benefit ratio of this treatment in patients with ISS. When used for other indications, GH appears to be safe. The metabolic consequences of GH used in ISS has been studied (again with pharmaceutical company support) with no adverse effects reported after 5 years [2]. However, since no long-term studies have been done, the potential for unforeseen complications exists. Psychological factors to consider include trauma associated with daily injections; treatment may also reinforce a negative self-image or generate a perception that short stature is a disease or disability [3].

What are the benefits of effective treatment? Severe short stature can pose physical limitations in a world that is geared to the average-sized individual. Driving a car or working at standard height desks and counters can be a challenge for the very short adult. Mr and Mrs Malcolm are convinced that short stature is associated with many other disadvantages, and Mr Malcolm attributes his own difficult social interactions to his short stature. The couple is concerned that David will be psychologically scarred by his short stature and assumes that GH treatment leading to taller stature will improve his psychosocial well-being. Although this notion has been a widely held, current data indicate that the psychological functioning of children and adults with short stature is indistinguishable from that of their peers. Moreover, studies do not support the claim that quality of life is improved after GH therapy [4, 5].

Dr Tyson should also consider whether providing David with GH is therapy or enhancement. GH therapy is routinely prescribed for children with GH deficiency, where there are few ethical dilemmas because GH is being used to treat a disease or disorder. Children with Turner's syndrome and renal insufficiency are not GH-deficient, but since they grow better on GH it is routinely prescribed as part of standard therapy in these conditions. The therapy/enhancement question is a tough one because children with ISS, though "normal," are as short when they are adults as

those with GH deficiency, Turner's syndrome, and renal insufficiency. Consequently, it seems reasonable to establish a minimum adult height below which one experiences physical limitations and, from there, to say any child who is unlikely to achieve a height above this minimum should be a candidate for GH therapy, regardless of diagnosis. The FDA arbitrarily approved GH for treatment in ISS of children whose predicted adult height fell below the first percentile, ie, lower than the height of 1 percent of adults. However, the height below which short stature is a true disability has not been determined and should be investigated. Moreover, the goal of treatment should be to achieve a normal adult height, not the maximum height that an individual can obtain. Once a child reaches a height at which his or her projected adult height is no longer associated with disability, GH should be discontinued. This approach attempts to prevent disability and normalize—rather than enhance—stature [6].

### **Social Inequities**

Matters relating to social justice should not be overlooked in the ethical analysis of GH treatment of short stature. The economic consequences of such treatment are significant. The annual cost of treatment of all children whose height falls below the first percentile for any reason including ISS, approaches \$4 billion [6]. When millions of Americans have no access to health care, should making healthy children taller be a priority? Currently, few insurers pay for GH treatment of ISS. But if society continues to medicalize short stature, insurers may be forced to pay for GH for all short children. For now, GH treatment for ISS is essentially available only to those, who, like the Malcolms, can afford to pay for it. If this inequality in access to GH were to continue, the already disadvantaged poor would become the shortest members of society.

Looking at the big picture, it's true that no matter how effective and accessible GH therapy is, someone will always be the shortest. By recommending GH treatment for ISS, society sends the message that taller is better and endorses prejudice against whoever is shortest—no matter what his or her actual height is.

After careful review of the medical and ethical issues involved in this case, Dr Tyson might assess this case as follows. David meets the FDA indication for GH therapy in ISS since his predicted adult height falls below the first percentile. A review of the literature suggests that it is unlikely that GH will benefit David since his tests, including IGF-1, are completely normal. Even if it were to benefit him, the expected increase in his height would be minimal, and he would still be a short adult. Current data does not support the theory that short stature impacts psychosocial well-being and, although the short-term risks of GH appear low, long-term risks are unknown. David may perceive that treatment of his short stature indicates that he has a serious disability, and this may reinforce a negative self-image regarding his stature. On a societal level, Dr Tyson must also consider the cost of treatment, unequal access to GH, and the “medicalization” of short stature. Weighing the potential risks—both social and medical—against the lack of evidence that David will either grow significantly taller or have improved quality of life if he does attain taller stature, Dr Tyson can confidently conclude that GH treatment is not warranted.

How do I honestly think Dr Tyson will fare in this matter? He will present all of this information to Mr and Mrs Malcolm who will still be adamant that their son be treated with GH even if there is only a small chance that it might make him taller. Dr Tyson will suggest that they monitor David's growth and re-evaluate him in 1 year and agree that he will continue to review the medical literature regarding treatment of ISS and notify the Malcolms of any new information. The Malcolms will leave the office, obviously unhappy with Dr Tyson's recommendations. The next day they will call and request that David's records be forwarded to another pediatric endocrinologist whom they will consult for a second opinion.

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*Wilma C. Rossi, MD, MBe, is a clinical associate professor of pediatrics at the University of Pennsylvania School of Medicine and attending pediatric endocrinologist at the Children's Hospital of Philadelphia.*

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# Virtual Mentor

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## Clinical Case

### Partial Androgen Insensitivity Syndrome

Commentaries by William G. Reiner, MD, David A. Diamond, MD, and by Tammy Camp, MD, and Surendra K. Varma, MD

While delivering Mrs Burdett's third child, her obstetrician observed that the baby had ambiguous external genitalia; on the evidence of the labioscrotal folds and incompletely formed penis or clitoris, the baby's sex could not be determined on sight. The obstetrician calmly answered the Burdett's question about whether their new baby was a boy or a girl by saying that some further examination would be needed. Then he called in Dr Leclerc, a pediatric endocrinologist, to explain the situation to the Burdett's and help them decide on their next steps.

Genetic tests performed the next day revealed that the baby had a 46,XY karyotype. Based on this and on the ratios of testosterone to luteinizing hormone and to dihydrotestosterone, the Burdett newborn was diagnosed with partial androgen insensitivity syndrome (PAIS). When the Burdett's learned of the diagnosis, they were sad and nearly speechless. Neither had ever heard of such an occurrence before. Dr Leclerc told them that the condition was not extremely rare and that parents of babies born with PAIS had taken a variety of approaches; some parents designated a sex for the newborn immediately and had surgery performed on the external genitalia if necessary. Other parents chose to wait until the child grew some and developed characteristics that appeared to favor one gender identity over another. But Mr Burdett protested, "I don't understand. If our child has XY genes why doesn't that make him a boy?" Dr Leclerc had been asked these questions before and knew that an overly medicalized answer would not be satisfying. He told the Burdett's that the decision about how to treat a child with PAIS was complicated by many factors beyond DNA and hormones. Understanding that Mr and Mrs Burdett were devastated by the confusion over their newborn's sex, Dr Leclerc wanted to give them all the information and options he could without making the process even more difficult. He knew, though, that most parents in the Burdett's' position ended up asking him what he would do if the child were his.

### Commentary 1

by William G. Reiner, MD

Dr Leclerc is in a unique position. He has the potential to mitigate the Burdett's' anxieties about their child's present and future growth and development while designing both a short-term and a long-range outline that can initially guide the parents and later the child. Within this framework he can begin to establish a trusting, open, and, presumably, mutually satisfying relationship. The care plan should be organized and written in a schematic format with new information and details added

as they become available—the child’s case is too complex to rely solely on parental memory. This written outline will then become a readily accessible reference for the Burdetts and everyone involved in Baby Burdett’s care. Schematics, such as charts, maintain a visual focus for clinical discussions over time. The framework should establish:

1. The overall clinical picture.
2. The clinical approach.
3. A plan for following the baby and the parents over time.

Using these techniques Dr Leclerc can gradually incorporate all clinical data, pertinent information, and answers to the Burdetts’ questions into the clinical record as they arise, while the corresponding schematic will allow the parents to have ongoing access to their child’s assessment and test results. This reference will also be helpful for all other physicians who see the baby. Dr Leclerc can immediately explain their baby’s clinical picture to the Burdetts and can share information on the baby’s overall growth and development as it occurs. But he must stress that he cannot predict their child’s gender identity with accuracy.

### **Establishing the Overall Clinical Picture**

The clinical picture of any given child begins with conception. Most of the genome is active in embryonic and fetal neuronal development. Precise gene functions or actions in brain development are mostly unknown, and it is important to emphasize to the parents that none of us ever really knows quite who or what our child is or will be at the time of its birth or how he or she will develop after birth, much less during gestation. Part of the joy and excitement, as well as the anxiety, about child rearing is this unpredictability, and any added unpredictability in a child with an intersex condition does not diminish the child. On the contrary, such a human variation may enrich the child’s life experience (although discussions of such a plausible development may not readily relieve typical parental anxieties at this time).

Physiologically speaking, the karyotype of the child is important, but causality of gender identity is separate from karyotype and has not been delineated. The Burdetts should be informed that the exact function of the genes on the Y chromosome and their actions in mediating the sexual differentiation of the brain are unknown. What *is* known and what the parents must know is that the presence of the Y chromosome by itself does *not* lead to a male gender identity.

In fact, few general relationships between sex-specific phenomena and their influences on gender identity have been discerned for typical children, let alone for children with intersex conditions. For example, the importance of the timing of prenatal hormonal effects on human brain development, or even dose-response relationships, is only poorly understood. Gender identity is a reductionistic construct that presupposes some knowledge of what identity, itself, means beyond the purely subjective and intuitive. Any concept of gender causality must preserve, explicate, and satisfy our human intuitions about what gender is.

During post-gonadal fetal development, this baby was exposed to substantial levels of androgen, but, because of the baby's partial androgen receptor defect, much of this androgen exposure was ineffective for establishing definitive male sexual differentiation. Some active androgen exposure was experienced and achieved real, but presently unknown, interactions with (other) direct or indirect Y-chromosome-induced functions.

After noting the clinical data presently available in the written outline, Dr Leclerc should convey what further data might be helpful and explain that the quantity, quality, and the timing of prenatal androgen exposure probably has a different relationship to brain development than it does to genital development—that is, the brain and genitalia do not necessarily have either synchronous or corresponding development. Then Dr Leclerc should interpret the clinical situation for the parents in lay terms: sex-assignment is important for this child, but the assigned sex may be discordant from the child's ultimate recognition of its gender.

Dr Leclerc can discuss their baby's diagnosis and the lack of urgency in this case (because of the absence of metabolic abnormalities). He can explore the parents' support systems including extended family, friends, and social contacts. He should also provide outside resources for the family. This can include a child psychiatrist, a pediatric urologist, and a nurse with specialized interests in developmental genital anomalies. Dr Leclerc can provide the names of willing individuals with similar conditions or parents in similar situations; he can direct them to web-based information for androgen insensitivity-specific or more generalized intersex support groups. Finally, Dr Leclerc can reaffirm that, despite the apparent ambiguity, their baby will know who he or she is.

### **Establishing the Clinical Approach**

A team approach to managing Baby Burdett is indicated because of the complexity and multispecialty needs of this child. The Burdetts should be encouraged to interview each of the assigned specialists. Dr Leclerc or one of the other specialists should be designated the chief spokesperson for the team. The specialized nurse would be an ideal contact and coordinating person for the parents. Other specialized personnel may not be based in the hospital, so communication or consultation with them would frequently be by telephone or e-mail. The nurse-specialist is in a good position to coordinate rapid communication among these consultants and the Burdetts.

### **Establishing the Plan for Following the Baby Over Time**

Short- and long-term plans should be established for following the baby and the parents. The outline and schematic chart will be updated whenever new information is available or decisions are made. The parents can record their own observations during their baby's growth and development in this chart. This follow-up plan provides a flexible approach for coordinated reassessments of the child at specific intervals. By providing routine input from the parents, the child, and from each of the subspecialists, the plan also encourages flexible clinical and parental strategizing as the baby's overall identity unfolds.

Unforgiving interventions should be discouraged until longer-range clinical goals are clear. One must be prudent in recommending surgical reconstructions—for that which is removed cannot be replaced. Dr Leclerc should emphasize that non-excisional reconstructions can always be undone at a later date if the child so desires, but tissues that are excised are lost. Vaginal or phallic reconstructions, for example, generally remove nothing, while genital or gonadal excision is permanent. The timing of surgery is less important than whether the surgery chosen is in the child's future best interest. Reproductive potential is a risky parameter for assigning sex. Virtually all people are sexual, but not all are reproductive. Some cannot reproduce, some choose not to, and some prefer that their mates carry out reproductive chores without their participation. A child's future (adult) desire for or rejection of reproduction is unpredictable and, hence, a poor guide for early sex-assignment decision making.

### **Conclusion**

The central theme of this approach to a baby with an intersex condition, then, is that only a given person can know who he or she is. As with each of our children, we parents must learn to adapt to our children as we (and they) begin to recognize who they are, and we must assist them in those developmental tasks and needs peculiar to each of them. Flexibility in our approach is critical because the ambiguity of the situation is ours, not the child's. The anxiety about the ambiguity is also ours. The child's privacy is important, but secrecy may be counterproductive. Indeed, as in many vital situations, openness with the child can aid in developing important bonds of mutual trust and communication between parents and child, parents and physician, and physician and child. Clinical data are unlikely to remain a secret forever. Ultimately, the parents must make the decision about initial assignment of sex, for social and legal reasons, generally within a few days of birth of the baby to about 1 to 2 weeks of age. It is important that the child's physicians aid in this decision-making process. It is also important that the child's physicians respond sensitively and remain available to the parents and to the child, over the time of the child's growth and development.

*William G. Reiner, MD, is an associate professor in the Department of Urology, adjunct associate professor in the Department of Psychiatry, and the director of the Psychosexual Development Clinic (Child and Adolescent) at the Oklahoma University Health Sciences Center.*

### **Commentary 2**

by David A. Diamond, MD

The obstetrician and Dr Leclerc have handled this difficult situation well by maintaining a calm and honest approach with the parents over the newborn child's ambiguous sex. The first order of business in the management of this child's care should be to make a definitive diagnosis of the specific intersex disorder. Based on karyotype and endocrine studies, the child appears to have a partial androgen insensitivity syndrome. This diagnosis can be further confirmed by PCR analysis of venous blood for chromosomal abnormalities of the androgen receptor. One means of explaining the abnormality to parents is to tell them that, despite an 46,XY

karyotype and the presence of a male hormone, the tissue is unable to "recognize" the hormone as it would under normal circumstances.

Findings from the physical examination and work-up need further clarification. The presence and position of gonads should be defined. The size and anatomy of the penis/clitoris and labioscrotal folds should also be determined to confirm the degree of virilization, and an abdominal ultrasound should be done to confirm absence of mullerian tissue.

The management issues for this newborn include sex assignment and appropriate treatment of the gonads and external genitalia. Partial androgen insensitivity, unlike complete androgen insensitivity, is an intersex condition for which no general consensus exists as to the better sex assignment. In other words, either sex may be assigned based on the anatomic findings. Indeed, a recent study of a modest number of partial androgen insensitivity patients raised as male or female demonstrated long-term satisfaction with either sex assignment [1]. Thus, more than 1 scenario is possible with this patient. One option may be to assign sex in the newborn period and carry out sex-appropriate surgical reconstruction.

If the decision were made to assign male sex to the child, hypospadias repair and scrotoplasty could be performed at 10 to 12 months of age. Undescended testes would require orchidopexy at this time. Although infertility is anticipated with partial androgen insensitivity, the potential for assisted reproductive techniques would be preserved.

If female sex were assigned, female genital reconstruction and gonadectomy could be performed after 6 months of age. The child would be infertile, and estrogen replacement would need to be started at the appropriate time to initiate puberty.

An alternative approach is to delay surgery for as long as possible with the hope that the child may develop a gender identity. In cases such as this, one could remain neutral until the time of anticipated puberty. Once pubertal stimulation occurs, however, the child would be virilized by the existing testes and a female sex assignment would be forever compromised. So, realistically, a relatively early decision must be made.

There are, however, risks to surgical reconstruction, the major one being an irreversible alteration in anatomy that may prove to be inconsistent with the child's developing gender identity. The technical outcomes of early reconstructive surgery have been criticized in some studies, but techniques have steadily improved, and an operation performed 30 to 40 years ago bears little resemblance to the surgery being performed today. Thus, surgical outcomes research based on the current adult population is imperfect, at best. There are also risks to deferring surgery, independent of pubertal virilization. The psychological consequences of being genitally ambiguous until age 10 or 11 is unstudied, but there has been wide speculation of distress associated with lengthy delays. Whichever course is taken, a team approach to managing Baby Burdett—including endocrinologists, urologists, and psychiatrists—is highly recommended.

### **Ethical Concerns**

The ethical issues raised by a case of partial androgen insensitivity include respect for autonomy and surrogate decision making, the meaning of informed consent, conflict between autonomy and beneficence, and veracity on the part of the treating physicians. The newborn with ambiguous genitalia must be regarded as a nonautonomous patient with the *potential* for autonomous decision making. Thus, appointment of a surrogate decision maker—most likely the parents—is necessary for decisions related to the infant's care with the understanding that, upon sexual maturity, the child will have developed a gender identity and gender orientation (choice of sexual partner). These gender decisions are unpredictable and may differ from the sex assigned by the parents and medical team years before. The standard most commonly applied by a surrogate for the pediatric patient is the "best interests standard," but in cases as complex as these, predicting what will be in the best interest of the future child is challenging for parents. This places a burden on the treating physicians to educate the parents sufficiently so they can act as responsible surrogates, capable of providing informed consent.

In a previous era, under the paternalistic model of a physician-patient relationship, physicians assumed a large—perhaps too large—a role in decision making for the infant. This attempt at beneficence usurped autonomy from the parents and has been a source of anger and frustration to some families many years after the treatment decisions were made. Honesty and good clinical judgment on the part of the treating physicians are essential for a trust-based relationship with the parents and, ultimately, the child. With these children, for whom medical science may be incapable of assuring a "right approach," physician transparency and humility seem especially appropriate. In addition, ongoing mutually trust-based relationships between the treating physicians and the maturing patient are critical in respecting the autonomy of the patient and avoiding the anger and shame experienced by some intersex patients whose diagnoses have been forced to remain secretive.

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*David A. Diamond, MD, is an associate in urology and associate clinical ethicist at Children's Hospital in Boston, Massachusetts. He is also an associate professor of surgery (urology) at Harvard Medical School.*

### **Commentary 3**

by Tammy Camp, MD, and Surendra K. Varma, MD

Cases of ambiguous genitalia are encountered by obstetricians and pediatricians with some frequency, and these health care professionals are often at a loss as to what to

tell the parents. Although pediatric endocrinologists are familiar with this dilemma, no guidelines apply to all cases; each must be considered unique.

When a baby is born with ambiguous genitalia, the parents immediately face a social dilemma. Extended family members waiting outside the delivery room and at home are anxious to know whether the baby is a “boy or a girl.” In cases of ambiguity, what should be the answer? During this time of confusion, the medical team should be cautious, using phrases such as “your baby” or “your child” rather than “he” or “she.” The infant’s genitalia should be shown to the parents, and the findings should be explained to them by the pediatrician and the pediatric endocrinologist. While the medical team may easily accept that the sex cannot be determined at this time, the sensitivity of the situation and the parents’ dilemma about what to tell the family should be considered and discussed.

Parents generally feel relief when they share the burden of a child’s physical anomalies, such as cardiac abnormalities or even facial clefts, with extended family. Unfortunately, because of its delicate and sensitive nature, parents often feel embarrassed to say that the sex of their new child is undetermined. Although there is no single “right” answer as to what parents should tell the extended family, it is our experience that parents are at greater ease if they share with their loved ones the fact that physicians are still determining the sex of the baby and that it may take a couple of days to do so because the external genitalia of the infant are not well defined.

Society’s concern about sex assignment is not a new phenomenon. Universally, one of the first questions asked after the birth of a baby is, “Is it a girl or a boy?” Throughout history, societies have been intrigued by the physical and psychosocial intricacies of reproduction and the roles of the sexes. Hence, the appearance of ambiguous anatomy is confusing and troubling.

Despite our current knowledge of the genetic and biochemical factors involved in the regulation of sexual differentiation and our ability to determine the physical adequacy (or inadequacy) of the genitalia, our approach to management of this abnormality remains problematic.

The inability of some genetic fetal males to masculinize sex duct development in external genitalia, as has happened in this case, can be divided into 2 groups: (1) a fetus that is unable to produce sufficient amounts of testosterone and dihydrotestosterone, or (2) fetal tissue that is unable to respond to and absorb androgens that are present in normal amounts [1].

Normal sexual differentiation requires the coordinated interaction between chromosomes, gonads, hormones, anatomical structure, and psychobehavioral factors. All of these factors combine to develop male or female characteristics. Infants with ambiguous genitalia are generally evaluated by a multidisciplinary health care team that includes a pediatric endocrinologist, geneticist, pediatric surgeon, urologist, ethicist, social worker, psychologist, psychiatrist, and nurses. After a comprehensive evaluation of the infant, this team assumes, along with the parents, the responsibility of assigning

the child a male or female sex and initiates a short- and long-term management plan, including medical and surgical treatment. In the past, the health care team's approach was more paternalistic and usually provided the parents with only basic information about the pathophysiology and possible cause of their baby's ambiguous genitalia. In our experience, it has been critical to involve the parents in the decision-making process.

The factors considered for proposing sex assignment include the size of the phallus and, most importantly, how this infant will be able to function as an adult. The judgment as to whether the baby would be better off as a nonreproducing, sexually functioning woman or a sexually impotent man possibly *with* reproductive capabilities must be made with careful evaluation, sometimes necessitating a second opinion [2]. It is desirable that the individual be able to function sexually with or without intercourse and that the individual be able to realize satisfaction and pleasure from sexual relations and activities. If necessary, psychiatrists or psychologists can help stem, avert, or manage dysphoria or psychiatric disturbance resulting from the condition.

Surgical correction should be carefully planned. It should be done by the time the infant is 6-12 months old so that as a toddler, the child does not consider himself or herself different from other children of the same age. We have learned that the goal of treatment should be to promote existence of an individual who is satisfied with his or her physical appearance and has a good quality of life.

It should be emphasized again that, even among infants with the diagnosis of partial androgen insensitivity, every child and family need to be evaluated individually. A child's sense of maleness or femaleness is not fixed at birth. Parents should be given accurate, easy-to-understand information, and ample time to help decide the sex of their newborn without feeling pressured to make a hasty choice. It should be explained that ongoing care and treatment will be required throughout the baby's childhood and perhaps on into adulthood. Medicine has not been able to provide all the answers or solve all of the problems associated with PAIS. There is some debate about whether it would be better for these individuals to make their own sex assignment decisions and, if so, when that decision would best be made. It is also debatable whether parents should bear the ultimate responsibility for making treatment and sex assignment decisions for their infant child [3].

It is hoped that, with advances in surgical techniques and procedures to treat intersex abnormalities and with better medical and psychosocial support for patients and their families, the quality of life experienced by individuals who are affected by syndromes of ambiguous genitalia will be further improved.

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*Tammy Camp, MD, is an assistant professor of pediatrics at Texas Tech University Health Sciences Center in Lubbock, Texas. She is also the assistant residency program director in pediatrics and is a practicing general pediatrician.*

*Surendra K. Varma, MD, is a distinguished professor of pediatrics and vice-chair of the Department of Pediatrics at Texas Tech University Health Sciences Center School of Medicine in Lubbock, Texas. He holds a joint appointment in the Department of Physiology and is the residency program director in pediatrics. Dr Varma is currently chair of the Endocrinology Section of the American Academy of Pediatrics.*

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# Virtual Mentor

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## Journal Discussion

### In the Left Corner: The Starving Endocrinologist

by Christina Fradelos

**Levetan CS, Jablonski KA, Passaro MD, Ratner RE. Effect of physician specialty on outcomes in diabetic ketoacidosis. *Diabetes Care*. 1999;22:1790-1795.**

Since the time of Hippocrates, physicians have been ethically bound to practice within the scope of their expertise [1]. When a physician is confronted with a patient whose care requires treatment beyond the physician's training, a specialist is summoned to examine the patient more effectively. A physician who specializes in endocrinology is frequently asked to treat patients with diabetes, reproductive complications, or hormone deficiencies. Under the recent pressures of managed care, however, more and more primary care physicians are themselves administering medical treatment previously delegated to endocrinologists [2]. This, along with decreasing enrollment of physicians entering training fellowships in endocrinology, bears the early signs of an ensuing crisis in this area of specialized treatment [3].

Consider a study that sought to determine whether endocrinologists' care of patients hospitalized for diabetic ketoacidosis (DKA) was more cost-effective than care by general physicians. In the US more than 100 000 people are hospitalized every year for DKA, accruing over \$65 billion in hospital charges annually. The study investigated 257 DKA patients over a period of 3½ years and logged physician specialty, length of patient stay (LOS) in the hospital, and re-admission rates for each patient treated [4].

### Results

The study found that the average LOS for endocrinologist-treated patients was shorter—3.3 days—than the average LOS for generalist-treated patients, which was 4.9 days. The endocrinologist-treated group also had a re-admission rate one third (2 percent) of the rate of the generalists-treated group (6 percent). Since DKA patients treated by endocrinologists had shorter hospital stays they also incurred lower hospital charges (mean \$5463) than did patients treated by general physicians (mean \$10 109). Therefore, the authors conclude, endocrinologists "provide more cost-effective care than generalists" [5], a fact the authors attribute to the "greater experience, more narrow area of focus, and the time these specialist dedicated to continuing education in the field of diabetes" [6]. The medical implications of these findings were not specifically addressed.

The study controlled for factors—including age, sex, and severity of illness—that might affect a patient's recovery and re-admission rate regardless of treatment.

### **Shortcomings**

The study was conducted in a large inner-city hospital whose patient demographic may not represent that of an average community-based hospital in other parts of the US. Socio-economic factors, such as the employment status or insurance plans of each patient, were not considered and may have influenced the patient's past care and desire to stay hospitalized. Similarly, patient autonomy was not discussed. The study neglected to give possible reasons why a patient might have preferred a general physician over a specialist or the possibility of a patient's having requested or refused additional testing. These are significant contributions to patient outcomes that may not be retrievable from medical records alone.

The study also failed to detail the qualifications, demographics, and treatment patterns of the physicians studied. There are many types of physicians: young, old, those who prefer family or general practices, those with better bedside manners, and so on. Endocrinologists, especially, vary in the type and extent of training they receive in particular disorders and technologies after initial certification. Without specific criteria to clarify the physician's background and training, the researchers risked blurring the distinction made between generalists and endocrinologists—a fundamental aspect of the study.

Yet the greatest weakness of this study lies in the exclusively economic endpoint it chose to consider. The study's primary focus is the financial cost-benefit of treatment by specialists versus treatment by generalists. It does not adequately represent their respective *medical* advantages or disadvantages which, ethically speaking, harbor greater significance.

### **Implications**

Aside from these shortcomings, however, the study highlights a number of important issues facing endocrinologists today. One question that comes to mind is why this group of endocrinologists was inspired to promote their discipline as *financially* friendly. Are endocrinologists feeling threatened within the general medical profession, and are articles like this one trying to counteract this fear? Are general physicians, themselves under the financial constraints of managed care, infringing on the endocrinologists' area of expertise? Why has there been a recent decline in the number of physicians entering training fellowships in endocrinology? Are young physicians faced with other career obstacles that discourage them from further training? Are patients, or their insurance policies, preferring general physicians over specialists these days? These questions, their answers, and their ethical implications apply not only to endocrinologists but to all specialists and generalists alike and will certainly require further discussion by the entire profession.

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# Virtual Mentor

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## Clinical Pearl

### **Post Women's Health Initiative—Menopausal Women and Hormone Therapy**

by JoAnn V. Pinkerton, MD

In July 2002, the first results from the Women's Health Initiative (WHI) trial found an increased risk of heart disease, breast cancer, deep vein thrombosis, stroke and gall bladder disease for post-menopausal women who received hormone therapy [1]. Although this study primarily targeted older women—the average age was 63—it raised the question: “Who are appropriate candidates for hormone therapy (HT)?” The study results suggested a narrower use of HT than expected: women who may be appropriate candidates for hormone therapy include those under 40 with premature menopause as a result of surgery or endocrine-system deficiencies; women with symptoms of menopause who don't respond to lifestyle adaptations; and older menopausal women who experience persistent severe symptoms and bone loss.

#### **The Women's Health Initiative**

The Women's Health Initiative was a prospective, randomized, double-blind, placebo-controlled study of more than 16 000 healthy, postmenopausal women between the ages of 50 and 79, who received either estrogen plus progestin [EPT] (0.625 mg CEE/2.5 mg MPA), estrogen alone [ET] (CEE 0.625 mg), or a placebo. The primary outcome studied was the effect of the 2 treatment types on prevention of cardiovascular disease (coronary artery disease and stroke), breast and colorectal cancer, and bone fractures. A separate study of women over 65 enrolled in the WHI assessed the effects on dementia and Alzheimer's disease (see table). Neither study was designed to assess the effect of the specific hormone treatment on hot flashes or vaginal dryness. Four percent of WHI participants had moderate to severe vasomotor symptoms (ie, hot flashes).

### Event-Attributable Risk or Benefit Per 10 000 Women/Year\*

	EPT Arm <sup>7</sup>	E Arm
<b>CHD</b>	<b>Risk (6)</b>	<b>Benefit (5)</b>
<b>Breast Cancer</b>	<b>Risk (8)</b>	<b>Benefit (7)</b>
<b>Dementia</b>	<b>Risk (23)</b>	<b>Risk (12)</b>
<b>Stroke</b>	<b>Risk (7)</b>	<b>Risk (12)</b>
<b>Venous Thromboembolism</b>	<b>Risk (18)</b>	<b>Risk (7)</b>
<b>Pulmonary Embolism</b>	<b>Risk (8)</b>	<b>Risk (3)</b>
<b>Colorectal Cancer</b>	<b>Benefit (6)</b>	<b>Risk (1)</b>
<b>Hip Fractures</b>	<b>Benefit (5)</b>	<b>Benefit (6)</b>
<b>Total Fractures</b>	<b>Benefit (47)</b>	<b>Benefit (56)</b>

\*Numerals in parentheses indicate absolute increases in risk or benefit attributable to either EPT or ET. That is, a risk (or benefit) of 6 means that 6 additional cases of a given outcome were experienced (or avoided) among subjects who received HT than among subjects on placebo [1-8]. Source: WHI

The WHI findings suggest that older women should *not* take hormone therapy to prevent heart disease or Alzheimer's disease. In the absence of clinical trial data for various estrogen and progestin compounds, the clinical trial results should probably be generalized to all agents within the same family, especially with regard to adverse effects. In particular, many women are requesting “bio-identical” hormones, which are either FDA-approved hormones or hormones compounded by pharmacies prepared in unique individualized dosage forms. The scientific evidence regarding both safety and efficacy for compounded therapies is currently lacking, and thus the same generalized risk and benefit data should apply.

#### Menopausal Women

Women often start hormone therapy at menopause to control vasomotor instability or urogenital atrophy or to prevent bone loss. Seventy-five percent of HT users initiate therapy within 5 years of menopause. In a 1999 national survey, 24 percent had used HT—3 percent EPT for =5 years, and 10 percent used ET for =5 years. In addition to over 90 percent relief of vasomotor symptoms, estrogen therapy has been found to improve (particularly REM) sleep, thus mitigating the fatigue associated with sleep disturbances [9].

Women often stop hormone therapy because of fear of breast cancer; hormone therapy-related bleeding; side effects such as breast tenderness, bloating, headaches, or mood changes; resolution of symptoms over time; fear of long-term use, or because they prefer natural methods.

#### Current Position Statements

The FDA has approved hormone therapy for the treatment of moderate-to-severe vasomotor symptoms associated with menopause, the treatment of vulvar and vaginal atrophy, and the prevention of postmenopausal osteoporosis [10].

The 2004 American College of Obstetricians-Gynecologists executive summary on hormone therapy states that, for selected women, HT remains an effective treatment for controlling vasomotor symptoms or vaginal atrophy and for retarding osteoporosis [11]. An individualized risk/benefit analysis by the physician and patient is recommended along with informed discussion before initiation of HT and periodic re-assessments after it is prescribed. In older postmenopausal women, the risks of HT are often felt to exceed the benefits for the prevention of chronic diseases. Future research is needed to clarify optimal timing and duration of hormone therapy because many believe that recent data does not address the effect of HT during or soon after the menopausal transition, its subsequent impact on disease processes, or the benefits and risks in women with premature menopause.

The 2004 North American Menopause Society Position Statement 12 on HT states similarly that the primary indication for systemic HT is the treatment of moderate-to-severe menopausal symptoms. Local estrogen is recommended for moderate-to-severe vulvar and vaginal atrophy. The primary indication for progestin is endometrial protection. HT should not be used for first or second degree prevention of coronary heart disease (CHD) or stroke. The lowest effective dose of HT for the shortest duration needed is recommended. Candidates for extended use of HT include women who decide, after thoughtful discussion with a physician and in the context of ongoing medical supervision, that the benefits of symptom relief outweigh risks. Such decisions usually follow a failed attempt to withdraw from HT. Other possible candidates are women with moderate-to-severe menopausal symptoms who are at high risk for osteoporotic fractures and women at high risk for osteoporosis for whom alternate therapies are not appropriate.

### **Lower Doses of Hormone Therapy**

Research findings show that lower doses of EPT and ET relieve vasomotor symptoms, prevent vaginal atrophy, are associated with a reduced incidence of endometrial bleeding—especially in the early months of therapy—provide effective endometrial protection, and prevent early postmenopausal bone loss [13-16]. These lower-dose options provide clinicians and patients with expanded options for individualizing ET/EPT.

### **Counseling Women about HT**

When counseling women, it is important to document each individual woman's reasons for considering ET/EPT (eg, quality-of-life, severity of symptoms), consider the individual risks and benefits of short-term ET/EPT use, and review indications for ET/EPT annually. The WHI data are not relevant for women with premature menopause or for symptomatic menopausal women. For women younger than 50 or those at low risk for CHD, stroke, osteoporosis, and breast or colon cancer, the absolute risk or benefit from ET or EPT is likely to be even smaller than for the women in the WHI, although the relative increase in risk may be similar [17-18].

### **Non-HT Alternatives for Menopausal Symptoms**

Lifestyle modifications may provide limited relief for women with mild symptoms or those for whom hormone therapy is not desired, not recommended, or

contraindicated. Possible lifestyle changes include exercise, cooling body core temperature with fans or layered clothing, avoiding hot and spicy foods that may trigger hot flashes, paced respirations, or other relaxing activities.

Alternative nonprescription therapies being studied include phytoestrogens/isoflavones, soy-derived dietary supplements, red clover, and black cohosh. Studies have shown no significant effect over placebo on hot flashes with Vitamin E, dong quai, ginseng, and evening primrose oil [19, 20]. For many alternative or complementary products, side effects and drug interactions occur but are not well known. Long-term safety and efficacy data are lacking. Small pilot studies suggest efficacy on hot flash reduction with low dose antidepressants and gabapentin [21, 22]. Long-term, adequately powered, randomized, placebo-controlled clinical trials with defined entry criteria are needed.

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*JoAnn V. Pinkerton, MD, is medical director of Midlife Health Center and professor of obstetrics and gynecology at the University of Virginia, in Charlottesville.*

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# Virtual Mentor

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## Health Law

### The Importance of Standard of Care and Documentation

by Allison Grady

On first glance, the case of *Conner v Ofreneo* might not seem that compelling. The alleged infractions took place in Chicago, Illinois, and litigation never went beyond the Illinois Appellate court. But if one looks beyond its regional nature and lack of precedent setting, aspects of this trial are important and interesting, especially for physicians. The case was settled in favor of the defendant, Dr Danilo Ofreneo, during the original jury trial. The decision was later affirmed by the appellate court. Yet the case should serve as a warning to all physicians: adherence to practice standards of care and documentation are essential and should not be compromised without good reason.

On February 5, 1980, Deborah Conner took her daughter, Karla (whose age is never disclosed in the appeals court's opinion), to Chicago's Uptown Clinic. Karla had been experiencing excessive thirst, slurred speech, abdominal pain, rapid weight loss, and significant bladder activity [1]. At the clinic, the Connors met with Dr Danilo Ofreneo who spent 15-20 minutes with Karla, during which time she was unresponsive to his questions. Dr Ofreneo did not document any medical history or record any allergies or immunizations; he stated during his testimony that Karla's history was within "normal limits" [1]. Unsure of a definitive diagnosis, Dr Ofreneo ordered blood tests and several x-rays. After the tests were completed he told Ms Conner to call him if anything new developed and to check with the office in about 3 days for the test results. Dr Ofreneo conceded to the court that he did not tell the Connors when to return to the office [1]. Concerned about Karla's worsening condition, Ms Conner took her to Children's Memorial Hospital later that same day where she was examined and had tests run by the hospital staff. It was found that her glucose level was 1126 (compared to the normal level of 126), and she was diagnosed with dehydration, poor circulation of blood to the brain, severe metabolic acidosis, and complications of diabetic ketoacidosis (DKA) [1]. The ketone levels of her urine and her dehydration were discovered when the treating doctor learned by taking Karla's history of her rapid weight loss, increased sleeping, and intense drinking and ran tests to uncover an explanation for these symptoms [1]. Karla was treated for dehydration, acidosis, and high ketone levels [1]. Treating the dehydration and DKA simultaneously was complicated, and the procedures to correct both were high risk. Karla experienced heart failure during the treatment phase and later died. The official cause of her death was listed as cardiorespiratory arrest that caused irreversible brain damage [1]. Following the death of her daughter, Deborah Conner sued Dr Ofreneo for medical malpractice and Children's Memorial Hospital, with whom she settled out of court.

This case is important for 2 reasons. First, it brings attention to the role of standard of care. Standard of care can be defined as "...not a guideline or list of options; instead, it is a duty determined by a given set of circumstances that present in a particular patient, with a specific condition, at a definite time and place" [2]. In other words, standard of care is sensitive to time, place, and person. This is a challenge to physicians who try to adhere strictly to clinical guidelines because the absence of absolute standards forces physicians to make judgments that may prove in hindsight to have been incorrect.

In this case, it appears that Dr Ofreneo missed the typical signs and symptoms of DKA. Patients afflicted with DKA typically present with "nausea, vomiting, and particularly in children, abdominal pain" [3]. Dr Ofreneo's decisions not to test the patient's glucose level or do a urinalysis also proved to be poor decisions. A prominent medical manual states that "a presumptive bedside diagnosis is justified if the patient's urine or blood is strongly positive for glucose and ketones" [3]. Had Ofreneo performed these simple tests he would have found that Karla's glucose level of 1126 was almost 10 times the norm, but instead he claimed that "Karla had no signs or symptoms specifically indicating that condition [DKA]" [1]. Although the jury found that Ofreneo had not deviated from standard of care, the symptoms that Karla was experiencing were identical to those of DKA, and it seems that he did not make the best medical treatment decisions. In his article, "A Model for Validating an Expert's Opinion in Medical Negligence Cases," Howard Smith reminds doctors that "the standard of care is a measure of the duty practioners owe patients to make medical decisions in accordance with any other prudent practioner's treatment of the same condition in a similar patient" [2]. This definition of standard of care, coupled with the ability of the physicians at Children's Medical Hospital to affirmatively diagnosis Karla based on an interview and routine tests, suggests that Ofreneo was not as diligent as he should have been.

The second aspect of medical care that this case highlights is the need for a physician to document a patient history thoroughly. Documentation is important, secondarily, for the legal protection that it affords. The primary purpose of the documentation is to provide the physician with a record of a patient's history and other details that he or she might not otherwise remember between visits. In a recent *Student BMJ* article, the author explains that "the patient's narrative gives important clues as to the diagnosis and the patient's perspective..."[4]. In this case, even though Karla was nonresponsive, her mother would have been able to fill in some of the history. Karla's own lack of response might also have been indicative of more serious health problems.

Taking a complete history is not always possible, especially in an urgent care situation, but a diligent effort should be made to engage both the patient and the patient's caregiver. Histories do not serve simply as footnotes in a chart but should be ongoing conversations with the patient or the patient's caregiver so that the physician can establish patterns and trends and provide the best possible treatment course. In taking a history, the physician listens to the patients' past medical experiences and hears how the patients perceive their own illnesses. As stated in the *Student BMJ* article, "to a large extent, this means making sense of the symptoms that the patient presents with...You

can attempt to link the symptoms to the diagnosis” [4]. A verbal exchange with the patient, however, is not the only responsibility of a doctor. Physicians must also *write down* the responses of the patient as well as their own medical impressions of a particular situation. Ofreneo did not document allergies, past illnesses, or vaccinations that might have provided clues about Karla's current condition [1]. As a result he was forced to give testimony from memory. Luckily for him, the jury found that this shortcoming was not a significant factor in Karla's death.

Ethical, as opposed to legal, responsibility might rest at least in part on Dr Ofreneo. His failure to recognize some of the obvious symptoms of DKA may have contributed to pushing Karla's illness to a critical level. The jury found that he did not deviate enough from the accepted standard of care to be legally liable, but he seems to have failed in his professional obligation to recognize and treat a serious illness. The professional duties of a physician extend beyond the clinical encounter. Physicians must effectively communicate with the patient, his or her caregivers, and other members of a patient care team. Dr Ofreneo's failure to accomplish this puts him in a compromised ethical position.

Based on the court records, Dr Ofreneo is lucky that his defense was presented to a sympathetic jury. His professional conduct with Karla Conner appears to have met minimal basic standards, and his medical decision making seems to have been weak, at best. It is vital that physicians learn from this case that they must be aware of the symptoms and patterns that a patient has been experiencing—information often best gathered via a complete medical history and a thorough exam. Physicians should also adhere closely to standards of care as a general rule and, before deviating from them, be convinced that the planned departure is soundly justified.

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# Virtual Mentor

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## Policy Forum

### Implications of Viewing Obesity as a Disease

by Joylene John-Sowah, MD, MPH

The American Medical Association (AMA) has a longstanding history of commitment to the betterment of the public's health and to the eradication of obesity on all fronts that stems back even further than the Surgeon General's Call to Action [1]. AMA policy *H.150.953* includes the statement that the AMA:

urges physicians as well as managed care organizations and other third-party payers to recognize obesity as a complex disorder involving appetite regulation and energy metabolism that is associated with a variety of comorbid conditions...[and to] work...to educate physicians about the prevention and management of overweight and obesity in children and adults...[The AMA] urges federal support of research to determine...the causes and mechanisms of overweight and obesity...[and] urges the appropriate federal agencies to work with organized medicine and the health insurance industry to develop coding and payment mechanisms for the evaluation and management of obesity [2].

Resolution 421 (A-04), introduced at the 2004 Annual Meeting of the AMA by the delegation of the Medical Society of the State of New York and referred to the Board of Trustees, asked:

That the American Medical Association urge the Centers for Medicare and Medicaid Services (CMS) to change the coverage issue for bariatric surgery so that obesity with the appropriate body mass index (BMI) is in itself considered as the appropriate criteria for coverage of this service under the Medicare Program; and

That the AMA urges CMS to recognize that obesity is a disease unto itself and Medicare beneficiaries should not be discriminated against by the requirement of a co-morbidity before having their disease treated [3].

That second point places the AMA in a bit of an awkward position since the AMA has neither policy nor a position statement to the effect that we have explored the science and do, in fact, consider obesity a disease. The absence of such policy makes it difficult to request that another national agency of recognized authority take that particular position. The closest the AMA has come to a formal position on qualifying

obesity is in policy *D-440.980 Recognizing and Taking Action in Response to the Obesity Crisis* which states that:

Our AMA will: (1) collaborate with appropriate agencies and organizations to commission a multidisciplinary task force to review the public health impact of obesity and recommend measures to better recognize and treat obesity as a chronic disease [4].

Additionally, policy *H-160.938 Disease-Specific Self-Management Programs* says the AMA “will seek to have physician-directed benefits of evidence-based, disease-specific education and self-management training provided to the beneficiaries of Medicare, Medicaid, other publicly supported programs, and all other payers” [5].

By way of background to this debate, those who argue that obesity is a disease often claim that “obesity is a physiological dysfunction of the human organism with environmental, genetic, and endocrinological etiologies” [6]. Obesity modifies vital bodily processes, places excess burden on the heart, alters pulmonary functions, and increases stress on weight-bearing joints. Disease-model proponents would also argue that overweight and obesity are associated with large decreases in life expectancy [7]. It is harder to point to characteristic signs and symptoms that are diagnostic of the “disease” because the only sign or symptom of obesity is obesity—ie, excess adipose tissue.

Those on the other side of the argument may say that obesity is an overproduction of adipocytes and that overproduction is not necessarily an impairment. They may go on to say that the tendency of the body to increase fat stores is a useful biological adaptation that has only been identified as dysfunctional because of drastic changes in the health care economics environment [8]. They may point to the fact that the “characteristic signs and symptoms” criterion for calling a condition a disease is weak at best in the case of obesity. They may even argue that, while it is true that obesity has been linked to the development of other disorders, a direct causal relationship has yet to be established.

The present commentary does not attempt to decipher the arguments over whether or not obesity is a disease. The topic tends to arouse passion in many a scientist, physician, public health official, and other professional, and one can debate either side of the argument until blue in the face—indeed many do. Moreover, a corollary to *D-440.980, Resolution 421, D-440.971 Recommendations for Physician and Community Collaboration on the Management of Obesity* asks that the AMA:

...work with the Centers for Disease Control and Prevention to convene relevant stakeholders to evaluate the issue of obesity as a disease, using a systematic, evidence-based approach... [9]

Since 2 sides of the question are already being addressed, this commentary sets out to explore a third side of the discussion, namely, *what is the goal of the debaters and can we reach this goal without having the argument?*

The answer to the question, “What is the goal?” is easy enough. It is found in the first concern that Resolution 421 addresses—coverage and reimbursement for bariatric surgery as treatment of obesity. We’ll take this a step further and say that the goal is not reimbursement solely for bariatric surgeons but for all physicians who manage obesity.

It is safe to say that the AMA has demonstrated willingness to promote the idea that obesity is a public health menace that must be recognized as a potential threat and subsequently and effectively dealt with. Hence, the AMA and debaters on all sides agree on the same endpoint, namely, that obesity *is* a *major* public health problem and that it is poised only to worsen unless given the societal, federal, public health, and financial endorsement needed to confront effectively a health threat of its magnitude. All sides also agree that a very effective method of achieving widespread treatment for any condition is ensuring that those who treat it, even in uncomplicated cases, are reimbursed for their services. So why the AMA emphasis on CMS? Simple. It is well established in the health arena that once CMS sets a precedent for covering medical conditions under Medicare and Medicaid, other health care payors follow suit.

But do we have to call obesity a disease in order to attain this goal? Perhaps not. To borrow from the words of the AMA's Council of Scientific Affairs (CSA) Report 4:

It is true that the ability to call a condition a disease gives enhanced credibility to the condition and its outcomes. It allows the public health community to feel confident and justified about the call to action and enlisting aid to fight the condition's untoward effects. To classify a condition as a disease strengthens public health's voice and position. In the case of obesity, it may even help enlist the aid of the government, scientific revenues, and social concern that is lacking in the current effort to control the epidemic, [and] it is true that obesity [and its] related illnesses deserve far more attention than they currently receive. Even if obesity is not classified as a disease, its public health impact is severe enough that the AMA *should* advocate strongly for policies such as reimbursement for management of obesity alone in addition to its co-morbid conditions and increased awareness of its effects” [9].

Classification as a disease may not be the only approach that will attract the public health backing, the federal recognition, the social limelight, and the financial support we need to make headway as a community in controlling the spread of obesity. I tend to see parallels in this argument with the recent nomination of Harriet Miers to the Supreme Court. There was major outcry since she had never been a judge, and many seemed to feel that she was thus poorly qualified to be a member of the Supreme Court. The administration’s strategy was to point out quickly that this is not an unprecedented move, since 29 prior Supreme Court justices had no previous judicial history. Okay, the original 9 justices notwithstanding, we can again take a further step back and point out that, to date, there has been no lasting legacy of poorly performing Supreme Court justices (presidents, yes, justices, no). Therefore, one does not have to

have been a judge in order to be a satisfactory justice. Same way with obesity; it does not necessarily have to be classified a disease before it can be reimbursed.

Let's look at other medical conditions that have gone the same route, by which I mean conditions that do not meet all the criteria for "diseases" but for which treatment reimbursement is currently received. The CSA Report 4-A-05, lists as the common characteristics of disease: (1) an impairment of the normal functioning of some aspect of the body; (2) that has characteristic signs or symptoms; and (3) results in harm or morbidity to the entity affected. Let's apply this standard to, for example, common dermatological disorders, eczema, scarring, and acne. According to the above definition, all of these are conditions rather than diseases. Yes, each represents an abnormality of function of the integumentary system. Yet, for any given one, there is no multitude of accompanying signs, there are no related symptoms, and each has little if any impact on morbidity and mortality of the individual affected. Nevertheless, each of these has an ICD-10 code and a CPT code that allow reimbursement for its medical management. One can make this argument for many other conditions currently covered under the CMS reimbursement system.

Perhaps all this will cause some to think that, instead of taking on obesity as a disease and urging CMS to accept it as such, it might be better to point to past instances in which treatment for conditions like those mentioned above has been reimbursed and then to appeal to the general sense of justice and urgency about obesity that would drive the same result. There is a considerable amount of text within AMA policy that emphasizes the importance the AMA places on this health concern and that would enable the AMA to unreservedly support this tactic.

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*Joylene John-Sowah, MD, MPH, works as a senior scientist in Medicine and Public Health at the American Medical Association, where she leads their initiatives on obesity and family violence and holds the AMA seat on the United States Preventive Services Task Force. Her professional interests include health policy, maternal/child and adolescent health, and health communications.*

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# Virtual Mentor

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## Op-Ed

### Medical Ethics and Performance-Enhancing Drugs

by Carlos R. Hamilton, MD

Our society, already obsessed with physical appearance and sporting success, has become inundated with reports of the effects and misuse of drugs that enhance athletic performance. These substances have tarnished the health, reputations, and records of many world-class athletes. Unfortunately the biologic effects of many drugs have led to their use by recreational athletes and school-aged competitors. One of the most rapidly growing markets for anabolic-androgenic steroids (AAS) comprises middle and high school-aged girls who value the appearance of muscle definition and reduced subcutaneous fat.

The cardiac toxicities of AAS, stimulants, and other performance-enhancing drugs are well known [1, 2] and include sudden death, thromboembolic phenomena, cardiomyopathy, and arrhythmias. These drugs have also been implicated in stroke, seizures, and such adverse psychiatric conditions as anxiety, mood changes, and autonomic hyperactivity [3]. “Steroid rage” has been cited as a cause of aberrant behavior in some adolescent males. AAS have unique adverse outcomes in adolescents because they accelerate bone epiphysis maturation, leading, ultimately, to reduced matured height. The overdevelopment of muscle strength can cause serious injury to ligaments, bone, and cartilage that have not experienced equivalent growth. And AAS may profoundly alter adolescent ovarian function, a change that can persist long after steroid use has ceased.

The recognition of life-threatening and serious nonfatal consequences of performance-enhancing drug use and treatments has led sports organizations and governments to cooperatively initiate an international campaign to eliminate doping by athletes. A World Anti-Doping Code has been universally accepted, and research, laboratory testing, and education are promoted by the World Anti-Doping Agency (WADA). As a result of these initiatives, urine specimen collection for drug testing has become a routine activity at international sports events such as the Olympic Games, the Tour de France, and the World Cup.

Since doping and other forms of cheating have been present throughout the recorded history of sport, it is clear that prohibition is ineffective without systematic detection procedures and enforcement of sanctions. Improvements in drug testing have revolutionized anti-doping initiatives and appear to be reducing the use of drugs, at least among elite international competitors. Unfortunately, the use of AAS and other drugs by noncompetitive bodybuilders, recreational athletes, and school children—groups among whom routine testing is lacking—seems to be growing rapidly.

From the medical ethics perspective, the role of physicians in anti-doping efforts is clear. The prescribing of potentially harmful drugs for nontherapeutic uses not only violates federal and state drug laws but is contrary to all standards of medical practice. We must also, however, guard against inadvertently facilitating the abuse of legitimate drugs for performance enhancement effects by, for example, prescribing beta agonists for a youth with asthma whose clinical record does not indicate a need for such drugs. This category of drugs may be abused by certain athletes such as sprint runners or swimmers and is included in the World Anti-Doping Code's list of prohibited substances and treatments [2].

Anabolic drugs such as testosterone and growth hormone have many important applications in clinical medicine, but careful monitoring of these prescriptions is needed. Physicians should become aware of the range of substances on the prohibited list and advise their athlete-patients accordingly. This list, determined by WADA, includes legal drugs that "have the potential to enhance sport performance, have actual or potential health risks or violate the 'spirit of sport'" [4]. The WADA Code precludes the "administration or attempted administration of a prohibited substance or prohibited method to any athlete, or any other type of complicity involving an anti-doping rule violation or any attempted violation" [4]. These violations apply not only to physicians but also to nurses, nutritionists, trainers, coaches, and others.

There is certainly no intent to deny athletes appropriate medical treatment of conditions, even if the best therapy is a "prohibited substance." Athlete-patients with medical conditions that call for treatment with a "prohibited substance" can request a "therapeutic use exemption" to gain approval for access to these drugs [4].

To maintain a high ethical standard, physicians should adopt a proactive response to the request for performance-enhancing drugs by patients. But it is not enough to refuse to prescribe the agents because an active (and lucrative) black market exists for them. We should inform patients of the harms associated with these drugs and encourage them to adopt safe and appropriate training programs. It is well known that the desired effects of AAS on muscle growth and strength are not sustained beyond the time of use and may actually result in decreased long-term performance. Undesirable side effects such as short stature, vascular disease, prostate hypertrophy, and menstrual disturbances may last long after the "thrill of victory" has gone.

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*Carlos R. Hamilton, MD, practices clinical endocrinology and internal medicine and is the executive vice president of the University of Texas (UT) Health Science Center at Houston. He is a professor of internal medicine at the UT-Houston Medical School and serves on the Health, Services and Research Committee of the World Anti-Doping Agency.*

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## Op-Ed

### **Steroid Hysteria: Unpacking the Claims**

by Norman Fost, MD, MPH

Some assertions, such as, “Using anabolic steroids for performance enhancement in sports is immoral,” or “Iraq has weapons of mass destruction,” seem to be so clearly true that reliable evidence (in the latter case), or coherent arguments (in the former) aren’t considered necessary to justify coercive action.

The long campaign to demonize and prohibit the use of anabolic steroids in sports—in the press, by the Congress, and by the offices of the leaders of sports—has been so strident and one-sided that a literate person would have little reason to suspect there is another side to the story.

But it is the business of ethics to present justifications for actions, and the claims that have been made for prohibiting the use of anabolic steroids by competent adults appear to be incoherent, disingenuous, hypocritical, and based on bad facts. Let’s look at the common claims.

#### *1. Steroids result in unfair competition.*

Anabolic steroids clearly do enhance performance for many athletes, but there is no coherent argument to support the view that enhancing performance is unfair. If it were, we should ban coaching and training. Competition can be unfair if there is unequal access to such enhancements, but equal access can be achieved more predictably by deregulation than by prohibition. It is hypocritical for leaders in major league baseball to trumpet their concern about fair competition in a league that allows one team (the Yankees) to have a payroll 3 times larger than most of its competitors.

A particularly egregious example of this hypocrisy was the juxtaposition in the 1988 Olympics of Ben Johnson and Janet Evans. Johnson broke the world record for the 100-meter dash and not only had his gold medal taken away but became the permanent poster child for the immorality of steroids, which, though illegal, were available to virtually anyone who wanted them. Evans, after winning her medal in swimming, bragged about the key role of her greasy swimsuit, which the Americans had kept secret from their competitors, and went on a prolonged lecture tour as “America’s Sweetheart.”

#### *2. Steroids are coercive: if your opponents use them, you have to.*

“Coercion,” according to my dictionary, has to do with the use or threat of force, or the threat of depriving someone of something he or she is entitled to. No one in American sports is forced to use steroids. Nor is anyone entitled to be a professional athlete. It’s an opportunity, often involving high risks, which everyone is free to walk away from.

Nor is it the case that you have to use steroids to succeed at the highest level. In the first year that Major League Baseball required anonymous testing, solely to determine the incidence of steroid use as a guide to development of policy, fewer than 6 percent of the players had positive tests.

*3. Steroids cause life-threatening harms.*

Good ethics starts with good facts, and the claims on this point are, to understate the case, seriously overstated. Articles abound in the mass media on the life-threatening risks of anabolic steroids: cancer, heart disease, stroke, and so on. What is missing are peer-reviewed articles in scientific journals to support the claims. Quick: name an athlete who died, or was diagnosed, with steroid-related cancer, heart disease, or stroke. Cases are so hard to find that the prohibitionists have to make them up. So Lyle Alzado, the NFL all-star, is presented on the front page of the *New York Times* and the cover of *Sports Illustrated* because of an alleged steroid-related brain tumor. What is missing is a single article, or evidence, or even a quote from any authority on the topic to support any connection between steroids and Alzado's tumor.

Of course, even if steroids did have these dire effects, it wouldn't follow that a competent adult should be prohibited from assuming those risks in exchange for the possible benefits. We allow adults to do things that are far riskier than even the most extreme claims about steroids, such as race car driving, and even playing football. There are far more deaths reported from the sport itself than from steroids. Why are the paternalists not using these data to ban the sport? The claim by the leader of the National Hockey League that they test for steroids because they're concerned about the health and safety of the players is, well, hysterical.

*4. Steroids are unnatural, and undermine the essence of sport.*

This claim seems predicated on the notion that there is some essence of sports. Sports are games, invented by humans, with arbitrary rules that are constantly changing. Since the beginning of recorded history, athletes have used an infinite variety of unnatural assists to enhance performance, from springy shoes to greasy swimsuits, bamboo poles to better bats, and endless chemicals from carb-filled diets to Gatorade drinks. Should vaulting poles be banned because they undermine the essence of the high jump? Why is there not a ban on training in high altitudes, or sleeping in a hypobaric chamber, for the purpose of raising hemoglobin to unnatural levels?

*5. Steroids undermine the integrity of records.*

Of all the proposed punishments for Rafael Palmeiro, the Baltimore Oriole slugger who was reported to have tested positive for steroids shortly after he testified under oath to a Senate committee that he had never used them, the favorite seemed to be to abolish his home run records. The implicit concern is that Babe Ruth or Roger Maris is being unfairly deprived of his place in history. But steroids are only one of many reasons why the old records keep falling. The fences are shorter, the pitching mound is lower, the ball is reputedly livelier, the strike zone keeps changing, and so on. The left field fence in Jacobs Field is more than 100 feet closer than it was in Municipal Stadium when it opened in the 1930s, so let's have some asterisks for home runs at "The Jake" and every other stadium with shortened fences.

6. *Fans will lose interest.*

It isn't clear what the moral issue is here, other than the possible dishonesty of the claim. It's pretty clear that the biggest draws in the sport over the past 10 years have been Barry Bonds, Sammy Sosa, and Mark McGwire, all suspected of steroid use and, in McGwire's case, a confessed user of the now-banned androstenedione. Chicks and guys love the long ball, and the steroid era has been accompanied by record-setting attendance.

7. *It's bad role modeling for kids.*

I'm against steroid use by children and favor harsh penalties for suppliers, but I'm more concerned about tobacco and alcohol use, which account for approximately 500 000 more deaths per year than steroids, most traceable to behaviors that begin in childhood. Baseball is presided over by the former owner of the Milwaukee *Brewers*, who play in *Miller Park*, where *beer* is consumed in prodigious quantities. President Bush and various senators are outraged at the message sent by steroid use, but have little or nothing to say about athletes arrested for drunk driving with little punishment from the leagues, or the larger number found guilty of sexual assault and battery. What message does that send to the kids? And battery is not confined to off-hours behavior. Professional hockey promotes illegal violence and infliction of injury, and it is taught in the junior leagues. Professional football glorifies hurting your opponents.

Steroids aren't good for kids, but there's something fishy going on when the number of articles and congressional hearings about protecting our children are inversely proportional to the seriousness of the problem.

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*Norman Fost, MD, MPH, is professor of pediatrics and bioethics, director of the Program in Medical Ethics, head of the Child Protection Team, and works as a general pediatrician at the University of Wisconsin-Madison.*

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