

of the population. It is speculated that there are many consumers still at risk, but total vCJD mortality appears to be lower at this time than previously predicted.

Many pathologists have begun to screen tonsil and appendix tissue since they were found to be positive in 1 affected individual 8 months prior to the onset of vCJD symptoms. For practical purposes, no positive specimens have been found when doing population screening (~3,500 cases).

Andrews NJ, et al. Incidence of variant Creutzfeldt-Jakob disease in the UK. *Lancet* 2000;356:481-482.
 Brown P. BSE and transmission through blood. *Lancet* 2000;356:955-956.
 Dieter RS. Prion protein in tonsil and appendix tissue. *Lancet* 2000;356:505.
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 Markham D. Prion protein in tonsil and appendix tissue. *Lancet* 2000;356:505-506.

Editor's comment: HIV and hepatitis have led to concerns about the safety of the blood transfusion system. This new report about blood transfusion transmission of prion disease in sheep is quite worrisome. There has not been a single documented case of human CJD, such as observed following contaminated GH injection, that could be related to blood transfusion. Nevertheless, it is of great concern from the standpoint of screening and excluding potential donors of blood products. It took Houston et al 3 years to produce 1 vCJD-positive sheep. Although methodologies to minimize the risk of blood transfusion are improving, there still is concern about whether an epidemic could occur. The good news is that the number of people affected with vCJD seems to be less than was predicted. The good news also is that many lessons are being learned about transmissible diseases, which is important for future public health practices.

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Effect of Growth Hormone Treatment on the Adult Height of Children With Chronic Renal Failure

Previous studies have demonstrated that GH therapy increases the growth rate and improves standardized height in prepubertal children with chronic renal failure. What has not been known, however, is whether such therapy actually improves final height. It has been speculated that GH therapy could accelerate the onset or progression of puberty and negate any effect of early prepubertal treatment. Haffner et al report for the German Study Group for Growth Hormone Treatment in Chronic Renal Failure their analyses of 38 initially prepubertal children with chronic renal failure who were treated with GH for 5.3 years until they reached their adult height. Their growth was compared with 50 matched children with chronic renal failure who were not treated with GH. Of note, the 50 children who did not receive GH had growth retardation that was less marked than that of the treated children.

All subjects in the study had chronic renal failure with a height SD of -2 or below and a height velocity below the 25th percentile during the year prior to the onset of treatment. The 38 children (32 boys and 6 girls) who were treated with GH were 10.4 ± 2.2 years at the initiation of GH and their bone age was 7.1 ± 2.3 years with an SD score of -3.1 ± 1.2. During the study, 11 of the children were started on dialysis and 9 subsequently received a renal transplant. GH was administered in a total weekly dose of 0.33 mg/kg body weight. Fifty children (31 boys) in the control group were matched with respect to age at first observation, underlying renal disease, treatment, residual renal function, and cumulative dose of glucocorticoids. They were not treated with GH because they had relatively little or no growth retardation at baseline. Standard anthropometric measurements were obtained at 3- to 6-month intervals during the study and bone age was determined by the Tanner-Whitehouse II (TW2) method approximately every 12 months. The genetic target was calculated as a midparental height +10 cm for boys and -2.6 cm for girls.

During the prepubertal observation period, height velocity in the GH-treated children increased over baseline and exceeded

values in both the controls and in normal children. After the prepubertal peak, the height velocity decreased until the start of the pubertal growth spurt. The total height gained during the prepubertal observation period was twice as much as that

Table
 Predictors of Growth During the Observation Period in the Growth Hormone-Treated and Control Children Combined

Period and Predictor	Effect	Partial R ²	Cumulative R ²	P Value
Prepubertal period (change in cm of height)				
Increased duration of prepubertal period	Positive	0.67	0.87	<0.001
Increased duration of growth hormone therapy	Positive	0.13		<0.001
Greater initial target-height deficit	Positive	0.04		<0.001
Greater % of time spent on dialysis	Negative	0.03		0.006
Pubertal growth period (change in cm of height)				
Increased duration of pubertal period	Positive	0.45	0.61	<0.001
Increased duration of growth hormone therapy	Positive	0.11		<0.001
Male sex	Positive	0.05		0.005
Total observation period (change in cm of height)				
Greater initial target-height deficit	Positive	0.58	0.78	<0.001
Increased duration of growth hormone therapy	Positive	0.06		0.002
Greater % of time spent on dialysis	Negative	0.04		0.004
Total observation period (change in standard deviation score)				
Increased duration of growth hormone therapy	Positive	0.58	0.64	<0.001
Greater initial target-height deficit	Positive	0.06		0.008

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in the control children. During puberty, peak height velocity was not significantly higher in the GH-treated children than in the controls. The onset of the pubertal growth spurt was delayed in these children by approximately 2½ years (compared with normal children) and the duration of the growth spurt was 1.6 years shorter compared with that of normal children.

The total pubertal height gain was similar in the GH-treated and the control children, but was 65% of that in normal children because the pubertal growth spurt was shorter.

Catch-up growth was sustained in the GH-treated children whereas the control children had progressive growth failure. The standardized height increased from the baseline mean of -1.4 SD. The mean final height was 1.6 SD below normal in the treated group, whereas in the control children the standardized height decreased by a mean of 0.6 SD to a final mean adult height of 2.1 SD below normal. Sixty-five percent of the GH-treated children reached an adult height within the normal range, but the mean final adult height was approximately 10 cm below the genetic target height for boys and 12 cm below the genetic target height for girls. The final height in the control children was 15.8 cm lower than the genetic target in boys and 16.1 cm lower than the genetic target in girls. Although the bone age increased faster during the prepubertal period in the GH-treated children than in the controls, it did not reduce overall height gain. Multiple regression analysis revealed that the absolute as well as the standardized height gain during the observation period was significantly associat-

ed with the longer duration of the prepubertal and pubertal observation periods, a longer duration of GH therapy, a greater initial target height deficit, a lower percentage of time spent on dialysis, and male sex. These factors explain 61% to 87% of the variability in the outcome data.

The authors point out that this study provides evidence that GH treatment can sustain catch-up growth in the majority of children with growth failure due to chronic renal failure.

Haffner D, et al. *N Engl J Med* 2000;343(13):923-929.

Editor's comment: *This is a particularly important study because it is the first to look at final height achieved in this population. Clearly, GH therapy is of significant benefit to final height in children with chronic renal failure. The particular strengths of this study are the variety of causes of chronic renal failure in these children and the careful matching of the etiologies between the treated and control groups. An unanswered question is the effect of GH therapy on adult height in children who begin such treatment during their pubertal years. The data in the current study cannot be used to answer this question. The children in this study had glomerular filtration rates of <60 mL/min/m². It also will be important to evaluate the effect of GH therapy on children with lesser degrees of renal insufficiency but similar degrees of growth retardation.*

William L. Clarke, MD

The Impact of Recombinant Human Growth Hormone Treatment During Chronic Renal Insufficiency on Renal Transplant Recipients

Fine et al described the posttransplant outcome for renal transplant patients who were treated with GH therapy during the course of their chronic renal insufficiency. Subjects were identified from 2 control studies (n=194) and matched with patients in the North American Pediatric Renal Transplant Cooperative Study (NAPRTS) database; 95 "likely" matches and 7 "possible" matches were made. These 102 patients formed the GH-treated cohort group and were compared with a control group of 4913 transplant recipients in the database who did not receive GH therapy during their chronic renal insufficiency. Interestingly, the treated cohort tended to have more males, a larger percentage of subjects between 6 and 12 years of age, and more (67% vs 45%) living parent donors.

Two deaths occurred in the cohort, after 78 days and 5 years. The survival rate for the cohort at 3 years was 98.9%, while that for the control group was 95.1%. In the cohort group, 11.8% of grafts failed; 21% of the grafts failed in the control group. There is no statistically significant difference between graft survival rates for either donor source. The percentage of failed grafts with chronic rejection as the cause was marginally significantly higher than in the control group ($P=0.05$). However, the percentage of all grafts that failed as a result of chronic rejection was similar for the 2 groups (6.9 for the GH-treated cohort and 6.5 for the control).

The mean height Z score at 60 months was slightly improved in the treated group compared with a slight worsening in the control group. In both groups, the delta Z score was positive, indicating continued improvement from baseline. Adverse events in the treated cohort included 2 posttransplant lymphoproliferative disorders and 38 other events, including appendicitis, gastroenteritis, pneumonia, other infections, and hypertensive crisis.

There was no core of adverse events but a broad spectrum of unrelated events. The authors' data did not support the assertion that recombinant human growth hormone (rhGH) treatment during the course of chronic renal insufficiency predisposed to the development of malignancy after transplant.

The authors conclude that GH therapy was not associated with an increase in adverse effects on graft function, nor were there more malignancies posttransplantation. There were concerns that "catch-down" growth would occur after renal transplantation in individuals who received GH during renal insufficiency, which might nullify gains in height. These data do not substantiate these concerns.

Fine R, et al. *J Pediatr* 2000;136(3):376-382.