

2. *Patients with slowly progressive cerebral disease, with or without Addison's disease. MRI shows slow progression of demyelination. BMT is to be considered. Disease severity is evaluated by scoring the extent of demyelination on the MRIs and performance on neuropsychological tests. MRIs are scored using a demerit scale ranging from 0 to 34 devised by Loes et al. BMT is recommended for patients whose cognitive abilities exceed a VIQ or PIQ of 80.*
3. *Patients with stable cerebral disease. Included are patients with MRI and neuropsychological abnormalities at diagnosis and in whom follow-up shows no evidence of MRI and neuropsychological deterioration. Close monitoring is required to detect change that may signal decline. (Not stated, but implied, is that those who are declining but whose IQ remains >80 might be candidates for BMT.)*
4. *Patients with advanced cerebral disease. These include patients with rapid progression of disease who decline rapidly to a vegetative state and have marked VIQ or PIQ dysfunction (<80) and neurologic signs. Current methods of BMT are not beneficial.*

The authors also state: "The absence of any correlation between the clinical phenotype and the ALD gene mutation or the biochemical defect, and the effectiveness of BMT ONLY at an early stage of the disease, lead us to recommend careful planning and frequent observation of all boys biochemically identified with X-ALD with normal brain MRI. No biological marker predicting the onset of cerebral demyelination is as yet available. Therefore continued MRI and neuropsychological testing are the only tools allowing the identification of patients who will benefit from BMT. Similarly no existing marker predicts whether or when a patient with a "slowly progressive cerebral disease" will enter into the "advanced cerebral disease" stage. Observations raised the hope that VLCFA could be decreased or even normalized by new pharmacological approaches. BMT, however, remains the only effective therapeutic approach in the cerebral form of X-ALD. The opportunity to recommend BMT at an early stage of cerebral X-ALD should not be missed."

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Loes DJ, et al. *Am J Neuroradiol* 1994;15:1767-1771.

Transmission of BSE (Bovine Spongiform Encephalopathy) by Blood Transfusion in Sheep

Houston et al published an early warning report before completion of a study that they were doing to look at cross-species transmission of bovine spongiform encephalopathy (BSE) through blood transfusion. This study was aimed at answering the question of whether there is a concern about blood transfusions transmitting the variant Creutzfeldt-Jakob (vCJD) disease in Britain from anyone living in Britain or who traveled in Britain between 1980 and 1996. Several countries have banned blood donations from people who spent time in Britain during the time of potential exposure to BSE.

Houston et al were engaged in a study to see if it is possible to transmit BSE between sheep by blood transfusion after the blood donor sheep had orally ingested the infecting agent. It turns out that sheep blood types are very complex, so this study was not a simple matter. It had been thought that there was a barrier to cross-species transmission of infectious agents. BSE-infected sheep harbor infection in peripheral tissues (tonsils, for example) prior to becoming symptomatic and thus are similar to humans infected with vCJD. A group of sheep were orally challenged with 5 g of BSE-affected cattle brain. At a later time, their blood was taken and transmitted into scrapie-free sheep. For the most part, whole blood was used for the transfusions and only a single transfusion was made. BSE clinical signs and pathologic changes have occurred in 1 of the sheep who received blood from a BSE-infected animal who was asymptomatic at the time of the transfusion. The donor had been challenged by oral BSE cattle brain 318 days before whole blood was taken. The BSE developed in the recipient animal 629 days after the transfusion. This suggests that the blood was taken from the orally challenged sheep halfway through the incubation period and yet it was nevertheless able to infect the recipient sheep.

This experiment does indicate that BSE can be transmitted between individuals of the same species by whole blood transfu-

sion and thus has implications for the blood transfusion system in general. The United Kingdom has been utilizing leukocyte-depleted blood; however, this may not be sufficient to avoid the problem.

A number of models have been utilized to predict the incidence of vCJD in the United Kingdom. There has been concern that as many as 500,000 individuals could become affected. The models have varying lengths of incubation and various calculations as to the number of people who would become infected and symptomatic after eating meat from an infected cow. The observed number of cases affected in early 2000 was 75 (Table). There appears to be a susceptible prion genotype, which is present in about 40%

Table
Annual Number of Onsets, Classifications, and Deaths From vCJD in the UK

Year	Onsets	Classified as vCJD	Deaths
1994	8	0	0
1995	10	7	3
1996	11	8	10
1997	14	12	10
1998	16	17	18
1999	16	17	14
2000	0	14	14
Total	75	75	69

Based on current classification criteria, applied retrospectively where appropriate.

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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.
 Ghani AC, et al. Predicted vCJD mortality in Great Britain. *Nature* 2000;406:583-584.
 Houston F, et al. Transmission of BSE by blood transfusion in sheep. *Lancet* 2000;356:999-1000.
 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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