

1998

# Heidi Peterson on behalf of Markelle Frei-Peterson v. Utah Department of Health, Division of Health Care Financing : Brief of Appellee

Utah Court of Appeals

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IN THE UTAH COURT OF APPEALS

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HEIDI PETERSON on behalf of	)	
MARKELLE FREI-PETERSON,	)	
	)	
Petitioner and Appellant,	)	Case No. 98-0078-CA
	)	
vs.	)	Category No. 14
	)	
UTAH DEPARTMENT OF HEALTH,	)	
DIVISION OF HEALTH CARE	)	
FINANCING,	)	
	)	
Respondent and Appellee.	)	

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BRIEF OF APPELLEE

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Appeal from Final Agency Order entered January 15, 1998, by the Director of the Division of Health Care Financing, Utah Department of Health, which adopted the Recommended Decision of the administrative law judge to deny Medicaid benefits.

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ORAL ARGUMENT AND PUBLISHED OPINION NOT REQUESTED

UTAH COURT OF APPEALS  
BRIEF

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DOCKET NO. 98-0078-CA

**FILED**

Utah Court of Appeals

JUN 12 1998

Julia D'Alesandro  
Clerk of the Court

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BRIEF OF APPELLEE

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**JURISDICTION**

In accordance with Rule 410-14-2, Utah Administrative Code, a hearing requested by Petitioner Peterson was conducted as a formal hearing before the Division of Health Care Financing. The provisions of Chapter 46b of Title 63, Utah Administrative Procedures Act, are applicable and pursuant to § 63-46b-16(1) "all final agency action[s] resulting from formal adjudicative proceedings" fall under the jurisdiction of either the Supreme Court or the Court of Appeals. In this instance, under § 78-2a-3(2)(a), Utah Code Ann. (1997), the Court of Appeals has appellate jurisdiction over this matter.

**STATEMENT OF NATURE OF PROCEEDINGS BELOW**

This appeal is taken from the Final Agency Order of the Division of Health Care Financing (Division/DHCF) adopting the

Recommended Decision issued by the Administrative Law Judge denying Medicaid funds for growth hormone to treat Markelle Freil-Peterson for short bowel syndrome. In the time leading up to the administrative hearing, Markelle had received growth hormone for a few months, paid for by Primary Children's Medical Center charitable funds. Her treating physician wanted to treat Markelle for a period of time with the growth hormone, prompting the request for Medicaid coverage. The Division issued its denial dated July 16, 1997, from which the petitioner sought a hearing. The hearing was conducted December 8, 1997, resulting in the Recommended Agency Decision dated January 7, 1998. The Final Agency Order, adopting the Recommended Decision, was dated January 15, 1998. Petitioner timely filed her notice of appeal with this court February 11, 1998.

#### **STATEMENT OF THE ISSUE PRESENTED FOR REVIEW**

Whether the use of growth hormone to treat short-bowel syndrome is properly categorized as experimental and therefore properly denied coverage under the Medicaid program.

#### **STANDARD OF REVIEW**

In an instance requiring the reviewing court to consider a mixed question of law and fact, the court will review the question of law for correctness but apply some degree of deference to the agency's determination in its application of the law to the facts. *Drake v. Industrial Commission*, 939 P.2d 177,

181 (Utah 1997). The degree of discretion granted to the agency must be evaluated in light of the particular circumstances. Some reasons which support a broader grant of discretion are when (1) the facts to which the rule are to be applied are "complex and varying [and] no rule [would] adequately address the relevance of all . . . [the] facts . . . ; (2) the matter to be decided is sufficiently new that a reviewing court would not be able to "anticipate and articulate definitively what factors should be outcome determinative;" and (3) the witnesses' demeanor is relevant and the record cannot adequately reflect those factors. *State v. Pena*, 869 P.2d 932, 939 (Utah 1994). The listing in *Pena* is not exhaustive and additional factors would also be considered under the particular situation of a specific case. Given the nature of the legal rule and the grant of discretion accorded the Division by statute to administer the Medicaid program to meet the objectives, see § 26-18-3, Utah Code Ann. (1995), this court should grant a degree of discretion to the Division in its application of the rule to the set of facts. *Drake*, 939 P.2d at 182, citing *Pena*, 869 P.2d at 939. Whether the decision to deny Medicaid coverage for the Petitioner was proper "is a mixed question of law and fact. [A] . . . determination of the law is reviewed for correctness, while . . . findings of fact are reviewed for clear error. [The agency's] application of the law to the facts is reviewed for abuse of any

discretion granted the [agency] in applying the stated rule . . . to the facts of the case." *Woodhaven Apartments v. Washington*, 942 P.2d 918, 924, citing *Pena*, 869 P.2d at 937.

#### **DETERMINATIVE STATUTES AND RULES**

1. 42 U.S.C. § 1396a(a)(5)
2. 42 U.S.C. § 1396(a)(10)(A)
3. 42 U.S.C. § 1396d(a)(4)(B)
4. 42 U.S.C. § 1396d(r)
5. Utah Code Ann. §§ 26-18-3; 26-18-4
6. Utah Administrative Code R414-1A-200
7. Utah Administrative Code R414-1A-300
8. Utah Administrative Code R414-10-6
9. Utah Administrative Code R414-13x-1.(5)(a)

#### **STATEMENT OF THE CASE**

Appellant, Markelle Frei-Peterson, diagnosed with short bowel syndrome, receives parenteral nutrition. Her treating physician wanted to try a regimen of growth hormone, hoping it would induce increased function of the intestines thereby reducing or eliminating parenteral nutrition. The associated problems of short bowel syndrome include the risk of central line catheter infections, the loss of intravenous access sites, and, potentially, liver dysfunction. The Medicaid program requires prior authorization for certain treatments, including the treatment proposed for Markelle. The application for Medicaid

coverage for the growth hormone was submitted to DHCF. Upon the initial review, the factors of the case did not meet the applicable criteria. Because the proposed use for the drug did not meet the usual criteria, additional documentation supporting the use was requested from the physician. The documentation received was reviewed and submitted to the Check Utilization Review Committee. The Committee determined the proposed use was experimental. Accordingly, the Health Program Manager of the Utilization Management staff in DHCF notified the parents of Markelle that the request for growth hormone therapy was denied on the basis the procedure was experimental. The Notice of Denial, dated July 16, 1997, included information of the right to a hearing if the applicant for Medicaid disagreed with the decision. Thereafter, Appellant filed a request for hearing on July 28, 1997. During the time from the request for hearing to the date the hearing was conducted on December 8, 1997, Markelle received growth hormone therapy paid by charitable funds of the Primary Children's Medical Center. At the hearing, testimony was presented by witnesses for Markelle and on behalf of DHCF as well as documentation and exhibits in support of the parties' positions. Thereafter, the Administrative Law Judge made the Recommended Decision to uphold DHCF's denial of Medicaid coverage on the basis it was experimental. This Decision dated January 7, 1998, was adopted as the Final Agency Order on January 15, 1998.



## STATEMENT OF FACTS

Markelle Frei-Peterson, at the time of the Formal Hearing in December 1997, was described as a 24-month old child with short bowel syndrome. To briefly acquaint this court with the nature of the condition, as described more fully in the articles submitted by Markelle's physician and made a part of the formal hearing record, it is a disorder characterized by "diarrhea, dehydration, electrolyte disturbances, malabsorption, and progressive malnutrition" resulting from "extensive loss or dysfunction of the intestinal absorptive surface area." The severity "depends upon the length, location, and absorptive function of the remaining bowel and its ability to accommodate the reduced absorptive surface area." Compensatory function can occur; meanwhile, parenteral nutrition is often necessary. Parenteral nutrition may be total (TPN) or partial and may be temporary or permanent.<sup>1</sup> Also at the time of the hearing, Markelle received parenteral nutrition for approximately 90 percent of her needs (T-126-10)<sup>2</sup>. For perhaps the three- to

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<sup>1</sup>This short definition is taken from Theresa A. Byrne, et al., *Growth Hormone, Glutamine, and a Modified Diet Enhance Nutrient Absorption in Patients With Severe Short Bowel Syndrome*, **Journal of Parenteral and Enteral Nutrition** (1995) (R-41-47). For additional description of the syndrome, articles submitted by Petitioner's physician to DHCF and included in the record are found at R-21 to 66.

<sup>2</sup>References to the transcript of the formal hearing before the Utah Department of Health, Division of Health Care Financing, shall be designated by the initial "T"; references to other

four-month period prior to the hearing, Markelle's enteral feedings had been increasing but she remained dependent upon parenteral nutrition. (T-126-10, 11). One of the concerns expressed by Markelle's physician, Dr. William D. Jackson, was the condition of her liver because the syndrome is characterized by progressive liver disease (T-126-31). Liver tests in approximately June 1997 showed some marked abnormalities which subsequently normalized (T-126-19) independent of the growth hormone therapy which had been initiated late in 1997 (T-126-29, 30). The impetus to the growth hormone therapy was concern for the potential of liver disease (T-126-31); however, the basic objective of any treatment was to stimulate the ability of the intestinal tract to tolerate increasing enteral nutrition, this in turn providing the natural protection for the liver function. (T-126-31). At the time the growth hormone therapy was considered, Markelle was having health problems necessitating hospitalization and the liver tests with marked abnormalities concerned Dr. Jackson. A few things in her treatment were changed in addition to adding growth hormone. (T-126-19). The factors changed were not specified and were not definitively related to any improvement in enteral feedings; the maturation process may have played a role in adapting to increased enteral

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portions of the record before the Division shall be designated by the letter "R."

feeding or the growth hormone may have provoked a change. (T-126-19). Markelle had begun to tolerate increasing enteral feedings. (T-126-19, 21). The progress in Markelle's condition admittedly did not prove the efficacy of the therapy. (T-126-38).

In addition to describing Markelle's condition, Dr. Jackson, board certified in pediatrics and pediatric gastroenterology and nutrition, made reference to recent articles on the topics of short bowel syndrome and growth hormone studies published in professional journals. The studies reported were small and short term, consisting of eight to 47 study patients in three- to four-week trials. (R-41; R-28; R-25). Dr. Jackson referred to the study results demonstrating some increased measures for absorption and function, but over very short terms, with small groups of adults. (T-126-28). This is an area of new therapy generating active work and controversy. (T-126-15, 16, 28).

Asked to comment on the therapy as experimental, Dr. Jackson elaborated as follows:

I think there's a lot of therapies that we use that are rightfully considered experimental which in terms of -- if you think of it in terms of data being accumulated and evaluating the efficacy, the appropriate dosage, the appropriate indications, things like that. And this one particularly as early a therapy as this is, as young a therapy I guess as this is would definitely I think have to be considered that.

(T-126-35). Dr. Jackson's continuing testimony on this point addressed his interpretation of his use of the growth hormone for

Markelle as not being an experiment in the strict sense inasmuch as no protocol were being followed and a study of one patient wouldn't constitute an experiment in his mind. (T-126-35). Dr. Jackson likened his decision to the "art of medicine" wherein available data is applied to a "desperate clinical situation" and in "adding up pluses and minuses" a judgment is made which "could be deemed erroneous by peers or other people," but on the other hand other peers agree with trying this as a therapy. He stated that as Markelle's physician it was his "judgment . . . that [he] would like to try this." Further, he stated he had a certain idea about its use but certainly did not have all the information . . . and "we often don't in making practice decisions and making clinical decisions. . . . We don't know that this indeed is what cured the patient or this indeed is what did anything." (T-126-36). Further questioning elicited testimony that Markelle did not have growth hormone deficiency. (T-126-41). The theory presented was that growth hormone would be given to "stimulate growth factor production in the body, including epidermal growth factors, things like that work on the lining of the intestine to stimulate growth." Experimental animal studies in which excessive amounts of growth hormone are given have produced animals expressing hyperplasia (tumors) in the small bowel. (T-126-42). The theory is to use the growth hormone as a pharmacological agent to "actually stimulate the kind of growth

factors that would be required to try to make the small bowel develop and grow more." (T-126-43). No known level of dosage is recognized. (T-126-43).

Upon receipt of the request for Medicaid coverage for the growth hormone, DHCF reviewed the information presented and applied the applicable criteria; at this point Markelle did not meet the criteria. (T-126-47, 48). Specifically, Markelle did not have documented failure of growth nor of insufficiency caused by kidney failure. (T-126-49). The proposed use was not a common use for the drug, therefore, DHCF requested additional documentation, including any supporting literature, as well as liver function tests, clinical records, parenteral and enteral nutrition information. (T-126-48). This information was reviewed and submitted to the Check Utilization Review Committee. The Committee, composed of physicians, nurses, consultants, social workers, reviewed the documentation and found the use proposed was not typical but was experimental. (T-126-48, 49). The Notice of Decision denying Medicaid coverage stated it was based on Utah Administrative Code R414-10-5, Physician's Covered Services, wherein it provides that "[e]xperimental or medically unproven physician services or procedures are excluded from coverage." (T-126-51). Duane Park, a registered pharmacist with a master's degree in health administration, testified on behalf of DHCF concerning effective drug utilization as required by the

Medicaid law. Mr. Park develops and coordinates the drug utilization review process for the State as mandated by federal law. (T-126-52).

Dr. John Hylen testified on behalf of DHCF. He stated he had a doctorate in medicine, a master's degree in public health, and was board certified in internal, cardiovascular, and geriatric medicine. Dr. Hylen's statements reiterated issues raised previously and particularly indicated his concerns that growth hormone used as proposed had not yet been proven effective in preventing liver disease nor were data available concerning toxicities for children. Dr. Hylen's testimony centered on concerns that since side effects were unknown, its efficacy in preventing progressive liver disease or the need for a liver transplantation remained undocumented, and it is an expensive medication and alternative cost-effective means exist to address the nutritional concerns, that he found many unanswered questions weighed against the therapy. (T-126-60, 61).

#### **SUMMARY OF THE ARGUMENT**

At issue is the proposed use of a drug, humatrope, a recombinant human growth hormone, to stimulate gastrointestinal function for a child suffering from short bowel syndrome. Under applicable Medicaid rules, the drug is approved for use under circumstances where a person is deficient in the growth hormone. The Appellant Markelle has no growth hormone deficiency. Rather,

her treating physician proposes to use growth hormone in the hope it will stimulate gastrointestinal function. However, the use proposed in the instant case is considered experimental. Under Medicaid law, coverage is not permitted for experimental procedures. This approach is justifiable because the Medicaid program's objectives are not directed toward research. In compliance with federal law, Utah, by its designated agency charged with the efficient and effective administration of the Medicaid program, has established rules addressing Medicaid payment policy for experimental or unproven medical practices and treatments.

The agency has defined an "experimental or unproven medical practice" as one not proven medically efficacious. Medically efficacious practices have been determined effective and widely utilized as a standard practice. These practices are approved as a covered Medicaid service on the basis of medical necessity. Proven effective treatments widely utilized are covered services when medically necessary. The determination of medically necessary is a proper exercise of agency discretion. A medically necessary service must be reasonably calculated to effectively address the patient's situation. This entails a consideration of the treatment for its preventive, diagnostic or curative use for the patient's condition as well as for its effectiveness and suitability.

The Division has essentially defined "necessary treatment" as used in the Medicaid Act to exclude experimental treatments. This is a valid interpretation by the Division fulfilling its role in meeting the objectives of the Act. Absent proven effectiveness for a treatment necessary for the patient's medical condition, the Division reasonably may deny funds.

#### **ARGUMENT**

##### **POINT I:**

**THE MEDICAID PROGRAM, A COOPERATIVE FEDERAL-STATE ENDEAVOR, CREATED TO ASSIST PARTICIPATING STATES BY PROVIDING FEDERAL FINANCIAL ASSISTANCE, PROVIDES MEDICAL ASSISTANCE TO NEEDY INDIVIDUALS WHO ARE ELIGIBLE UNDER THE STATE'S APPROVED PLAN.**

In 1965 Congress established the Medicaid program by enacting Title XIX of the Social Security Act. The program is a cooperative federal-state endeavor by which federal grants are paid to states enabling them to provide medical assistance to persons otherwise unable to pay for necessary medical care. Although Medicaid is entirely optional, once a state elects to participate, the state must comply with all the federal statutory and regulatory requirements. *Harris v. McRae*, 448 U.S. 297, 301, 100 S.Ct. 2671, 2680 (1980). Participating states must have a State plan approved by the Secretary. See 42 U.S.C. § 1396. A single agency must be selected to administer the plan. See 42 U.S.C. § 1396a(a)(5). Although states must comply with the federal requirements, they retain broad discretion in determining



which medical services will be covered under their plans. However, to qualify for federal funds the state plan must include the seven mandatory medical services referenced at 42 U.S.C. § 1396a(a)(10)(A), which include inpatient hospital services, various outpatient hospital services, laboratory and X-ray services, specified nursing facility services, early and periodic screening, diagnostic, and treatment services for eligible individuals under 21, (42 U.S.C. § 1396d(r)) various physician services, nurse-midwife services, and services of certified pediatric or family nurse practitioners. 42 U.S.C. § 1396d(a)(4)(B).

Utah is a participating Medicaid state having opted to participate by adopting the Medical Assistance Act in 1981. See Utah Code Ann. §§ 26-18-1 to -11 (1995 and Supp. 1997). Having opted into the federally created medical assistance program, Utah assumes complete administration of its program. Utah designated the Division of Health Care Financing as the single administrative agency for the state. As the designated agency, the Division is responsible for administering the Medicaid program in accordance with federal and state law. The Utah legislature granted the Division broad authority to develop standards and to develop and administer policies in implementing the state's plan. Utah Code Ann. §§ 26-18-3(2), -4(1) (1995). Utah has complied with federal requirements by creating a state

Medicaid plan which has received approval by the Secretary of Health and Human Services. Utah Admin. Code R414-1-4.

**A. A state's medical assistance plan must be consistent with the objectives of Title XIX; the plan must employ reasonable standards for determining eligibility for and extent of medical assistance.**

Title XIX's overarching objective is to enable participating states, "as far as practicable, to furnish medical assistance to individuals whose income and resources are insufficient to meet the costs of necessary medical services." *Beal v. Doe*, 97 S.Ct. 2366, 2371, 432 U.S. 438 (1977). Title XIX does not specify particular medical procedures to be provided; although participating states must provide financial assistance for five (the Medicaid statute now mandates seven categories) broad categories of medical treatment, states are not required to fund every medical procedure falling within the general categories.

Indeed, the statute expressly provides: "A State plan for medical assistance must . . . include reasonable standards . . . for determining eligibility for and the extent of medical assistance under the plan which . . . are consistent with the objectives of this [Title]. . . ." 42 U.S.C. § 1396a(a)(17) (1970 ed., Supp. V).

*Beal v. Doe*, 97 S.Ct. at 2370-71; *A.M.L. v. Department of Health*, 863 P.2d 44, 47 (Utah App. 1993).

To retain the integrity of the program, each participating state must submit and receive approval for its state plan. However, receiving approval does not mean the state plan is minutely managed by federal oversight. In fact, the *Beal* Court

goes on to state, "[t]his language confers broad discretion on the States to adopt standards for determining the extent of medical assistance, requiring only that such standards be 'reasonable' and 'consistent with the objectives' of the Act." *Beal*, 97 S.Ct. at 2371.

**B. Utah's standards of eligibility and coverage are reasonable and in conformance with the objectives of the Act.**

In conformance with Title XIX and by the authority granted under § 26-18-3(2), Utah Code Ann. (1995), Utah's designated Medicaid office has established standards enabling the Division to administer its Medicaid program. The specific standards applicable to this case provide in pertinent part:

R414-1A-300. Policy.

(1) Experimental or unproven medical practices are not covered Medicaid services.

(2) Division staff and physician consultants shall establish criteria to determine whether a service or procedure is a covered Medicaid service.

(3) Procedures or services proven to be medically efficacious for specific medical conditions may be provided as covered Medicaid services only for the conditions specified. Such procedures or services are not covered for any other conditions or for experimental trials. . . .

The issue before this court concerns DHCF's denial of Medicaid coverage for an experimental use of a drug. The policy excludes experimental or unproven medical practices; it does not exclude procedures or services proven to be medically efficacious. Furthermore, the criteria applied to a given situation is the result of the combined efforts of Division staff and physician

consultants. This is an important issue on which the agency should be permitted broad discretion to fashion rules which promote the objectives of the Medicaid program. Medicaid was not created to promote research for new treatments. In fact, using the population of Medicaid-covered individuals as a potential pool of research subjects would raise public policy and ethics concerns. This population of persons is already vulnerable because of lack of sufficient personal funds to obtain needed medical services. While the concept of public funding of medical research is not a foreign or repugnant one, it would be unacceptable to combine the dual purpose of needed medical treatment and experimental medical treatment within the single program of Medicaid. The Medicaid program is not a research program.

In addition to the rule establishing the Medicaid payment policy for experimental or unproven medical practices, the agency has by rule defined certain terms which govern the agency in its assessment of the set of facts applicable to the particular individual. The definitions established by rule provide in pertinent part:

R414-1A-200. Definitions.

(1) Terms used in this rule [R414-1A. Medicaid Policy for Experimental or Unproven Medical Practices.] are defined in R414-1-1.

(2) In addition:

(a) "experimental or unproven medical practice" means any procedure, medication product, or service that is:

- (i) not proven to be medically efficacious for a given procedure; or
  - (ii) performed for or in support of purposes of research, experimentation, or testing of new processes or products; or
  - (iii) both;
- (b) "medically efficacious" means a medical practice that:
- (i) has been determined effective and is widely utilized as a standard medical practice for specific conditions; and
  - (ii) has been approved as a covered Medicaid service by division staff and physician consultants on the basis of medical necessity, as defined in R414-13x-1.(5)(a),. . . .

When determining the application of "experimental medical practice" to the facts of the case, the question of "medical necessity" may arise because of the specific circumstances. A service is "medically necessary" if it is:

- (1) reasonably calculated to prevent, diagnose, or cure conditions in the recipient that endanger life, cause suffering or pain, cause physical deformity or malfunction or threaten to cause a handicap; and
- (2) there is no other equally effective course of treatment available or suitable for the recipient . . . which is more conservative or substantially less costly.

Utah Admin. Code R414-13x-1.(5)(a).

Under both the Medicaid Act and Utah law, the Division has been granted discretion to establish and implement a program designed to furnish medical assistance within the scope and intent of the law. The Division has designed a program to meet those objectives. Nothing in federal or state law prevents the state from denying coverage for medical practices or services which do not satisfy reasonable criteria designed to achieve the

program's objectives. As the *Beal* Court noted, "[a]lthough serious statutory questions might be presented if a state Medicaid plan excluded necessary medical treatment from its coverage, it is hardly inconsistent with the objectives of the Act for a State to refuse to fund unnecessary---though perhaps desirable---medical services." *Beal*, 97 S.Ct. at 2371. The terminology of "unnecessary" is not precisely the correct question in the instant case. Rather, the reference to the quote in *Beal* helps clarify the determination in this case. The agency's decision denied the request because the proposed use was experimental. The medical procedure is unproven; and without a certain quantum of reliable authority establishing a procedure's safety and effectiveness, the agency is justified in exercising its discretion not to fund a questionable medical service.

**POINT II:**

**UTAH'S STANDARD GOVERNING EXPERIMENTAL  
MEDICAL PRACTICES IS REASONABLE AND AS  
APPLIED TO THE FACTS OF THE CASE WAS A  
REASONABLE EXERCISE OF AGENCY DISCRETION.**

The rule applied in this case denied Medicaid coverage for an experimental use of growth hormone to treat short bowel syndrome. In essence, if the practice or service is determined experimental, then it has not been proven medically efficacious for that purpose. In *Rush v. Parham*, 625 F.2d 1150, 1156 (5th Cir. 1980), that court had occasion to consider the question

presented when applying the standard of experimental within the definition of medically necessary services. The case concerned a request for transsexual surgery and presented that court with the problem of whether the Georgia Medicaid program's definition of medically necessary services could exclude experimental treatments. The court concluded that it was a valid exercise of the agency's discretion to exclude experimental treatments. Its support was found in a letter Medicare<sup>3</sup> uses to explain why certain services are ineligible for reimbursement. The supportive information contained in the opinion at footnote 11 states:

The clearest articulation of the considerations that go into determining whether a particular service is experimental is found in a letter Medicare uses to explain to its clients and providers why a service is ineligible for reimbursement:

In making such a decision [whether to provide payment for a particular service], a basic consideration is whether the service has come to be generally accepted by the professional medical community as an effective and proven treatment for the condition for which it is being used. If it is, Medicare may make payment. On the other hand, if the service or treatment is not yet generally accepted, is rarely used, novel or relatively unknown, then authoritative evidence must be obtained that it is safe and effective before Medicaid may make payment. Enclosure # 2 to Intermediary Letters Nos. 77-4 & 77-5,

---

<sup>3</sup>The Medicare program, which is administered directly by the federal government on a nationwide basis, shares similarities with the Medicaid program, including the relationship between the private physician and the federal government wherein the physician's judgment plays a central role yet the physician must operate within the reasonable limits established by the state.

[1976 Transfer Binder] Medicare & Medicaid Guide (CCH)  
¶ 28,152 (1976).

*Rush v. Parnam*, 625 F.2d at 1156 n. 11.

Following *Rush*, the question of experimental treatment has been considered in a variety of settings, not all of which actually turn on the application of that standard to the facts of the case. A number of cases cited by Appellant as having followed *Rush*'s lead on this point are, in fact, distinguishable.

In *Weaver v. Reagan*, 886 F.2d 194 (8th Cir. 1989), a class of Medicaid-eligible individuals were denied coverage for AZT to treat their AIDS. The Missouri Department of Social Services defended their action claiming the coverage was limited to only those patients whose condition met the FDA labeling statement and, secondarily, any use outside the labeling statement was *per se* experimental. Not only did an FDA bulletin refute the Department's position with respect to the controlling nature of the labeling statement, but the *Weaver* court applying the *Rush* definition found the use of AZT beyond the labeled uses was not experimental inasmuch as it was commonly prescribed for the use requested by plaintiffs and was generally accepted in the medical community as an effective treatment. In sum, Missouri's action was arbitrary since the rule created an irrebuttable presumption. Such is not the case with Utah's standard which takes into consideration factors such as acceptance in the medical community as an efficacious treatment.



In *Montoya v. Johnston*, 654 F.Supp. 511 (W.D.Tex. 1987), the Texas Department of Human Services placed a cap of \$50,000 on the amount Medicaid would pay for inpatient hospital services during any 12-month period. This effectively precluded the liver transplants, costing approximately \$200,000, sought by two young children otherwise eligible for Medicaid. In support of the request, the children's physicians submitted affidavits stating that liver transplants were not considered experimental. Additionally, the court found the Texas Medicaid cap was arbitrary and unreasonable. The cap was contrary to Medicaid regulations which prohibit restrictions which "arbitrarily deny or reduce the amount, duration or scope of a required service . . . to an otherwise eligible recipient solely because of the diagnosis, type of illness or condition." *Montoya v. Johnston*, 654 F.Supp. at 513. While the *Montoya* court cited to *Rush* and the definition of experimental treatment, the facts of *Montoya* distinguish it from the instant case. Appellant Markelle did not come up against an arbitrary cap or restriction nor did the evidence submitted state unequivocally the procedure was not experimental. Rather, the contrary situation exists in that there is no unequivocal statement that the use of growth hormone for the use requested is not experimental.

In *Miller by Miller v. Whitburn*, 10 F.3d 1315 (7th Cir. 1993), the issue of experimental is framed in a somewhat

different manner. The question decided was that the district court could review Wisconsin's Department of Health and Social Services' definition of experimental to ensure it complied with federal mandates that standards applied by states be reasonable. The court took care to reiterate that states retained significant discretion in deciding which treatments to cover. The actual determination of whether the liver-bowel transplantation at issue was covered by Medicaid remained to be considered. The court noted the record did not contain facts addressing matters such as efficacy or the opinion of the medical community. In citing to *Rush*, the *Miller* court cited the definition of experimental in its entirety; it then made further comments on the term. It stated "[c]learly, the best indicator that a procedure is experimental is its rejection by the professional medical community as an unproven treatment." *Miller by Miller v. Whitburn*, 10 F.3d at 1320. This would be correct if the scientific studies had been properly conducted and confirmed the conclusion the treatment was worthless. As it stands, it perhaps states too much until the confirming results; therefore, it is of dubious use in analyzing the instant matter. However, further on the *Miller* court states that "certain procedures may be so new and . . . relatively unknown, that the medical community may not yet have formed an opinion as to their efficacy." *Miller by Miller v. Whitburn*, *Id.* The court then stated "[i]f

'authoritative evidence' exists that attests to a procedure's safety and effectiveness, it is not 'experimental.'" *Miller by Miller v. Whitburn, Id.* Taken together these statements indicate that experimental determinations require authoritative evidence establishing safety and effectiveness. Therefore, DHCF's determination in the present case is reasonable if the same factors are applied.

And, finally, in *McLaughlin v. Williams*, 801 F.Supp. 633 (S.D. Fla. 1992), the court considered Florida's denial of Medicaid for a liver-small bowel transplantation because it was deemed experimental. The definition of experimental found in *Rush* was applied as binding precedent as the *McLaughlin* court considered a possibly fatal situation and so the court found useful the determination that a relatively new procedure can be found medically necessary if "authoritative evidence" established it was "safe and effective." *McLaughlin v. Williams*, 801 F.Supp. at 639, citing from *Rush*. Of concern to the court were factors of safety and effectiveness where new procedures are considered. Risks and benefits must be balanced. Rapid medical advances made determinations difficult and rigid standards applied by the state compounded the problem. The court identified in some detail that "simple demarcation" was not a workable means of defining experimental. *McLaughlin v. Williams*, 801 F.Supp. at 638-40. Such is not the case in the instant matter. The standard applied

by DHCF permits evaluation of the effectiveness of the procedure and its utilization in the medical community along with the physician's determination of medical necessity. Appellant argues that DHCF's definition of experimental should include specific demarcation to define "how widely used" a practice should be to avoid the same fate as the court identified in *McLaughlin*. In point of fact, this would not benefit the decision making process. In these cases the Division needs to be able to exercise its discretion so that a reasoned and reasonable decision is made.

The Recommended Decision, adopted as the Final Agency Order, (R-109-114), sets forth the decision to deny on the basis of experimental treatments not being covered by Medicaid. In her findings, the administrative law judge (ALJ) identified Markelle's diagnosis and prior and current condition. She also identified the proposed treatment as still controversial notwithstanding a number of reputable physicians were motivated to prescribe the treatment. She also alluded to the fact growth hormone was not included in the package labeling statement. The record transcript and exhibits and submitted articles when taken as a whole justify the ALJ's conclusion even though the findings are somewhat cursory. Further, the reasoning given by the ALJ identifies those additional factors necessary to support the conclusion. Of importance is the recognition that the testimony

does not refute the experimental nature of the treatment and that it remains controversial. (R-113). Also, while the ALJ writes "Dr. Jackson made compelling arguments for the medical necessity of using growth hormone" (R-113), that is not the same as stating he established the medical necessity. A careful reading of the transcript and the recommended decision shows the ALJ did not reject the treating physician's testimony. Her decision weighed all the evidence and finding the treatment remained controversial even by Dr. Jackson's own testimony gave reason and credibility to the decision. *Frey v. Bowen*, 816 F.2d 508 (10th Cir. 1987). In fact, nowhere in the record does Dr. Jackson unequivocally state the treatment is medically necessary.

Even assuming the Division has applied the wrong standard to the facts of this matter, Appellant's position is not supported upon a review of the entire record. Assuming the review standard applied by Appellant is to succeed in claiming that the ALJ's decision should fail for lack of sufficient evidence, Appellant must marshall all the evidence presented and show that notwithstanding the evidence contrary to the decision there is insufficient evidence to adequately support the conclusion. *A.M.L. v. Department of Health*, 863 P.2d at 46-47; *Zissi v. State Tax Comm'n of Utah*, 842 P.2d 848, 852-53 (Utah 1992). The record as a whole provides sufficient evidence which a reasonable person could accept as adequate to support the conclusion reached by the

administrative law Judge. Appellant's position is that even if the procedure is not widely utilized as a standard medical practice, novel or relatively unknown procedures can be found medically necessary if authoritative evidence shows the treatment is safe and effective. Appellant claims the authoritative evidence to be relied upon in this case is the "testimony of Dr. Jackson, together with extensive medical literature" (Appellant's Br. at 20). Appellant's summary of Dr. Jackson's testimony identifies eight points as determinative. Point 1: ["higher indicated" use of the drug] While using a drug to possibly save a life could reasonably be classified as a "higher indication" for the drug than its approved use for short statured persons, this does not equate with effectiveness. Point 2: [cost effective alternative] While the limited data suggests growth hormone treatment costs less than either TPN or a liver transplant, the critical factor is whether the drug effectively eliminates or prevents either of the alternative treatments and the attendant costs; and, the evidence does not establish that fact. (T-126-26, 27, 29-31). Point 3: [studies by "mainstream" professionals supporting use] While Dr. Jackson testified the proposed use found support among "mainstream" professionals, the fact remains that these studies describe limited trials which remain in the investigational stage and are still controversial. (T-126-27-28). Point 4: [short-term studies show some increase

in absorption and amino acid uptake] While study trial results may show some of the hoped-for benefits, the results obtained suggested to those conducting the trials that additional trials should be undertaken to determine effectiveness. (R-25, 28-29, 37-38). Point 5: [apparent improvement in Markelle's enteral nutrition while taking growth hormone] While testimony indicated some increased ability to tolerate oral feedings, Dr. Jackson testified he could not tie that change to any treatment and it could be the result of the maturation process. (T-126-18, 19). Point 6: [use of growth hormone reasonably calculated to prevent death, improve quality of life] While Dr. Jackson did testify that his goals with respect to the use of growth hormone would be to achieve the definitional elements contained in the "medically necessary" rule read at the hearing, he further testified that it was a new therapy, still controversial and it may not turn out to be effective. (T-126-26). Point 7: [growth hormone would lessen suffering] While eliminating the need for TPN would also eliminate suffering caused by infections, and so forth, this would only occur if the treatment proved safe and effective and in fact eliminated the parenteral nutrition; that was one of Dr. Jackson's goals but that is different than stating the proposed experimental use will achieve that goal. Point 8: [no alternative treatment for less cost] Assuming the proposed growth hormone treatment worked as hoped and was of limited duration,

the testimony supports this conclusion. As further testimony indicates, Markelle receives TPN which is expensive; however, her oral feedings have increased. (T-126-18).

Four published studies, previously referred to generally, were submitted at the time of the administrative hearing; and, unfortunately and inexplicably, the literature had not been received for the Division's medical expert to review and comment upon during testimony. Whether this legitimately constitutes extensive, authoritative evidence which proves safety and effectiveness is questionable. If Appellant's standard should apply, one question to be addressed is what constitutes authoritative evidence. It is not unreasonable to require a certain quantum of such evidence such that a person would reasonably believe it established the safety and effectiveness of the experimental procedure. Are these studies sufficient to meet the proposed standard. The studies submitted for support contain statements of reservation and these reservations are acknowledged by Dr. Jackson in his testimony. The studies state their initial results suggest a potential alternative treatment and therefore further trials are required to determine matters such as timing, dosage, combinations for optimal effect, and safety and effectiveness. The studies were very small and conducted over very short periods of time using adult subjects. One reference is made to a group of 12 children having received treatment (R-



17); however, the details of treatment and results are limited and cannot reasonably justify finding the treatment proposed for Markelle is not experimental. The study size and duration, participant composition, and multiple factors (growth hormone, glutamine and specialized diet) administered to the participants in the clinical trials combine to raise significant concerns justifying the Division's decision. Since the elements of the proposed standard of "safe and effective" require a factual analysis, this should be left to the agency's discretion and the reviewing court should grant deference to the agency's expertise.

#### **CONCLUSION**


The Medicaid program is a publicly funded program designed to assist individuals who lack sufficient funds to obtain needed medical services. Since it is a public program, it must function according to rules and regulations to ensure efficient and effective use of limited resources. Medicaid never has been considered a research program. While new, evolving treatments in medical research are anticipated, it is unacceptable to contemplate using a vulnerable population as potential research subjects. To protect both the individuals needing the Medicaid services necessary and appropriate to the specific condition and the integrity of the Medicaid program, the Division should have policies in place to prevent unintended as well as intended

abuses. It is entirely appropriate for the Division to exclude experimental medical services.

The agency's application of the rule to the facts of the case resulted in a final agency order denying Medicaid coverage for an experimental treatment. In reviewing the record as a whole, and in the absence of an abuse of the discretion granted the agency to establish and administer the State's Medicaid program, the agency's decision is reasonable and should be affirmed.

Respectfully submitted this 11th day of June, 1998.

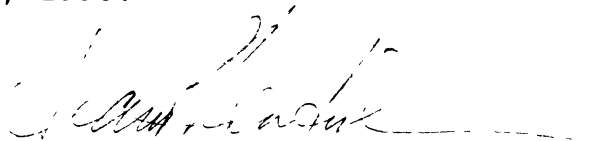
JAN GRAHAM  
Attorney General

  
\_\_\_\_\_  
Jean P. Hendrickson  
Assistant Attorney General  
Attorney for Appellee

#### **CERTIFICATE OF DELIVERY**

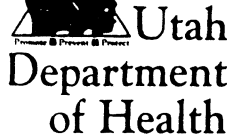
I hereby certify that I caused to be delivered 4 copies of the foregoing Appellee's Brief to the attorneys for the Appellant, Michael E. Bulson, Utah Legal Services, Inc., 550 24th Street, Suit 300, Ogden, Utah 84401, and, W. Paul Wharton, Utah Legal Services, Inc., 254 West 400 South, Second Floor, Salt Lake City, Utah 84101.

DATED this 15th day of June, 1998.

  
\_\_\_\_\_

## Addenda

## Addendum A



## DIVISION OF HEALTH CARE FINANCING

# State of Utah

**Michael O. Leavitt**  
Governor

**Rod L. Betit**  
Executive Director

**Michael J. Deily**  
Division Director

288 North 1460 West  
Box 142901  
Salt Lake City, Utah 84114-2901  
Telephone: (801) 538-6406  
Fax: (801) 538-6099

**MARKELLE FREI-PETERSON**  
Petitioner

**VS.**

UTAH DEPARTMENT OF HEALTH  
DIVISION OF HEALTH CARE FINANCING,  
Respondent.

## FINAL AGENCY ORDER

Case No. 97-209-11

IF YOU ARE NOT SATISFIED WITH THIS DECISION, YOU MAY REQUEST A RECONSIDERATION FROM THE DIRECTOR OF HEALTH CARE FINANCING WITHIN TWENTY (20) DAYS AFTER THIS DECISION IS SIGNED. IF YOU WOULD LIKE TO APEAL THIS DECISION, YOU MAY FILE A PETITION IN THE UTAH COURT OF APPEALS WITHIN THIRTY (30) DAYS AFTER THIS DECISION IS SIGNED. IF YOU DECIDE TO APPEAL, YOU ARE NOT REQUIRED TO ASK FOR A RECONSIDERATION FIRST, BUT YOU MAY DO SO IF YOU WISH. IF YOU HAVE QUESTIONS, CALL (801) 538-6576.

The enclosed Recommended Decision has been reviewed pursuant to Section 63-46b-12 Utah Code Ann. 1953, as amended, entitled "Agency Review - Procedure," and Department of Health Administrative Rule R410-14, entitled "Division of Health Care Financing Administrative Hearing Procedures for Medicaid/UMAP Applicants, Recipients, and Providers."

**I hereby adopt Recommended Decision No. 97-209-11 in its entirety.**

## RIGHT TO JUDICIAL REVIEW

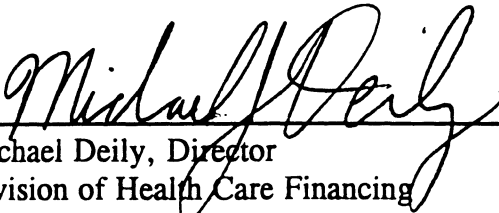
Within twenty (20) days after the date that this Final Agency Order is issued, you may file a written request for reconsideration with the Director of the Division of Health Care Financing. Any request for reconsideration must state the specific grounds upon which relief is requested. The filing of such a request is not a prerequisite for seeking judicial review.

Judicial review may be secured by filing a petition in the Utah Court of Appeals within thirty (30) days of the issuance of this Final Agency Action or, if a request for reconsideration is

filed and denied, within thirty (30) days of the denial for reconsideration. The petition shall be served upon the Director of Health Care Financing and shall state the specific grounds upon which review is sought. Failure to file such a petition within the 30-day time limit may constitute a waiver of any right to appeal the Final Agency Order.

A copy of this Final Agency Order shall be sent to Petitioner or representative at the last known address by certified mail, return receipt requested.

DATED this 15 day of January 1998

BY:   
Michael Deily, Director  
Division of Health Care Financing  
UTAH DEPARTMENT OF HEALTH

BEFORE THE UTAH DEPARTMENT OF HEALTH

DIVISION OF HEALTH CARE FINANCING

STATE OF UTAH

-----ooOoo-----

MARKELLE FREI-PETERSON	:	
Petitioner,	:	
	:	<b>RECOMMENDED DECISION</b>
vs.	:	
	:	
UTAH DEPARTMENT OF HEALTH	:	Case No. 97-209-11
DIVISION OF HEALTH CARE	:	Margaret J. Clark
FINANCING,	:	Administrative Law Judge
Respondent.	:	

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Pursuant to Rule R410-14 of the Utah Department of Health and the Utah Administrative Hearing Procedures Act, Title 63, Chapter 46b, Utah Code Annotated, 1953, as amended, a formal administrative hearing for the above captioned case was held on December 8, 1997, at 8:00 a.m., in Room 344, Cannon Health Building, 288 North 1460 West, Salt Lake City, Utah 84116, Margaret J. Clark, Administrative Law Judge, presiding. Daniel Jackson, M.D., testified on behalf of the petitioner. The petitioner's mother was present at the hearing. Steven Gatzemeier represented the Division of Health Care Financing ("DHCF"). John C. Hylan, M.D., and Duane Parke testified on behalf of DHCF.

ISSUE

SHOULD UTAH MEDICAID COVER GROWTH HORMONE TO TREAT SHORT BOWEL SYNDROME FOR MARKELLE FREI-PETERSON?

## FINDINGS OF FACT

1. Markelle Frei-Peterson is approximately twenty four months old, suffers from short bowel syndrome, and is dependent on parenteral nutrition for approximately 90% of her nutritional needs.
2. In the past three or four months she has begun to tolerate some oral feedings, but remains dependent on parenteral nutrition.
3. Short bowel syndrome requires expensive technology and possibly a lifetime of parenteral nutrition.
4. The goal of Markelle's treating physician is to accelerate her gastrointestinal adaptation by administering the growth hormone for about one year.
5. Because she has short bowel syndrome, Markelle is at risk of central line catheter infections, eventual loss of intravenous access sites, and progressive liver dysfunction.
6. Markelle has been receiving growth hormone for approximately three months. The hormone has been supplied by a Primary Children's Hospital charity.
7. Usage of growth hormone for short bowel syndrome is considered an "off-label" use by the Federal Food and Drug Administration.
8. The data is sufficient to motivate a number of reputable physicians to prescribe growth hormone for short bowel syndrome, but it is still considered to be controversial.

## RECOMMENDED CONCLUSIONS OF LAW

The use of growth hormone to treat small bowel syndrome is "experimental" as defined in: Utah Administrative Code R414-1A-200, and is therefore not covered by Utah Medicaid [see R414-1A-300(1)].

## REASONS FOR PRESIDING OFFICER'S DECISION

DHCF denied reimbursement for growth hormone for Markelle because it contended that the drug is experimental for usage in treating short bowel syndrome, and it has not been approved by the Federal Drug Administration for that purpose.

DHCF's policy regarding experimental or unproven medical practices is contained in Utah Administrative Code R410A. R410A-300 states in relevant part:

- (1) Experimental or unproven medical practices are not covered Medicaid



services.

R410A-200 defines "experimental or unproven medical practice" as "(2)(i) not proven to be medically efficacious for a given procedure." "Medically efficacious" is defined in R410-1A-200(iii)(b) as "a medical practice that has been determined effective and is widely utilized as a standard medical practice for specific conditions."

W. Daniel Jackson, M.D., Markelle's treating physician testified on her behalf. Dr. Jackson is board certified in pediatrics and pediatric gastroenterology and nutrition. He is an Assistant Professor of Pediatrics at the University of Utah School of Medicine, and Medical Director of Nutrition Support Services at Primary Children's Hospital.

Dr. Jackson testified that growth hormone for short bowel syndrome is being used by a number of reputable physicians in the United States. He testified that it was controversial, but it had promise.

Dr. Jackson testified that growth hormone is commonly used in many children to treat short stature, and since Medicaid covers the drug for that use, it should also cover its usage for short bowel syndrome, which he believes has a "higher indication."

Dr. Jackson made compelling arguments for the medical necessity of using growth hormone for Markelle. He testified that he thought that use of growth hormone in this case would be a cost effective approach when compared to the potential cost of lifetime parental nutrition or liver transplantation, both of which could result from small bowel syndrome. He testified that more conservative approaches to treat Markelle were not successful, and as her treating physician, he had weighted the pluses and minuses of using the growth hormone.

Dr. Jackson testified that the impetus for trying the growth hormone was the fact that Markelle was showing signs of accelerated liver disease. Upon cross examination, John C. Hylen, M.D., and Physician Consultant for DHCF asked Dr. Jackson if he could provide documentation of whether or not Markelle's liver function had normalized as a result of receiving the growth hormone. Dr. Jackson replied that he did not know why her liver functions had improved, but he thought that it had normalized "independent of growth hormone." He testified that Markelle had improved after receiving growth hormone, but that improvement could also have come from the maturation process and the oral feedings Markelle has recently begun to tolerate.

Dr. Jackson conceded that the use of growth hormone for short bowel syndrome is an area where there is active work and controversy, and, "The indications are not in your code for using it this way."

As the expert witness for the moving party, the burden of proof was on Dr. Jackson to prove by the preponderance of the evidence that the growth hormone should be covered. Despite his convincing testimony regarding the medical necessity of using the drug for Markelle, he was not able to overcome DHCF's evidence that the use of growth hormone to treat short bowel

syndrome is an off-label usage of the drug, and it has not yet been proven to be effective for that usage. Although treatment of short bowel syndrome with growth hormone might be more highly indicated than its usage for children of short stature, the law prohibits the use of experimental treatments, and Dr. Jackson's testimony clearly indicated that the use of growth hormone to treat short bowel syndrome was not "widely utilized as a standard medical practice," and therefore meets the criteria for an "experimental procedure."

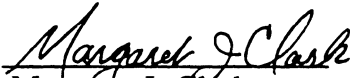
#### RECOMMENDED AGENCY ACTION

I recommend that DHCF's action be UPHELD.

#### RIGHT TO REVIEW

This Recommended Decision will be automatically reviewed by the Department of Health, Division of Health Care Financing, prior to its release. Both the Recommended Decision and a Final Agency Action, which represent the results of that review, will be released simultaneously by the Department of Health, Division of Health Care Financing.

DATED this 7 day of January 1998

  
Margaret J. Clark  
Administrative Law Judge

The following exhibits were admitted into evidence:

RESPONDENT'S EXHIBIT 1: Off-Label Drug Policy

PETITIONER'S EXHIBIT 1: Medical Literature Regarding Short Bowel Syndrome and  
Growth Hormone

PETITIONER'S EXHIBIT 2: Billing Records for Markelle

No: 97-209-11

CERTIFICATE OF MAILING

I hereby certify that on the 15 day of January 1998, I mailed a true and correct copy of the foregoing FINAL AGENCY ORDER AND RECOMMENDED DECISION, to the following parties:

POSTAGE PREPAID

HEIDI PETERSON  
2694 ORCHARD DRIVE  
BOUNTIFUL, UTAH 84010-6466

DR. DAN JACKSON  
PEDIATRIC GASTROENTEROLOGY  
PRIMARY CHILDRENS MEDICAL CENTER  
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EVY SMITH, PEDIATRIC CONTINUUM CARE MANAGER  
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IHC HOME CARE  
MCKAY-DEE HOSPITAL CENTER  
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INTER-DEPARTMENTAL MAIL

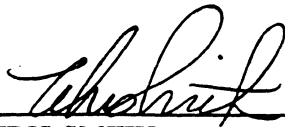
STEVE GATZEMEIER  
HEALTH PROGRAM MANAGER  
COVERAGE & REIMBURSEMENT POLICY  
DIVISION OF HEALTH CARE FINANCING  
UTAH DEPARTMENT OF HEALTH

DR. JOHN HYLEN  
COVERAGE & REIMBURSEMENT POLICY  
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PENNI NAHLEY  
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DUANE PARKE  
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UTAH DEPARTMENT OF HEALTH

MICHAEL DEILY, DIRECTOR  
DIVISION OF HEALTH CARE FINANCING  
UTAH DEPARTMENT OF HEALTH

  
CHRIS SMITH

## Addendum B

## Note 2

When state voluntarily elects to participate in Medicaid program, it must comply with requirements of the Act and applicable regulations. *Morgan v. Idaho Dept. of Health and Welfare*, Idaho 1991, 813 P.2d 345, 120 Idaho 6.

## 3. Eligibility

Omnibus Budget Reconciliation Act does not prevent otherwise eligible pregnant women who are not permanently residing in this country under color of law (PRUCOL) from receiving Medicaid sponsored prenatal care where their children, if born in the United States, will become United States citizens. *Lewis v. Grinker*, C.A.2 (N.Y.) 1992, 965 F.2d 1206.

State and federal regulations arbitrarily and capriciously limited to \$1,500 the automobile exclusion in calculating family resources for purposes of eligibility for Aid to Families with Dependent Children (AFDC) and Medicaid in that reason initially offered for automobile asset limitation, in allowing recipients to retain possession of a car, could no longer provide rational basis for the regulation in light of inflation, even though Congress did not mandate review to adjust for inflation. *Hazard v. Sullivan*, M.D.Tenn.1993, 827 F.Supp. 1348, reversed 44 F.3d 399.

## § 1396a. State plans for medical assistance

## (a) Contents

A State plan for medical assistance must—

(1) provide that it shall be in effect in all political subdivisions of the State, and, if administered by them, be mandatory upon them;

(2) provide for financial participation by the State equal to not less than 40 per centum of the non-Federal share of the expenditures under the plan with respect to which payments under section 1396b of this title are authorized by this subchapter; and, effective July 1, 1969, provide for financial participation by the State equal to all of such non-Federal share or provide for distribution of funds from Federal or State sources, for carrying out the State plan, on an equalization or other basis which will assure that the lack of adequate funds from local sources will not result in lowering the amount, duration, scope, or quality of care and services available under the plan;

(3) provide for granting an opportunity for a fair hearing before the State agency to any individual whose claim for medical assistance under the plan is denied or is not acted upon with reasonable promptness;

(4) provide (A) such methods of administration (including methods relating to the establishment and maintenance of personnel standards on a merit basis, except that the Secretary shall exercise no authority with respect to the selection, tenure of office, and compensation of any individual employed in accordance with such methods, and including provision for utilization of professional medical personnel in the administration and, where administered locally, supervision of administration of the plan) as are found by the Secretary to be necessary for the proper and efficient operation of the plan, (B) for the training and effective use of paid subprofessional staff, with particular emphasis on the full-time or part-time employment of recipients and other persons of low income, as community service aides, in the administration of the plan and for the use of nonpaid or partially paid volunteers in a social service volunteer program in providing services to applicants and recipients and in assisting any advisory committees established by the State agency, and (C) that each State or local officer or employee who is responsible for the expenditure of substantial amounts of funds under the State plan, each individual who formerly was such an officer or employee, and each partner of such an officer or employee shall be prohibited from committing any act, in relation to any activity under the plan, the commission of which, in connection with any activity concerning the United States Government, by an officer or employee of the United States Government, an individual who was such an officer or employee, or a partner of such an officer or employee is prohibited by section 207 or 208 of Title 18;

(5) either provide for the establishment or designation of a single State agency to administer or to supervise the administration of the plan; or provide for the establishment or designation of a single State agency to administer or to supervise the administration of the plan, except that the determination of eligibility for medical assistance under the plan shall be made by the State or local agency administering the State plan approved under subchapter I or XVI of this chapter (insofar as it relates to the aged) if the State is eligible to participate in the State plan program established under subchapter XVI of this chapter, or by the agency or agencies administering the supplemental security income program established under subchapter XVI or the State plan approved under part A of subchapter IV of

this chapter if the State is not eligible to participate in the State plan program established under subchapter XVI of this chapter;

(6) provide that the State agency will make such reports, in such form and containing such information, as the Secretary may from time to time require, and comply with such provisions as the Secretary may from time to time find necessary to assure the correctness and verification of such reports;

(7) provide safeguards which restrict the use or disclosure of information concerning applicants and recipients to purposes directly connected with the administration of the plan;

(8) provide that all individuals wishing to make application for medical assistance under the plan shall have opportunity to do so, and that such assistance shall be furnished with reasonable promptness to all eligible individuals;

(9) provide—

(A) that the State health agency, or other appropriate State medical agency (whichever is utilized by the Secretary for the purpose specified in the first sentence of section 1395aa(a) of this title), shall be responsible for establishing and maintaining health standards for private or public institutions in which recipients of medical assistance under the plan may receive care or services,

(B) for the establishment or designation of a State authority or authorities which shall be responsible for establishing and maintaining standards, other than those relating to health, for such institutions, and

(C) that any laboratory services paid for under such plan must be provided by a laboratory which meets the applicable requirements of section 1395x(e)(9) of this title or paragraphs (13) and (14)<sup>1</sup> of section 1395x(s) of this title, or, in the case of a laboratory which is in a rural health clinic, of section 1395x(aa)(2)(G) of this title;

(10) provide—

(A) for making medical assistance available, including at least the care and services listed in paragraphs (1) through (5), (17) and (21) of section 1396d(a) of this title, to—

(i) all individuals—

(I) who are receiving aid or assistance under any plan of the State approved under subchapter I, X, XIV, or XVI of this chapter, or part A or part E of subchapter IV of this chapter (including individuals eligible under this subchapter by reason of section 602(a)(37), 606(h), or 673(b) of this title, or considered by the State to be receiving such aid as authorized under section 682(e)(6) of this title),

(II) with respect to whom supplemental security income benefits are being paid under subchapter XVI of this chapter or who are qualified severely impaired individuals (as defined in section 1396d(q) of this title),

(III) who are qualified pregnant women or children as defined in section 1396d(n) of this title,

(IV) who are described in subparagraph (A) or (B) of subsection (l)(1) of this section and whose family income does not exceed the minimum income level the State is required to establish under subsection (l)(2)(A) of this section for such a family;<sup>1</sup>

(V) who are qualified family members as defined in section 1396d(m)(1) of this title;<sup>1</sup>

(VI) who are described in subparagraph (C) of subsection (l)(1) of this section and whose family income does not exceed the income level the State is required to establish under subsection (l)(2)(B) of this section for such a family, or

(VII) who are described in subparagraph (D) of subsection (l)(1) of this section and whose family income does not exceed the income level the State is required to establish under subsection (l)(2)(C) of this section for such a family;

(ii) at the option of the State, to any group or groups of individuals described in section 1396d(a) of this title (or, in the case of individuals described in section 1396d(a)(i) of this title, to any reasonable categories of

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### Note 32

Undocumented alien whose chronic alcoholism had so compromised her liver and central nervous system before she appeared at hospital that lack of immediate medical attention would not have resulted in more serious jeopardy to her health did not possess "emergency medical condition," such that would be eligible for assistance under Medical Care and Assistance Program. *Norwood Hosp. v. Commissioner of Public Welfare*, Mass.1994, 627 N.E.2d 914, 417 Mass. 54.

Statute which states that Medicaid payment shall be made for care and services to alien who is not lawfully admitted for permanent residence, only if such care and services are necessary for treatment of emergency medical condition and alien otherwise meets eligibility requirements for medical assistance of a State plan, is exception to rule that prohibits Medicaid not only to nonresident aliens, but also to resident aliens whose residency is unlawful; it does not affect status of nonresident aliens. *Salem Hosp. v. Commissioner of Public Welfare*, Mass.1991, 574 N.E.2d 385, 410 Mass. 625.

### 33. Relief from judgment or order

State of New York was entitled to relief from consent decree establishing Medicaid pharmacy reimbursement methodology, where Secretary of Health and Human Services had subsequently established reimbursement cap on Medicaid reimbursements for certain defined medications, creating risk that state would lose federal financial participation if it did not comply. *Pharmaceutical Soc. of the State of New York, Inc. v.*

## PUBLIC HEALTH AND WELFARE

*Cuomo*, S.D.N.Y.1991, 774 F.Supp. 826, affirmed in part, reversed in part 981 F.2d 632.

### 34. Similarly situated individuals—Generally

Under federal Medicaid statute pursuant to which federal payment for organ transplant will not be made unless state plan provides for written standards and such standards provide that similarly situated individuals are treated alike, "similarly situated" means all patients who can be treated effectively by same organ transplant procedure. *Salgado v. Kirschner*, Ariz.1994, 878 P.2d 659, 179 Ariz. 301, certiorari denied 115 S.Ct. 1102, 130 L.Ed.2d 1069.

### 35. — Other necessary services

Provision of state Medicaid plan that allowed state to deny life-sustaining liver transplant coverage to otherwise eligible Medicaid recipient solely because she was over 21 years of age violated requirement of federal Medicaid statute that state standards for organ transplants treat similarly situated individuals alike; recipient was within class of all patients who could be treated effectively by liver transplant, and catch-all provision of Medicaid statute dealing with federal early and periodic health screening diagnostic and treatment services (EPSDT) did not, as state apparently contended, define substantive scope of medically necessary procedures and draw distinction for such procedures between children and adults. *Salgado v. Kirschner*, Ariz.1994, 878 P.2d 659, 179 Ariz. 301, certiorari denied 115 S.Ct. 1102, 130 L.Ed.2d 1069.

## § 1396c. Operation of State plans

### NOTES OF DECISIONS

#### 9. Hearing

Decision of Secretary of Health and Human Services (HHS) as to whether to hold hearing on

compliance with federal Medicaid requirements is discretionary. *Phoenix Baptist Hosp. and Medical Center, Inc. v. U.S.*, C.A.9 (Ariz.) 1991, 937 F.2d 452.

## § 1396d. Definitions

For purposes of this subchapter—

### (a) Medical assistance

The term "medical assistance" means payment of part or all of the cost of the following care and services (if provided in or after the third month before the month in which the recipient makes application for assistance or, in the case of medicare cost-sharing with respect to a qualified medicare beneficiary described in subsection (p)(1) of this section, if provided after the month in which the individual becomes such a beneficiary) for individuals, and, with respect to physicians' or dentists' services, at the option of the State, to individuals (other than individuals with respect to whom there is being paid, or who are eligible, or would be eligible if they were not in a medical institution, to have paid with respect to them a State supplementary payment and are eligible for medical assistance equal in amount, duration, and scope to the medical assistance made available to individuals described in section 1396a(a)(10)(A) of this title) not receiving aid or assistance under any plan of the State approved under subchapter I, X, XIV, or XVI, or part A of subchapter IV, and with respect to whom supplemental security income benefits are not being paid under subchapter XVI of this chapter, who are—

(i) under the age of 21, or, at the option of the State, under the age of 20, 19, or 18 as the State may choose,



(ii) relatives specified in section 606(b)(1) of this title with whom a child is living if such child is (or would, if needy, be) a dependent child under part A of subchapter IV of this chapter,

(iii) 65 years of age or older,

(iv) blind, with respect to States eligible to participate in the State plan program established under subchapter XVI of this chapter,

(v) 18 years of age or older and permanently and totally disabled, with respect to States eligible to participate in the State plan program established under subchapter XVI of this chapter,

(vi) persons essential (as described in the second sentence of this subsection) to individuals receiving aid or assistance under State plans approved under subchapter I, X, XIV, or XVI of this chapter,

(vii) blind or disabled as defined in section 1382c of this title, with respect to States not eligible to participate in the State plan program established under subchapter XVI of this chapter,

(viii) pregnant women,

(ix) individuals provided extended benefits under section 1396r-6 of this title,

(x) individuals described in section 1396a(u)(1) of this title, or

(xi) individuals described in section 1396a(z)(1) of this title,

but whose income and resources are insufficient to meet all of such cost—

(1) inpatient hospital services (other than services in an institution for mental diseases);

(2) (A) outpatient hospital services, (B) consistent with State law permitting such services, rural health clinic services (as defined in subsection (l)(1) of this section) and any other ambulatory services which are offered by a rural health clinic (as defined in subsection (l)(1) of this section) and which are otherwise included in the plan, and (C) Federally-qualified health center services (as defined in subsection (l)(2) of this section) and any other ambulatory services offered by a Federally-qualified health center and which are otherwise included in the plan;

(3) other laboratory and X-ray services;

(4) (A) nursing facility services (other than services in an institution for mental diseases) for individuals 21 years of age or older; (B) early and periodic screening, diagnostic, and treatment services (as defined in subsection (r) of this section) for individuals who are eligible under the plan and are under the age of 21; and (C) family planning services and supplies furnished (directly or under arrangements with others) to individuals of child-bearing age (including minors who can be considered to be sexually active) who are eligible under the State plan and who desire such services and supplies;

(5) (A) physicians' services furnished by a physician (as defined in section 1395x(r)(1) of this title), whether furnished in the office, the patient's home, a hospital, or a nursing facility, or elsewhere, and (B) medical and surgical services furnished by a dentist (described in section 1395x(r)(2) of this title) to the extent such services may be performed under State law either by a doctor of medicine or by a doctor of dental surgery or dental medicine and would be described in clause (A) if furnished by a physician (as defined in section 1395x(r)(1) of this title);

(6) medical care, or any other type of remedial care recognized under State law, furnished by licensed practitioners within the scope of their practice as defined by State law;

(7) home health care services;

(8) private duty nursing services;

(9) clinic services furnished by or under the direction of a physician, without regard to whether the clinic itself is administered by a physician, including such services furnished outside the clinic by clinic personnel to an eligible individual who does not reside in a permanent dwelling or does not have a fixed home or mailing address;

(10) dental services;

(11) physical therapy and related services;

(12) prescribed drugs, dentures, and prosthetic devices; and eyeglasses prescribed by a physician skilled in diseases of the eye or by an optometrist, whichever the individual may select;

(13) other diagnostic, screening, preventive, and rehabilitative services, including any medical or remedial services (provided in a facility, a home, or other setting) recommended by a physician or other licensed practitioner of the healing arts within the scope of their practice under State law, for the maximum reduction of physical or mental disability and restoration of an individual to the best possible functional level;

(14) inpatient hospital services and nursing facility services for individuals 65 years of age or over in an institution for mental diseases;

(15) services in an intermediate care facility for the mentally retarded (other than in an institution for mental diseases) for individuals who are determined, in accordance with section 1396a(a)(31)(A) of this title, to be in need of such care;

(16) effective January 1, 1973, inpatient psychiatric hospital services for individuals under age 21, as defined in subsection (h) of this section;

(17) services furnished by a nurse-midwife (as defined in section 1395x(gg) of this title) which the nurse-midwife is legally authorized to perform under State law (or the State regulatory mechanism provided by State law), whether or not the nurse-midwife is under the supervision of, or associated with, a physician or other health care provider, and without regard to whether or not the services are performed in the area of management of the care of mothers and babies throughout the maternity cycle;

(18) hospice care (as defined in subsection (o) of this section);

(19) case-management services (as defined in section 1396n(g)(2) of this title) and TB-related services described in section 1396a(z)(2)(F) of this title;

(20) respiratory care services (as defined in section 1396a(e)(9)(C) of this title);

(21) services furnished by a certified pediatric nurse practitioner or certified family nurse practitioner (as defined by the Secretary) which the certified pediatric nurse practitioner or certified family nurse practitioner is legally authorized to perform under State law (or the State regulatory mechanism provided by State law), whether or not the certified pediatric nurse practitioner or certified family nurse practitioner is under the supervision of, or associated with, a physician or other health care provider;

(22) home and community care (to the extent allowed and as defined in section 1396t of this title) for functionally disabled elderly individuals; and

(23) community supported living arrangements services (to the extent allowed and as defined in section 1396u of this title);

(24) personal care services furnished to an individual who is not an inpatient or resident of a hospital, nursing facility, intermediate care facility for the mentally retarded, or institution for mental disease that are (A) authorized for the individual by a physician in accordance with a plan of treatment or (at the option of the State) otherwise authorized for the individual in accordance with a service plan approved by the State, (B) provided by an individual who is qualified to provide such services and who is not a member of the individual's family, and (C) furnished in a home or other location; and

(25) any other medical care, and any other type of remedial care recognized under State law, specified by the Secretary.

except as otherwise provided in paragraph (16), such term does not include—

(A) any such payments with respect to care or services for any individual who is an inmate of a public institution (except as a patient in a medical institution); or

(B) any such payments with respect to care or services for any individual who has not attained 65 years of age and who is a patient in an institution for mental diseases.

For purposes of clause (vi) of the preceding sentence, a person shall be considered essential to another individual if such person is the spouse of and is living with such individual, the needs of such person are taken into account in determining the amount of aid or assistance furnished to such individual (under a State plan approved under subchapter I, X, XIV, or XVI of this chapter), and such person is determined, under such a State plan, to be essential to the well-being of such individual. The payment

In the case of any State which is providing medical assistance to its residents under a waiver granted under section 1315 of this title, the Secretary shall require the State to meet the requirement of section 1396a(a)(10)(E) of this title in the same manner as the State would be required to meet such requirement if the State had in effect a plan approved under this subchapter.

**(q) Qualified severely impaired individual**

The term "qualified severely impaired individual" means an individual under age 65—

(1) who for the month preceding the first month to which this subsection applies to such individual—

(A) received (i) a payment of supplemental security income benefits under section 1382(b) of this title on the basis of blindness or disability, (ii) a supplementary payment under section 1382e of this title or under section 212 of Public Law 93-66 on such basis, (iii) a payment of monthly benefits under section 1382h(a) of this title, or (iv) a supplementary payment under section 1382e(c)(3) of this title, and

(B) was eligible for medical assistance under the State plan approved under this subchapter; and

(2) with respect to whom the Commissioner of Social Security determines that—

(A) the individual continues to be blind or continues to have the disabling physical or mental impairment on the basis of which he was found to be under a disability and, except for his earnings, continues to meet all non-disability-related requirements for eligibility for benefits under subchapter XVI of this chapter,

(B) the income of such individual would not, except for his earnings, be equal to or in excess of the amount which would cause him to be ineligible for payments under section 1382(b) of this title (if he were otherwise eligible for such payments),

(C) the lack of eligibility for benefits under this subchapter would seriously inhibit his ability to continue or obtain employment, and

(D) the individual's earnings are not sufficient to allow him to provide for himself a reasonable equivalent of the benefits under subchapter XVI of this chapter (including any federally administered State supplementary payments), this subchapter, and publicly funded attendant care services (including personal care assistance) that would be available to him in the absence of such earnings.

In the case of an individual who is eligible for medical assistance pursuant to section 1382h(b) of this title in June, 1987, the individual shall be a qualified severely impaired individual for so long as such individual meets the requirements of paragraph (2):

**(r) Early and periodic screening, diagnostic, and treatment services**

The term "early and periodic screening, diagnostic, and treatment services" means the following items and services:

(1) Screening services—

(A) which are provided—

(i) at intervals which meet reasonable standards of medical and dental practice, as determined by the State after consultation with recognized medical and dental organizations involved in child health care and, with respect to immunizations under subparagraph (B)(iii), in accordance with the schedule referred to in section 1396s(c)(2)(B)(i) of this title for pediatric vaccines, and

(ii) at such other intervals, indicated as medically necessary, to determine the existence of certain physical or mental illnesses or conditions; and

(B) which shall at a minimum include—

(i) a comprehensive health and developmental history (including assessment of both physical and mental health development),

(ii) a comprehensive unclothed physical exam,

(iii) appropriate immunizations (according to the schedule referred to in

(iv) laboratory tests (including lead blood level assessment appropriate for age and risk factors), and

(v) health education (including anticipatory guidance).

(2) Vision services—

(A) which are provided—

(i) at intervals which meet reasonable standards of medical practice, as determined by the State after consultation with recognized medical organizations involved in child health care, and

(ii) at such other intervals, indicated as medically necessary, to determine the existence of a suspected illness or condition; and

(B) which shall at a minimum include diagnosis and treatment for defects in vision, including eyeglasses.

(3) Dental services—

(A) which are provided—

(i) at intervals which meet reasonable standards of dental practice, as determined by the State after consultation with recognized dental organizations involved in child health care, and

(ii) at such other intervals, indicated as medically necessary, to determine the existence of a suspected illness or condition; and

(B) which shall at a minimum include relief of pain and infections, restoration of teeth, and maintenance of dental health.

(4) Hearing services—

(A) which are provided—

(i) at intervals which meet reasonable standards of medical practice, as determined by the State after consultation with recognized medical organizations involved in child health care, and

(ii) at such other intervals, indicated as medically necessary, to determine the existence of a suspected illness or condition; and

(B) which shall at a minimum include diagnosis and treatment for defects in hearing, including hearing aids.

(5) Such other necessary health care, diagnostic services, treatment, and other measures described in subsection (a) of this section to correct or ameliorate defects and physical and mental illnesses and conditions discovered by the screening services, whether or not such services are covered under the State plan.

Nothing in this subchapter shall be construed as limiting providers of early and periodic screening, diagnostic, and treatment services to providers who are qualified to provide all of the items and services described in the previous sentence or as preventing a provider that is qualified under the plan to furnish one or more (but not all) of such items or services from being qualified to provide such items and services as part of early and periodic screening, diagnostic, and treatment services. The Secretary shall, not later than July 1, 1990, and every 12 months thereafter, develop and set annual participation goals for each State for participation of individuals who are covered under the State plan under this subchapter in early and periodic screening, diagnostic, and treatment services.

(s) Qualified disabled and working individual

The term "qualified disabled and working individual" means an individual—

(1) who is entitled to enroll for hospital insurance benefits under part A of subchapter XVIII of this chapter under section 1395i-2a of this title;

(2) whose income (as determined under section 1382a of this title for purposes of the supplemental security income program) does not exceed 200 percent of the official poverty line (as defined by the Office of Management and Budget and revised annually in accordance with section 9902(2) of this title) applicable to a family of the size involved;

(3) whose resources (as determined under section 1382b of this title for purposes of the supplemental security income program) do not exceed twice the maximum amount of resources that an individual or a couple (in the case of an individual with a spouse) may have and obtain benefits for supplemental security income benefits under subchapter XVI of this chapter; and

- (c) mandatory outpatient, rather than inpatient, surgery in appropriate cases;
  - (d) second surgical opinions;
  - (e) procedures for encouraging the use of outpatient services;
  - (f) coordination of benefits; and
  - (g) review and exclusion of providers who are not cost effective or who have abused the Medicaid program, in accordance with the procedures and provisions of federal law and regulation.
- (3) The director of the division shall periodically assess the cost effectiveness and health implications of the existing Medicaid program, and consider alternative approaches to the provision of covered health and medical services through the Medicaid program, in order to reduce unnecessary or unreasonable utilization.

**History:** C. 1953, 26-18-2.3, enacted by L. 1988, ch. 21, § 4.

**Federal Law.** — Title XIX of the federal

Social Security Act, cited in Subsection (1), is compiled as 42 U.S.C. § 1396 et seq.

#### NOTES TO DECISIONS

##### ANALYSIS

Discretion of division.  
Resource preservation.

##### **Discretion of division.**

The legislature has, by virtue of Subsection (1), explicitly granted the Division of Health Care Financing (DHCF) discretion to establish criteria concerning medical reimbursement. When a hospital failed to submit a physician certification before admission of a Medicaid-eligible patient and never obtained physician recertification at any time during the patient's three-month stay in acute care, the DHCF reasonably denied reimbursement to the hospital. *South Davis Community Hosp. v. Department of Health*, 860 P.2d 979 (Utah Ct. App. 1994).

##### **Resource preservation.**

Utah does not have a "resource spend down" provision in its Medicaid plan, nor any statement of policy expressing a desire to preserve the resources of potential beneficiaries. Utah's statutes seem to evince a legislative concern for economy and efficiency in the Medicaid program, not the preservation of applicants' assets. *Allen v. Utah Dep't of Health*, 829 P.2d 122 (Utah Ct. App. 1992), aff'd, 850 P.2d 1267 (Utah 1993).

It is not unreasonable for the division to apply a fixed asset limit forbidding persons to adjust their assets to become eligible for Medicaid benefits. *Allen v. Utah Dep't of Health*, 850 P.2d 1267 (Utah 1993).

### **26-18-3. Administration of Medicaid program by department — Disciplinary measures and sanctions — Funds collected.**

(1) The department shall be the single state agency responsible for the administration of the Medicaid program in connection with the United States Department of Health and Human Services pursuant to Title XIX of the Social Security Act.

(2) The department shall develop implementing policy in conformity with this chapter, the requirements of Title XIX, and applicable federal regulations.

(3) The department may, in its discretion, contract with the Department of Human Services or other qualified agencies for services in connection with the administration of the Medicaid program, including but not limited to the determination of the eligibility of individuals for the program, recovery of overpayments, and enforcement of fraud and abuse laws to the extent permitted by law and quality control services.

(4) The department shall provide, by rule, disciplinary measures and sanctions for Medicaid providers who fail to comply with the rules and procedures of the program, provided that sanctions imposed administratively may not extend beyond:

- (a) termination from the program;
- (b) recovery of claim reimbursements incorrectly paid; and
- (c) those specified in Section 1919 of Title XIX of the federal Social Security Act.

(5) Funds collected as a result of a sanction imposed under Section 1919 of Title XIX of the federal Social Security Act shall be deposited in the General Fund as nonlapsing dedicated credits to be used by the division in accordance with the requirements of that section.

**History:** C. 1953, 26-18-3, enacted by L. 1981, ch. 126, § 17; 1988, ch. 21, § 5; 1989, ch. 165, § 1; 1990, ch. 183, § 9.

**Federal Law.** — Title XIX of the federal

Social Security Act is compiled as 42 U.S.C. § 1396 et seq. Section 1919 of Title XIX is 42 U.S.C. § 1396r.

#### NOTES TO DECISIONS

##### ANALYSIS

**Children.**

—Temporary absence from home.  
Federal law.

**Children.**

—Temporary absence from home.

Federal law requires that eligibility for “medically needy” Medicaid benefits be determined consistently with the methods of the Aid to Families with Dependent Children program and the Supplemental Security Income Program. In the case of an unemancipated child, resources include those available from a par-

ent. By these standards, a child’s temporary absence from home will not qualify him or her for benefits independent of parental resources. *Bleazard v. Utah Dep’t of Health Care Fin.*, 861 P.2d 1048 (Utah Ct. App. 1993).

**Federal law.**

Medicaid is not intended to provide benefits to the medically needy in circumstances where financial need is not fully demonstrated and where benefits would be inconsistent with requirements for the higher priority classification of the categorically needy. *Bleazard v. Utah Dep’t of Health Care Fin.*, 861 P.2d 1048 (Utah Ct. App. 1993).

#### COLLATERAL REFERENCES

**C.J.S.** — 81 C.J.S. Social Security and Public Welfare § 126.

**Key Numbers.** — Social Security and Public Welfare ⇨ 241 et seq.

### 26-18-3.1. Medicaid expansion.

(1) The purpose of this section is to expand the coverage of the Medicaid program to persons who are in categories traditionally not served by that program.

(2) Within appropriations from the Legislature, the department may amend the state plan for medical assistance to provide for eligibility for Medicaid:

- (a) on or after July 1, 1994, for children 12 to 17 years old who live in households below the federal poverty income guideline; and
- (b) on or after July 1, 1995, for persons who have incomes below the federal poverty income guideline and who are aged, blind, or disabled.

(3) (a) Within appropriations from the Legislature, on or after July 1, 1996, the Medicaid program may provide for eligibility for persons who have incomes below the federal poverty income guideline.

#### **26-18-4. Department standards for eligibility under Medicaid — Funds for abortions.**

(1) The department may develop standards and administer policies relating to eligibility under the Medicaid program. An applicant receiving Medicaid assistance may be limited to particular types of care or services or to payment of part or all costs of care determined to be medically necessary.

(2) The department shall not provide any funds for medical, hospital, or other medical expenditures or medical services to otherwise eligible persons where the purpose of the assistance is to perform an abortion, unless the life of the mother would be endangered if an abortion were not performed.

(3) Any employee of the department who authorizes payment for an abortion contrary to the provisions of this section is guilty of a class B misdemeanor and subject to forfeiture of office.

(4) Any person or organization that, under the guise of other medical treatment, provides an abortion under auspices of the Medicaid program is guilty of a third degree felony and subject to forfeiture of license to practice medicine or authority to provide medical services and treatment.

**History:** C. 1953, 26-18-4, enacted by L. 1981, ch. 126, § 17; 1987, ch. 181, § 2. **Cross-References.** — Sentencing for felonies, §§ 76-3-201, 76-3-203, 76-3-301. Sentencing for misdemeanors, §§ 76-3-201, 76-3-204, 76-3-301.

#### **NOTES TO DECISIONS**

##### **ANALYSIS**

Federal law.  
Standards for eligibility.  
— Temporary absence from home.

##### **Federal law.**

Medicaid is not intended to provide benefits to the medically needy in circumstances where financial need is not fully demonstrated and where benefits would be inconsistent with requirements for the higher priority classification of the categorically needy. *Bleazard v. Utah Dep't of Health Care Fin.*, 861 P.2d 1048 (Utah Ct. App. 1993).

##### **Standards for eligibility.**

##### **— Temporary absence from home.**

Federal law requires that eligibility for “medically needy” Medicaid benefits be determined consistently with the Aid to Families with Dependent Children program and the Supplemental Security Income Program. In the case of an unemancipated child, resources include those available from a parent. By these standards, a child’s temporary absence from home will not qualify him or her for benefits independent of parental resources. *Bleazard v. Utah Dep't of Health Care Fin.*, 861 P.2d 1048 (Utah Ct. App. 1993).

#### **26-18-5. Contracts for provision of medical services — Federal provisions modifying department rules — Compliance with Social Security Act.**

(1) The department may contract with other public or private agencies to purchase or provide medical services in connection with the programs of the division. Where these programs are used by other state agencies, contracts shall provide that other state agencies transfer the state matching funds to the department in amounts sufficient to satisfy needs of the specified program.

(2) All contracts for the provision or purchase of medical services shall be established on the basis of the state’s fiscal year and shall remain uniform during the fiscal year insofar as possible. Contract terms shall include provisions for maintenance, administration, and service costs.

another state, to the same extent that Medicaid is furnished to residents in the state.

**R414-1-19. Retroactive Coverage.**

Individuals are entitled to Medicaid services under the plan during the three months preceding the month of application, if they were, or would have been, eligible at that time.

**R414-1-20. Freedom of Choice of Provider.**

Unless an exception under 42 CFR 431.55 applies, any individual eligible under the plan may obtain Medicaid services from any institution, pharmacy, person, or organization that is qualified to perform the services and has entered into a Medicaid provider contract, including an organization that provides these services or arranges for their availability on a prepayment basis.

**R414-1-21. Availability of Program Manuals and Policy Issuances.**

Program manuals and other policy issuances that affect recipients, providers and the public, including the Medicaid agency's rules governing eligibility, need and amount of assistance, recipient rights and responsibilities, and services offered by the agency are maintained in the state office and in each local and district office for examination and, upon request, are available to individuals for review, study, or reproduction. All requirements of 42 CFR 431.18 are met.

**R414-1-22. General Rule Format.**

(1) The following format is used generally throughout the rules of the Division. Section headings as indicated and the following general definitions thereunder are for guidance only. The section headings are not part of the rule content itself. In certain instances, such format may not be appropriate and will not be implemented due to the nature of the subject matter of a specific rule.

(a) Policy Statement. A concise statement as to what Medicaid service is covered by the rule.

(b) Authority. A listing of specific federal statutes and regulations and state statutes that authorize or require the rule.

(c) Definitions. Definitions that have special meaning to the particular rule.

(d) Client Eligibility. Categories of Medicaid clients eligible for the service covered by the rule: Categorically Needy or Medically Needy or both. Conditions precedent to the client's obtaining coverage such as age limitations or otherwise.

(e) Program Access Requirements. Conditions precedent external to the client's obtaining service such as type of certification needed from attending physician, whether available only in an inpatient setting or otherwise.

(f) Service Coverage. Detail of specific services available under the rule, including limitations such as number of procedures in a given period of time or otherwise.

(g) Prior Authorization. As necessary, a description of the procedures for obtaining prior authorization for services available under the particular rule.

(h) Other Sections. As necessary under the particular rule, additional sections may be indicated.

**References:** 26-1-5, 26-18-1.

**History:** 11559, NSC, 02/15/91; 14034, AMD, 02/08/93.

NOTES TO DECISIONS

ANALYSIS

Compliance with federal law.

Efficiently and economically operated.

Spend down.

**Compliance with federal law.**

A reasonable basis existed for the Department to find that proposed rates were reasonable and adequate to meet the costs of an efficiently and economically operated facility as required by federal law: Ninety-three percent of all long-term health care facilities in Utah were shown to be meeting their costs under the modified flat rate plan, with a majority showing a profit. Weber Mem. Care Ctr. v. Utah Dep't of Health, 751 P.2d 831 (Utah Ct. App.), cert. denied, 765 P.2d 1278 (Utah 1988).

**Efficiently and economically operated.**

Setting rates for payment for services that the state deems reasonable and adequate and maintaining that an "efficiently and economically operated facility" is one that is able to operate at or below that standard is a proper alternative to defining "efficiently and economically operated." Weber Mem. Care Ctr. v. Utah Dep't of Health, 751 P.2d 831 (Utah Ct. App.), cert. denied, 765 P.2d 1278 (Utah 1988).

Since the modified flat rate implicitly defines an efficiently and economically operated facility, evidence of a nursing home's costs and operation was irrelevant and, therefore, inadmissible in an action challenging the modified rate plan. Weber Mem. Care Ctr. v. Utah Dep't of Health, 751 P.2d 831 (Utah Ct. App.), cert. denied, 765 P.2d 1278 (Utah 1988).

**Spend down.**

Federal Medicaid regulations did not require states to allow an applicant to spend down excess resources by applying them to outstanding medical bills, thereby becoming eligible for Medicaid. (Former R810-304-411, R455-1 to R455-48.) Allen v. Utah Dep't of Health, 829 P.2d 122 (Utah Ct. App. 1992), aff'd, 850 P.2d 1267 (Utah 1993).

**R414-1A. Medicaid Policy for Experimental or Unproven Medical Practices.**

R414-1A-100. Authority and Purpose.

R414-1A-200. Definitions.

R414-1A-300. Policy.

**R414-1A-100. Authority and Purpose.**

(1) This rule establishes Medicaid payment policy for experimental or unproven medical practices.

(2) This rule is authorized by Sections 26-1-5, 26-1-15, and 26-18-6, and by Subsections 26-18-3(2) and 26-18-5(4).

**R414-1A-200. Definitions.**

(1) Terms used in this rule are defined in R414-1-1.

(2) In addition:



(a) "experimental or unproven medical practice" means any procedure, medication product, or service that is:

(i) not proven to be medically efficacious for a given procedure; or

(ii) performed for or in support of purposes of research, experimentation, or testing of new processes or products; or

(iii) both;

(b) "medically efficacious" means a medical practice that:

(i) has been determined effective and is widely utilized as a standard medical practice for specific conditions; and

(ii) has been approved as a covered Medicaid service by division staff and physician consultants on the basis of medical necessity, as defined in R414-13x-1.5(a), and in accordance with R414-26-1.2(f);

(c) "supporting services" means supplies or laboratory, X-ray, physician, pharmacy, therapy, or transportation services.

#### **R414-1A-300. Policy.**

(1) Experimental or unproven medical practices are not covered Medicaid services.

(2) Division staff and physician consultants shall establish criteria to determine whether a service or procedure is a covered Medicaid service.

(3) Procedures or services proven to be medically efficacious for specific medical conditions may be provided as covered Medicaid services only for the conditions specified. Such procedures or services are not covered for any other conditions or for experimental trials.

(4) Inpatient or outpatient hospitalization for the purpose of receiving services or procedures that are experimental or medically unproven, or in support of such services or procedures, is not a covered Medicaid service. However, when such services or procedures are provided incidentally during a hospitalization for an otherwise medically necessary and appropriate service, only the experimental or unproven medical procedures and any supporting services specifically identifiable with such services and procedures are excluded from payment.

**References:** 26-1-5, 26-18-3(2).

**History:** 13288, AMD, 10/08/92.

#### **R414-2A. Inpatient Hospital Services.**

R414-2A-100. Authority and Purpose.

R414-2A-300. Program Access Requirements.

R414-2A-400. Services.

R414-2A-500. Limitations.

R414-2A-600. Prior Authorization.

#### **R414-2A-100. Authority and Purpose.**

(1) This rule defines the scope of inpatient hospital benefits available for the care and treatment of Medicaid clients who meet the level of care criteria

for admission to an acute-care general hospital for treatment of disorders other than mental disease.

(2) Inpatient hospital services are required under Section 1901 et seq. and Section 1905(a)(1) of the Social Security Act, and by 42 CFR 440.10 (October 1, 1991, edition).

(3) This rule is authorized by Sections 26-1-5, 26-1-15, and 26-18-6, and by Subsections 26-18-3(2) and 26-18-5(3) and (4).

#### **R414-2A-300. Program Access Requirements.**

(1) Each hospital providing inpatient services must have a utilization review plan, as described in 42 CFR 482.30 (October 1, 1991, edition), which is incorporated by reference.

(2) The attending physician or other practitioner of the healing arts must sign a physician attestation statement that meets the requirements of 42 CFR 412.46 (October 1, 1991, edition), which is incorporated by reference.

(3) The attending physician must certify and recertify the need for inpatient care as described in 42 CFR 441.152 and 456.60 (October 1, 1991, edition), which are incorporated by reference.

(4) All hospital admissions are subject to review by the department for appropriateness and medical necessity as detailed in R414-2A.

(5) For purposes of reimbursement, the day of admission is counted as a full day; the day of discharge is not counted.

(6) When a patient receives SNF-level, ICF-level, or other sub-acute care in an acute-care hospital or in a hospital with swing-bed approval, payment shall be made at the SNF or ICF rate.

(7) Inpatient hospital psychiatric services are covered Medicaid services for clients who live in the counties identified in Table 1 only when such services are coordinated through the contractor identified for the specified county:

TABLE 1

I.	Counties:	Salt Lake County Summit County
	Contractor:	Salt Lake Valley Mental Health, Salt Lake City, Utah
II.	Counties:	Carbon County Emery County Grand County
	Contractor:	Four Corners Community Mental Health Center, Price, Utah
III.	Counties:	Beaver County Garfield County Kane County Iron County Washington County
	Contractor:	Southwest Utah Mental Health Center, St. George, Utah

#### **R414-2A-400. Services.**

(1) Inpatient hospital services encompass all medically necessary and therapeutic Medicaid services and supplies that are ordered by a physician or other practitioner of the healing arts and are appropriate for the adequate diagnosis and treatment of a patient's illness. These services include nursing, therapy services, use of hospital facilities, the tech-

Physician services are available to categorically and medically needy eligible individuals.

#### **R414-10-4. Program Access Requirements.**

- (1) Physician services are available only from a physician who meets all requirements necessary to participate in the Utah Medicaid Program and who has signed a provider agreement.
- (2) Physician services are available only from a physician who renders medically necessary physician services in accordance with his specific provider agreement and with Department rules.
- (3) An eligible Medicaid client may seek physician services from:
  - (a) a physician in private practice who is an enrolled Medicaid provider;
  - (b) a Health Maintenance Organization (HMO) that has a contract with the Department;
  - (c) a federally qualified community health center; or
  - (d) any other organized practice setting recognized by the Department for providing physician services.

#### **R414-10-5. Service Coverage.**

- (1) Physician services involve direct patient care and securing and supervising appropriate diagnostic ancillary tests or services in order to diagnose the existence, nature, or extent of illness, injury, or disability. In addition, physician services involve establishing a course of medically necessary treatment designed to prevent or minimize the adverse effects of human disease, pain, illness, injury, infirmity, deformity, or other impairments to a client's physical or mental health.
- (2) Physician services may be provided only within the parameters of accepted medical practice and are subject to limitations and exclusions established by the Department on the basis of medical necessity, appropriateness, and utilization control considerations.
- (3) Program limitations and noncovered services are established by specific program policy maintained in the Physician Provider Manual and updated by notification through Medicaid Provider Bulletins. Following is a general list of medical and health care services excluded from coverage:
  - (a) Services rendered during a period the recipient was ineligible for Medicaid;
  - (b) Services medically unnecessary or unreasonable;
  - (c) Services which fail to meet existing standards of professional practice, or which are currently professionally unacceptable;
  - (d) Services requiring prior authorization, but for which such authorization was not received;
  - (e) Services, elective in nature, based on patient request or individual preference rather than medical necessity;
  - (f) Services fraudulently claimed;
  - (g) Services which represent abuse or overuse;
  - (h) Services rejected or disallowed by Medicare when the rejection was based upon any of the reasons listed above.
- (4) Experimental or medically unproven physician services or procedures are excluded from coverage. Criteria established and approved by the Department staff and physician consultants are used to identify noncovered services and procedures. Policy statements developed by the Department of Health and Human Services, Health Care Financing Administration, Coverage Issues Bureau, are also used to determine Department policy for noncovered services.
- (5) Certain services are excluded from coverage because medical necessity, appropriate utilization, and cost effectiveness of the services cannot be assured. A variety of lifestyle factors contribute to the "syndromes" associated with such services, and there is no specific therapy or treatment identified except for those that border on behavior modification, experimental, or unproven practices. Services include:

- (a) Sleep apnea or sleep studies, or both;
- (b) Pain clinics; and
- (c) Eating disorders clinics.
- (6) When a service or procedure does not qualify for coverage under the Medicaid program because it is an elective cosmetic, reconstructive, or plastic surgery, all related services, supplies, and institutional costs are excluded from coverage.
- (7) Medications for appetite suppression, surgical procedures, unproven or experimental treatments, or educational, nutritional support programs for the treatment of obesity or weight control, are excluded from coverage.
- (8) Cognitive or Office Services:
  - (a) Cognitive services by a provider are limited to one service per client per day. These services are defined as office visits, hospital visits except for those following a package surgical procedure, therapy visits, and other types of nonsurgical services. When a second office visit for the same problem or a hospital admission occurs on the same date as another service, the physician shall combine the services as one service and select a procedure code that indicates the overall care given.
  - (b) Routine physical examinations, not part of an otherwise medically necessary service, are excluded from coverage, except in the following circumstances:
    - (i) Preschool and school age children, including those who are EPSDT (CHEC) eligible, participating in the ongoing CHEC program of scheduled services and follow-up care.
    - (ii) New patients seeing a physician for the first time with an initial complaint where a comprehensive physical examination, including a medical and social history, is necessary.
    - (iii) Medically necessary examinations associated with birth control medication, devices, and instructions.
  - (c) Family planning services may be provided only by or under the supervision of a physician and only to individuals of childbearing age, including sexually active minors. The following services are excluded from coverage as family planning services:
    - (i) Experimental or unproven medical procedures, practices, or medication.
    - (ii) Surgical procedures for the reversal of previous elective sterilization, both male and female.
    - (iii) Infertility studies.
    - (iv) In-vitro fertilization.
    - (v) Artificial insemination.
    - (vi) Surrogate motherhood, including all services, tests, and related charges.
    - (vii) Abortion, except where the life of the mother would be endangered if the fetus were carried to term, or where pregnancy is the result of rape or incest.
  - (d) After-hours service codes may be used only by a private physician, primary care provider, who responds to treat a patient in the physician's private office for a medical emergency, accident, or injury after regular office hours. Only one of the after hours CPT codes may be used per visit.
  - (e) Only the laboratory tests in the following list are covered as part of a physician's office service. An independent laboratory shall provide all other laboratory services. The independent laboratory completing the service must bill the Department directly to receive payment for the service.
    - (i) 81000 Urinalysis by reagent strips, any number of components: with microscopy;
    - (ii) 81002 Urinalysis without microscopy;
    - (iii) 82270 Blood: occult, feces, screening;
    - (iv) 82948 Glucose: blood, stick test;
    - (v) 84702 Gonadotropin, chorionic: quantitative;
    - (vi) 84703 Gonadotropin, chorionic: qualitative;

- (vii) 85007 Blood count: manual differential WBC (includes RBC morphology and platelet estimation);
- (viii) 85014 Blood count: hematocrit;
- (ix) 85021 Blood count: hemogram, automated (RBC, WBC, HgB, Hct and indices only);
- (x) 85022 Blood count: hemogram, automated, and manual differential WBC count (CBC);
- (xi) 85023 Blood count: hemogram and platelet count, automated, and manual differential WBC count (CBC);
- (xii) 85024 Blood count: hemogram and platelet count, automated, and automated partial differential WBC count (CBC);
- (xiii) 85025 Blood count: hemogram and platelet count, automated, and automated complete differential WBC count (CBC);
- (xiv) 85027 Blood count: hemogram and platelet count, automated;
- (xv) 85031 Blood count: hemogram, manual, complete CBC (RBC, WBC, HgB, Hct, differential and indices);
- (xvi) 85048 Blood Count: white blood cell (WBC);
- (xvii) 85650 Sedimentation rate (ESR): Wintrobe type;
- (xviii) 85651 Sedimentation rate: Westergren type;
- (xix) 86300 Heterophile antibodies: screening (includes monotype test) slide or tube;
- (xx) 86317 Immunoassay for infectious agent antigen or antibody, each;
- (xxi) 86403 Particle agglutination, rapid test for infectious agent, each antigen;
- (xxii) 86580 Skin test: tuberculosis, intradermal;
- (xxiii) 86585 Skin test: tuberculosis, tine test;
- (xxiv) 87081 Culture, bacterial, screening only, for single organisms;
- (xxv) 87082 Culture, presumptive, pathogenic organisms, screening only, by commercial kit; for single organisms;
- (xxvi) 87210 Smear, primary source: wet mount with simple stain, for bacteria, fungi, ova, and parasites;
- (xxvii) 87220 Tissue examination for fungi (e.g., KOH slide).
- (f) In addition to the above laboratory services, the following services are covered when a private physician personally collects the specimen:
  - (i) 85095 Bone marrow smear or cell block or both: aspiration only;
  - (ii) 85102 Bone marrow biopsy, needle or trocar.
- (g) A specimen collection fee is covered for service in a physician's office only when a specimen is to be sent to an outside laboratory, and the physician or one of his office staff under his personal supervision actually extracts the specimen from a patient, and only by one of the following procedures:
  - (i) Drawing a blood sample through venipuncture, i.e., inserting into a vein a needle with syringe or vacutainer to draw the specimen; or
  - (ii) Collecting a urine sample by catheterization.
- (h) Eye examinations are covered, but only once each calendar year.
- (i) Contact lenses are covered only for aphakia, nystagmus, keratoconus, severe corneal distortion, cataract surgery, and in those cases where visual acuity cannot be corrected to at least 20/70 in the better eye.
- (9) Psychiatric Services:
  - (a) Psychiatric services or psychosocial diagnosis and counseling are specialty medical services. Psychiatric services, whether in a private office, a group practice, or private clinic setting, may only be provided directly and documented and billed to the Department by the private physician. Charting and documentation must clearly reflect the private physician's direct provision of care.
  - (b) Nonphysician psychosocial counseling services are excluded from coverage as a

Medicaid benefit. The personal supervision policy, R414-45-1, may not be applied to psychiatric services.

(c) Admission to a general hospital for psychiatric care by a physician requires prior authorization and is limited to those cases determined by established criteria and utilization review standards to be of a severity that appropriate intensity of service cannot be provided in any alternate setting.

(10) Laboratory and Radiology Services:

(a) Laboratory services identified by CPT codes 80000 through 89999, and radiology services identified by CPT codes 70000 through 79999 are ancillary medical services with both a technical and professional component. The professional component, e.g., analysis, interpretation and written report, represented by modifier 26, may be provided only by a pathologist or a radiologist practicing in an independent or hospital laboratory or radiology setting. Private physicians who are not pathologists or radiologists may not bill for the service described by modifier 26 for telling a patient the results of laboratory or radiology procedures as noted on the laboratory or radiology printout or the written report. Providing such information to the patient is part of the office call rather than a separate service.

(b) Physicians prepared in a highly specialized field of practice, e.g., neurology or neurosurgery, who provide consultation and diagnostic radiology services in an independent setting at the request of a private physician may bill for both the technical and professional component of the radiology service.

(11) Hospital Services:

(a) A patient hospitalized for nonsurgical services may require more than one visit per day because of the patient's condition and treatment needs. Since physician visits are limited to one per day, the physician shall select one procedure code to define the overall care given. If intensive care services are provided, or critical care service codes are used to define service provided, the Department requires additional documentation from the physician. The medical record must show documentation of medical necessity and result of the additional service.

(b) If, for the convenience of the physician and not for medical necessity, a patient is transferred between physicians within the same hospital or from one hospital to another hospital, both physicians may only use subsequent hospital care service codes to define and bill for services provided. Under this policy limitation, services associated with the following codes are excluded from coverage as a Medicaid benefit:

- (i) Consultation; and
- (ii) Initial hospital care services.

(c) Treatment of alcoholism or drug dependency in an inpatient setting is limited to acute care for detoxification only.

(12) Abortion, Sterilization and Hysterectomy:

(a) Abortion procedures are limited only to those with medical certification of necessity as described in 42 CFR 441.203, October 1994 edition, which is adopted and incorporated by reference.

(b) Sterilization and hysterectomy procedures are limited to those which meet the requirements of 42 CFR 441, Subpart F, October 1994 edition, which is adopted and incorporated by reference.

(13) Cosmetic, Plastic, or Reconstructive Services:

(a) Cosmetic, plastic, or reconstructive surgery procedures may only be covered when medically necessary to:

- (i) correct a congenital anomaly;
- (ii) restore body form or function following an accidental injury; or
- (iii) revise severe disfiguring and extensive scarring resulting from neoplastic surgery.

(14) Surgical Services:

(a) Surgical procedures defined and coded in the CPT Manual are limited by Utah Medicaid policy to place of service, to prior authorization, or are excluded from coverage. Limitations are documented on the Medical and Surgical Procedures Prior Authorization List, reviewed and revised yearly and maintained in the Physician Provider Manual through notification by Provider Bulletins.

(b) Surgical procedures are "package" services. The package service includes:

(i) the preoperative examination, initiation of the hospital record, and development of a treatment program either in the physician's office on the day before admission, or in the hospital or the physician's office on the same day as admission to the hospital;

(ii) the operation;

(iii) any topical, local, or regional anesthesia; and

(iv) the normal, uncomplicated follow-up care covering the period of hospitalization and office follow-up for progress checks or any service directly related to the surgical procedure for up to six weeks post surgery.

(c) Interpretation of "package" services:

(i) A physician may not bill for an office visit the day prior to surgery, for preadmission or admission workup, or for subsequent hospital care while the patient is being prepared, hospitalized, or under care for a "package" surgical service.

(ii) Consultation services may be billed by the consulting physician only when consultation and no other service is provided. When a consulting physician admits and follows a patient, independently or concurrently with the primary physician, only admission codes and subsequent care codes may be used.

(iii) Office visits for up to six weeks following the hospitalization which relate to the same diagnosis are part of the "package" service. The only exception to either inpatient or office service is for service related to complications, exacerbations, or recurrence of other diseases or problems requiring additional or separate service.

(d) Procedures exempt from the "package" definition are identified in the CPT Manual by an asterisk. The CPT Manual outlines the surgical guidelines which apply to documentation and billing of procedures marked by an asterisk.

(e) Complications, exacerbations, recurrence, or the presence of other diseases or injuries requiring services concurrent with the initial surgical procedure during the listed period of normal follow-up care, may warrant additional charges only when the record shows extensive documentation and justification of additional services.

(f) When an additional surgical procedure is carried out within the listed period of follow-up care for a previous surgery, the follow-up periods continue concurrently to their normal terminations.

(g) Preoperative examination and planning are covered as separate services only in the following circumstances:

(i) When the preoperative visit is the initial visit for the physician and prolonged detention or evaluation is required to establish a diagnosis, determine the need for a specific surgical procedure, or prepare the patient;

(ii) When the preoperative visit is a consultation and the consulting physician does not assume care of the patient; or

(iii) When diagnostic procedures, not part of the basic surgical procedure, e.g., bronchoscopy prior to chest surgery, are provided during the immediate preoperative period.

(h) Exploratory laparotomy procedures confirm a diagnosis and determine the extent of necessary treatment. A physician may request payment only if the exploratory procedure is the only procedure done during an operative session. Exploratory laparotomy services identified by CPT Codes 49000-49060 may not be billed in conjunction with any services identified by the following CPT Codes: 43500 - 44346 - 44600 - 45180 - 47400 - 47490 - 47600 - 48999 - 49002 -

49999 - 58140 - 58285 - 58400 - 58960.

(i) The services of an assistant surgeon are covered only on very complex surgical procedures. Procedures not authorized for assistant surgeon coverage are listed in the Physician Provider Manual and updated by Medicaid Provider Bulletins as necessary. Medicare guidelines for limitation of assistant surgeon coverage are used, since those decisions are made at the national level with physician consultation.

(15) Diagnostic and Therapeutic Procedures:

(a) Diagnostic needle procedures, e.g., lumbar puncture, thoracentesis, and jugular, femoral vein, or subdural taps, when performed as part of a necessary workup for a serious medical illness or injury, are covered in addition to other medical care on the same day.

(b) Diagnostic "oscopy" procedures, e.g., endoscopy, bronchoscopy, and laparoscopy, are covered separately from any major surgical procedure. However, when an "oscopy" procedure is done the same day or at the same operative session as another procedure, the "oscopy" procedure may only be covered as a multiple procedure.

(c) Magnetic resonance imaging (MRI) is covered only for service to the brain, spinal cord, hip, thigh and abdomen.

(d) Therapeutic needle procedures, e.g., scalp vein insertion, injections into cavities, nerve blocks, are covered in addition to other medical care on the same day.

(e) Puncture of a cavity or joint for aspiration followed by injection of a medication is covered as one procedure and identified by specific CPT code.

(16) Anesthesia Services:

Anesthesia services are covered only when administered by a licensed anesthesiologist or nurse anesthetist who remains in attendance for the sole purpose of rendering general anesthesia services. Standby or monitoring by the anesthesiologist or anesthetist during local anesthesia is not a covered Medicaid anesthesia service.

(17) Transplant Services

Organ transplant services are limited to those procedures for which selection criteria have been approved and documented in R414-10A.

(18) Modifiers:

Modifiers may be used only, as defined in the CPT Manual, to show that a service or procedure has been altered to some degree but not changed in definition or code. The following limitations apply:

(1) The professional component, modifier 26, may be used only with laboratory and radiology service codes by a pathologist or radiologist and only when direct analysis, interpretation, and written report of findings are provided on a laboratory or radiology procedure. Private physicians may not use this modifier.

(2) Unusual services are identified by use of modifier 22, along with the appropriate CPT code. A prepayment review of unusual services shall be completed by Medicaid professional staff or physician consultants. A report of the service and any important supporting documentation must be submitted with the claim for review.

(3) Anesthesia by surgeon is identified by use of modifier 47. The operating surgeon may not use modifier 47 in addition to the basic procedure code. Anesthesia provided by the surgeon is part of the basic procedure being provided.

(4) Mandated services as defined by CPT and identified by modifier 32 are noncovered services.

(5) Reference laboratory services identified by modifier 90 are noncovered services.

(19) Medications:

(a) Drugs and biologicals are limited to those approved by the Food and Drug Administration (FDA). Medicaid coverage of drugs and biologicals is based on individual need and orders written by a physician when the drug is given in accordance with accepted standards

of medical practice and within the protocol of accepted use for the drug.

(i) Generic drugs shall be used whenever a generic product approved by the FDA is available. If the physician determines that a brand name drug is medically necessary, the physician may override the generic requirement by writing on the prescription in his own hand writing "name brand medically necessary". Preprinted messages, abbreviations, or notations by a second party, do not meet the override requirement. The pharmacist shall fill the prescription with the generic equivalent product if the override procedure is not followed.

(ii) Injectable medications approved in HCPCS are identified in the "J" code list published by the Health Care Financing Administration or the Department, or both. The list is reviewed and revised yearly and maintained in the Physician Provider Manual by notification and update through Medicaid Provider Bulletins.

(iii) The "J" code covers only the cost of an approved product.

(iv) Office visits only for administration of medication are excluded from coverage. However, an injection code which covers the cost of the syringe, needle and administration of the medication may be used with the "J" code when medication administration is the only reason for an office call.

(v) When an office service is provided for other purposes, in addition to medication administration, only the office visit and a "J" code may be used to bill for the service provided.

(vi) The office visit code and injection code may never be used together. Only one of the codes may be used to define the service provided.

(vii) Vitamin B-12 is limited to use only in treating conditions where physiological mechanisms produce pernicious anemia. Use of Vitamin B-12 in treating any unrelated condition is excluded from coverage.

(b) Vitamins may be provided only for:

(i) Pregnant women: Prenatal vitamins with 1 mg folic acid.

(ii) Children through age five: Children's vitamins with fluoride.

(iii) Children through age 15: Fluoride supplement.

(c) Human growth stimulating hormones are not a covered service.

(d) Methylphenidates, amphetamines, and other central nervous system stimulants require prior authorization and may be provided only for treatment of Attention Deficit Disorder (ADD) in children between the ages of six and 18 years.

(e) Medications for appetite suppression are not a covered service.

(f) Non-prescription, over-the-counter items are limited, and notification of changes consistent with this rule is made by Provider Bulletin and Provider Manual updates.

(g) Nutrients may be provided only as established in R414-24A.

**References:** 26-1-5, 26-18-3.

**History:** 11442, NEW, see CPR; 11442, CPR, 04/15/91; 17705, AMD, 06/07/96; 18823, 5YR, 03/18/97.

## **NOTES TO DECISIONS**

### **Breast reduction surgery.**

Breast reduction surgery is authorized in particular cases of "medical necessity." Therefore, because the patient's attending physicians testified regarding the medical necessity of the procedure and the Department of Health Care Finance failed to give a reasoned basis for declining to give deference to the testimony of the treating physician, the agency's finding that the breast reduction surgery was not medically necessary was not supported by substantial evidence and was reversed. (R414-10-6.) A.M.L. v. Department of Health, Div. of Health Care Fin., 863 P.2d 44 (Utah Ct. App. 1993).



2) the medical services for which payment is claimed were actually furnished to the person identified as the recipient at the time and in the manner stated;

3) the payment claimed does not exceed the provider's usual and customary charges (or the maximum amount negotiated under applicable regulations of the Division of Health Care Financing); and

4) the information submitted in, with, or in support of the claim is true, accurate, and complete. The Division of Health Care Financing may terminate any provider from further participation in the Title XIX program if the provider shall fail or cease to satisfy all applicable criteria for eligibility as a Medicaid Provider as explained in provider manuals.

**b. Ineligibility of Provider**

The Department may refuse to grant provider privileges to anyone who has been convicted of a criminal offense relating to that person's involvement in any program established under Title XVIII, XIX, or XX of the Social Security Act, or of a crime of such nature that, in the judgment of the Department, the participation of such Provider would compromise the integrity of the Medical Assistance Program.

**4. QUALITY ASSURANCE**

In order for the state to meet Title XIX requirements, certain procedures are required. The State is responsible to monitor all programs with respect to medical need, extent and appropriateness of care, and program effectiveness. These procedures include, but are not limited to:

- (a) Audit Procedures
- (b) On-Site Reviews
- (c) Quality Assurance
- (d) Utilization Review

**5. MEDICAL STANDARDS**

a. A Provider must furnish or prescribe medical services to the recipient only when, and to the extent that, it is medically necessary. A service is "medically necessary" if it is (1) reasonably calculated to prevent, diagnose, or cure conditions in the recipient that endanger life, cause suffering or pain, cause physical deformity or malfunction, or threaten to cause a handicap; and (2) there is no other equally effective course of treatment available or suitable for the recipient requesting the service which is more conservative or substantially less costly. Medical services shall be of a quality that meets professionally recognized standards of health care, and shall be substantiated by records including evidence of such medical necessity and quality. Those records shall be made available to the Department upon request.

**b. Determination of Compliance with Medical Standards**

A provider's failure to comply with medical standards may be determined by peer review. Initial determinations as to whether or not a provider has failed to comply with medical standards, will be made by Division of Health Care Financing employ-

ees or consultants. If the determination has been made by the Division of Health Care Financing that noncompliance exists, the Division of Health Care Financing will notify the provider of the failure to comply in writing pursuant to the notice provisions of the Division of Health Care Financing ADMINISTRATIVE HEARING PROCEDURES Section 2.

Either the Division of Health Care Financing or the provider may request to have formal peer review of the Department's determination.

A written request by either the Division of Health Care Financing or provider for formal review must be made within 30 days following the date of the original notice to the provider of the Division of Health Care Financing determination that noncompliance had occurred. The written request from the provider must be submitted by him/her to:

Division of Health Care Financing  
Bureau of Program Review  
ATTN: PEER REVIEW  
P. O. Box 16580  
Salt Lake City, Utah 84116-0580

This written request will be submitted to the appropriate Professional Society requesting that their Peer Review Committee conduct a formal peer review of the Division of Health Care Financing determination.

The informal hearing requirements of Section 26-23-2-(1) UCA, (1953) are satisfied by the professional peer review process.

If either the Division of Health Care Financing or the provider is dissatisfied with the results of the formal peer review they may request a formal hearing before the Department of Health pursuant to Section 23-32-2, UCA (1953) by complying with the formal hearing procedures set forth in the Division of Health Care Financing ADMINISTRATIVE HEARING PROCEDURES.

In situations of violations of compliance of professionally recognized medical standards, identified by peer review, the Division of Health Care Financing may pursue any legal sanction for recovery of overpayments.

Should Federal Financial Participation (the amount the federal government contributes to provider reimbursement) be disallowed on reimbursements made to the provider, the provider will reimburse to the State the total amount that the State paid for the services disallowed (including Federal audit, quality assurance review, or prior authorization requirements) only if the provider was at fault.

**References:** 26-1-5.

**History:** 13550, 5YR, 11/15/92.

**R414-14. Home Health Service.**

R414-14-0. Policy Statement.

R414-14-1. Authority and Purpose.

R414-14-2. Definitions.

R414-14-3. Eligibility Requirements/Coverage.

R414-14-4. Program Access Requirements.

R414-14-5. Service Coverage.

## Addendum C

UTAH DEPARTMENT OF HEALTH  
DIVISION OF HEALTH CARE FINANCING

MARKELLE FRET-PETERSON,

Petitioner,

vs.

UTAH DEPARTMENT OF HEALTH,  
Division of Health Care  
Financing,

Respondent.

Case No. 97-209-11

Margaret J. Clark,  
Administrative Law Judge

REPORTER'S TRANSCRIPT OF AUDIOTAPED PROCEEDINGS

December 8, 1997

Reported by JANE SAVILLE, CSR  
Utah CSR License 103680

*Kingsbury and Associates* Certified Shorthand Reporters

One Utah Center, Suite 900  
201 South Main Street  
Salt Lake City, Utah 84111

1 Reporter's transcript of audiotaped  
2 proceedings transcribed on behalf of Utah  
3 Department of Health of hearing held at the  
4 Cannon Health Building, Room 344, 288 North  
5 1460 West, Salt Lake City, Utah, commencing at  
6 8:30 a.m. on December 8, 1997, before  
7 Margaret J. Clark, Administrative Law Judge.

8

9

\* \* \* \* \*

10

BEFORE:

11

MARGARET J. CLARK  
Administrative Law Judge

12

13 IN ATTENDANCE:

14

For Petitioner: Heidi Peterson  
Dr. William D. Jackson  
(By telephone)

15

16 For I.H.C. Pediatric  
Home Care:

Juliana Rich

17

For Respondent: Mr. Steve Gatzemeier  
Dr. John Hylen  
Ms. Penelope S. Nahley  
Mr. Duane Park

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I N D E X

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HEIDI PETERSON	Direct Testimony	21
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RESPONDENT'S	ADMITTED
1	54

\* \* \* \* \*

1 SALT LAKE CITY, UTAH, DECEMBER 8, 1997, 8:30 A.M.

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THE COURT: I have Mrs. Peterson here and  
7 Juliana Rich. And then for Health Care Financing, Utah  
8 Medicaid, Dr. John Hylen and Penny Nahley who's an R.N.  
9 And then Steve Gatzemeier will be coming shortly. I  
10 think I'm going to have you testify first, Dr. Jackson,  
11 and I'll get into that a little bit more in a moment.

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Basically I need to tell you that the tape  
recorder is on now and it's a formal hearing in the  
matter of Markelle Frei-Peterson versus Utah Department  
of Health, Division of Health Care Financing and the  
Case Number is 97-209-11. My name is Margaret Clark.  
I'm the administrative law judge assigned to preside  
over today's hearing. Today is Monday, December 8th,  
and it's approximately 8:30 in the morning.

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Procedures for today's hearing are governed  
by the Utah Administrative Procedures Act, Title 63,  
Chapter 46(b) of the Utah Code and Utah Administrative  
Rule R410-14. Mr. Gatzemeier just entered the room and  
also Duane Park, who's a pharmacist for Health Care  
Financing.

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1           As I was saying the procedures are governed  
2 by Title 63, Chapter 46(b) and Utah Administrative Rule  
3 R410-14 which contain the Division of Health Care  
4 Financing's hearing policies. After today's hearing I  
5 will prepare what is called a Recommended Decision.  
6 That decision will contain my Findings of Fact and my  
7 Conclusions of Law. The director of the Division of  
8 Health Care Financing will then issue a final decision  
9 called a Final Agency Order and that order may affirm,  
10 reverse, remand or modify my Recommended Decision based  
11 only upon the evidence from the record as a whole, and  
12 that would be the sworn testimony taken today or any  
13 exhibits that are entered into evidence.

14           Should the outcome be unfavorable my  
15 assistant has provided copies of appeals rights to Mrs.  
16 Peterson. If you have any questions should you need  
17 them feel free to call our office.

18           First I'm going to have Health Care Financing  
19 enter their appearances. Are you going to be  
20 representing, Mr. Gatzemeier?

21           MR. GATZEMEIER: Yes.

22           THE COURT: Would you like to introduce  
23 yourself?

24           MR. GATZEMEIER: Okay. My name is Steven  
25 Gatzemeier. I'm a Health Program Manager for Coverage

1 and Reimbursement Policy, Division of Health Care  
2 Financing. Testifying today will be Penny Nahley, who  
3 is a registered nurse and who is the prior  
4 authorization reviewer and was the evaluator, the  
5 initial evaluator in this case. We also have Dr. John  
6 Hylen who is an M.D. who will be available for  
7 testimony. And we have Duane Park who is a registered  
8 pharmacist.

9 THE COURT: Okay. Dr. Peterson, are you able  
10 to hear? I'm sorry. Dr. Jackson, are you able to hear  
11 us okay.

12 DR. JACKSON: Yes. For the state was that  
13 Mr. Gatzemeier?

14 THE COURT: Yes. Okay. I'm having to move  
15 his speaker a little bit closer.

16 I'd like to have you testify first, Dr.  
17 Jackson, since you have the burden of proof, or Miss  
18 Peterson has the burden of proof of as the moving  
19 party. And the issues, as I understand it from the  
20 pleadings and the prehearing conference, is whether or  
21 not Utah Medicaid should cover payment for a growth  
22 hormone. And this is not normally covered by Health  
23 Care Financing as I understand it because it's  
24 considered to be experimental and experimental  
25 procedures are excluded from coverage by the



1 Administrative Code.

2 Is that the issue as everyone understands it?  
3 Mr. Gatzemeier?

4 MR. GATZEMEIER: Yes. Experimental and I  
5 believe it's our understanding that this drug is also  
6 being used for an off-legal use. That may or may not  
7 be but that's the understanding I have.

8 THE COURT: Okay. And, Dr. Jackson, is that  
9 the issue as you understand it?

10 DR. JACKSON: Right. It's the use of growth  
11 hormone for an indication other than stimulating  
12 somatic growth. It's for accelerating intestinal  
13 adaptation.

14 THE COURT: Okay.

15 DR. JACKSON: Although it's not within the  
16 specific experimental protocol like some other  
17 therapies that we sometimes used it's not exactly...

18 THE COURT: I'm sorry, doctor, before you go  
19 any further I need to swear you in so everything you  
20 say is accountable. If you'll raise your right hand,  
21 please.

22 DR. JACKSON: Okay.

23 WILLIAM DANIEL JACKSON, M.D.,  
24 appearing as a witness on behalf of the  
25 Petitioner, having been first duly sworn,

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1 testified as follows:

2 DIRECT TESTIMONY

3 THE COURT: State your name for the record  
4 again.

5 DR. JACKSON: William Daniel Jackson.

6 THE COURT: Thank you. I'm sorry. Now if  
7 you'd like to start testifying in narrative fashion if  
8 you'd like. I think a couple of things that you'd like  
9 to address being not -- not being represented by an  
10 attorney is the medical necessity role which I believe  
11 Health Care Financing was supposed to have sent you a  
12 copy. Did you receive that?

13 DR. JACKSON: Yes, I did.

14 THE COURT: Okay. If you could possibly in  
15 your testimony address those two elements of medical  
16 necessity, and then anything else you'd like to tell  
17 us, and also why you think this procedure, this use of  
18 the drug is not experimental in this case, if that's  
19 what you're contending. I'll just leave it up to you,  
20 but I'm just trying to kind of give you some guidance  
21 here.

22 DR. JACKSON:. Okay. Some of these issues we  
23 went over in the previous hearing.

24 THE COURT: Right. And that was just a  
25 prehearing and that wasn't on the record, so we need to

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1 reiterate anything that's important because this is the  
2 official hearing record.

3 DR. JACKSON: Okay. Markelle Frei-Peterson  
4 is a 24-month-old toddler now with short bowel  
5 syndrome. Is dependent upon parenteral nutrition  
6 support for much of her nutritional needs.

7 THE COURT: Okay. I need to back up just one  
8 more second. I'm sorry to do this to you again. I  
9 need to get your credentials for the hearing record.

10 DR. JACKSON: M.D.

11 THE COURT: Uh-huh.

12 DR. JACKSON: Do you need to know where I  
13 trained or what do you need to know?

14 MR. GATZEMEIER: Specialties.

15 THE COURT: Specialties, board certification,  
16 anything that tells us --

17 DR. JACKSON: I'm board certified in  
18 pediatrics and board certified in pediatric  
19 gastroenterology and nutrition. Recently recertified.  
20 Have fellowship training in pediatric gastroenterology  
21 and nutrition. Have an M.D. and a bachelor's degree.

22 THE COURT: Okay. And where are you working  
23 now?

24 DR. JACKSON: I'm an assistant professor of  
25 pediatrics at University of Utah School of Medicine and

1 I'm based at Primary Children's Medical Center where  
2 I'm the Medical Director of Nutrition Support Services.

3 THE COURT: Okay, thank you.

4 DR. JACKSON: And I practice in pediatric  
5 gastroenterology.

6 THE COURT: Thank you. I hope I won't be  
7 interrupting any more. I'll let you go ahead. You  
8 were starting to tell us that Markelle Frei-Peterson is  
9 a toddler about 24 months old?

10 DR. JACKSON: Yes, she's a two-year-old  
11 little girl with short bowel syndrome dependent upon  
12 parenteral nutrition support which is I.V. nutrition  
13 for I would say 90 percent of your nutritional needs.  
14 She is receiving continuous gastrostomy feeds which are  
15 feedings into her gastrointestinal tract. And around --  
16 variable amounts but generally around 20 cc's per hour.  
17 She has begun to eat and she does consume a certain  
18 amount, it's difficult to quantify, of oral feedings  
19 now. These are -- some of these are new changes that --

20 THE COURT: How recent approximately?

21 DR. JACKSON: This is over the last two to  
22 three -- you know, I'd say last two to three, maybe  
23 three to four months that she's having increasing  
24 intake of oral feedings.

25 THE COURT: Okay.

1 DR. JACKSON: And her stool consistency has  
2 changed at times. So there's been a number of changes  
3 that have occurred in the past few months since we  
4 started this appeal process.

5 THE COURT: Uh-huh.

6 DR. JACKSON: In any case she still remains  
7 dependent upon parenteral nutrition and our main  
8 project and the number one I guess impetus and concern  
9 in a patient with short bowel syndrome is dependent  
10 upon such an expensive technology and possibly lifetime  
11 technology of parenteral nutrition is to get them off  
12 of that and get there G.I. tract, the gastrointestinal  
13 tract to adapt and to accommodate enteral nutrition and  
14 basically take over all of their needs.

15 The other I guess omen along the path for her  
16 besides the risk of central line catheter infections  
17 and eventual loss of I.V. access sites is consequences  
18 on the liver. In children that have short bowel  
19 syndrome who can't be fed adequately enterally they  
20 develop liver dysfunction that is progressive. You can  
21 biopsy these patients' livers and you see fibrosis,  
22 like a scarring process --

23 THE COURT: Uh-huh.

24 DR. JACKSON: -- that occurs in the liver.  
25 And it goes at various different rates in different

1 patients. So I think that's probably the biggest  
2 concern is that a lot of our patients that have short  
3 bowel syndrome that are parenterally nutrition  
4 dependent who can't adequately adapt their G.I. tract  
5 have a risk of progressing to -- well, have a high risk  
6 of progressing to liver failure and require liver  
7 transplantation.

8 So not only do they have the cost of chronic  
9 TPN and the cost of maintaining the central line which  
10 requires repeated hospital admissions as well as they  
11 have the risk long term of possibly requiring a liver  
12 transplantation. Which is covered by Medicaid in  
13 certain situations as is the TPN.

14 So I guess my impetus in this case, the  
15 bottom line in my case is a clinical judgment as to --  
16 I consider it a medical judgment --

17 THE COURT: Uh-huh.

18 DR. JACKSON: -- rather than a legal  
19 judgment. Although I understand that, you know, her  
20 survival and her situation in this case and the  
21 reimbursement situation is from public funds.

22 THE COURT: Right.

23 DR. JACKSON: And there's a responsibility.  
24 I completely understand this. I've been over this with  
25 Dr. Hylen before with some other transplantation

1 issues. And those are larger ethical, economic --

2 THE COURT: Right.

3 DR. JACKSON: -- issues. And I completely  
4 understand all those. In this case on the other hand I  
5 think from both the citizen point of view and the  
6 public trust point of view and a money point of view,  
7 although perhaps it might be premature in terms of the  
8 letter of law and the indications for example, the off  
9 label, et cetera, the evidence that it's experimental,  
10 et cetera like that, even though that may be, from a  
11 medical point of view I -- and there are a number of  
12 other physicians around the country, many much smarter  
13 than I am, including Dr. Book who's a division chief,  
14 who feel that in certain situations using growth  
15 hormone which is commonly used in many, many children  
16 for the indications of just somatic growth, it's not  
17 going to threaten their life, it doesn't threaten much  
18 of anything except for their -- it threatens self  
19 esteem, et cetera. But growth hormone for  
20 short-stature patients, that is covered by Medicaid as  
21 an on-label use.

22 In this case we're using it off of that label  
23 but for what I think is a higher indication which is --  
24 and obviously has to do with judgment and making a  
25 guess of probabilities, but for saving someone's life.

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1 THE COURT: Okay. What --

2 DR. JACKSON: But also I think from an  
3 economic point of view the way I add up I thought that  
4 a reasonably short-term course of this would be -- if  
5 it worked would be a cost effective approach in terms  
6 of the huge magnitude of the cost of lifetime TPN  
7 and/or liver transplantation.

8 THE COURT: What is the growth hormone called  
9 specifically?

10 DR. JACKSON: It's called -- well, it's  
11 recombinant human growth hormone.

12 THE COURT: Okay.

13 DR. JACKSON: And it's called humatrope,  
14 h-u-m-a-t-r-o-p-e.

15 THE COURT: Thank you. Okay. So if I  
16 understand your testimony are you saying that this  
17 growth hormone in this procedure would be reasonably  
18 calculated to prevent liver dysfunction?

19 DR. JACKSON: Indirectly.

20 THE COURT: Okay.

21 DR. JACKSON: What it promotes -- its direct  
22 role -- and there's a lot -- in fact there's more  
23 than -- I said some to you, but there's been more since  
24 then. There's a lot of data about effects on  
25 adaptation in terms of absorption of electrolytes,

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1 amino acids. There's also a lot of data on protein,  
2 carbohydrate absorption and changes of stool output.  
3 There's -- from animal studies. And there's also some  
4 studies of human studies recently that are just been  
5 published.

6 The question is are these studies -- in my  
7 mind these studies are not large, they're not the kind  
8 of studies in which someone would say on a blanket case  
9 that this would be a -- that you will do this for  
10 everybody. But for certain indications there's enough  
11 promise there to motivate a number of different people  
12 to continue to work along these lines. And they're not  
13 fringe people, they're mainstream. In fact one of  
14 biggest protagonists of this is the person that  
15 actually developed total parenteral nutrition, Doug  
16 Wilmore, in 1968. It's been -- these are people that  
17 have been with this for a long time. And there's --  
18 there is controversy.

19 THE COURT: Uh-huh.

20 DR. JACKSON: It's like any other kind of  
21 burgeoning, you know, new therapy. But there's enough  
22 promise there. I don't think it's cold fusion. So  
23 anyway, there's a lot of data on growth hormone itself  
24 stimulating transcription of certain regulatory genes  
25 that turn on growth of the lining of the intestine.

1 And there's lots of demonstrations in certainly animal  
2 models and there's some reports in human studies of  
3 mucosal growth.

4 There's also some where they looked, for  
5 short term at least, like three-week studies, where  
6 they weren't able to see a change, but they were able  
7 to see some changes in absorption and amino acid  
8 uptake.

9 So it's -- it definitely is an area where  
10 there's active work and controversy. But there is --  
11 the basic science elements of it at least are the  
12 growth factors including those stimulated by growth  
13 hormone stimulating intestinal growth.

14 The big question is -- one of the big  
15 questions is what is the timing for doing this, what is  
16 the outcome? Wilmore's group, the group that's  
17 published some, has shown even in patients who have had  
18 their -- lost their intestine years and years ago still  
19 show response. And that doesn't make sense to some  
20 people. But anyway. So there's -- I've kind of sent  
21 most of that information over.

22 THE COURT: Okay. Actually I don't have  
23 copies of that. Will the Respondent's be entering --

24 DR. JACKSON: I sent some articles over with  
25 my appeal to Ms. Nahley back on June 23rd of '97. And

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1 then there was -- I just did a search and I found some  
2 more things. So there's --

3 THE COURT: What I'd like to do is keep the  
4 record open so you could submit whatever you found  
5 recently.

6 DR. JACKSON: One other piece of information,  
7 in the letters I read -- I read two letters. One was  
8 June 23rd, the other one was -- I didn't date it but it  
9 was a little bit later. I guess it was about seven  
10 months ago. Anyway, since then she has been able to  
11 get growth hormone and so she's been on that for a  
12 number of months now. And one of my recommendations  
13 was to do growth hormones for a short period of time, a  
14 limited time such as three months back in June.

15 THE COURT: Uh-huh.

16 DR. JACKSON: And the argument then was this  
17 is worth it, try it. If there is no -- if there is  
18 signs of some benefit then we would like to pursue this  
19 and keep going. The trial process or the hearing  
20 process has basically dragged on over this six months  
21 so in the meantime we've already used it. So can I  
22 attribute what's happening to her now on that?

23 THE COURT: Yes, I think it's relevant.

24 DR. JACKSON: It's circumstantial, but  
25 there's been some -- I mean I think Ms. Peterson can

1 probably attest to what's happening with respect to  
2 Markelle's ability to eat, take some solid foods, do  
3 some things that are often great -- one of the biggest  
4 challenges you have with some of these patients that  
5 have been chronically fed with TPN and tube feeding is  
6 inability to take things orally. So the fact that  
7 she's been able to get her to eat things is a big step  
8 forward.

9 THE COURT: Would you like --

10 DR. JACKSON: Billy Rich perhaps might be  
11 someone else from a medical or nursing background who  
12 could comment on things like that. So, you know, have  
13 there been some changes? Yeah, I think there have been  
14 some changes. Is that something that she would have  
15 done anyway without this? That's why we do randomized  
16 trials. And Dr. Hylen would certainly say, yes, of  
17 course. So this could all just be anecdotal, et  
18 cetera.

19 THE COURT: Could you -- do you know how  
20 long -- how long will she be needing this growth  
21 hormone? I mean is it indefinite or do you have any  
22 idea how long she would need it?

23 DR. JACKSON: I think it's self limited. I  
24 think that my original feeling would be to use it for a  
25 year. But I think that her ability to adapt or start

1 being able to accommodate to more enteral feeding, that  
2 by itself is somewhat protective on the liver. The  
3 feedings itself are stimulatory to the G.I. tract.

4           Though we are really stuck -- when we first  
5 proposed this in June the impetus behind this was --  
6 and I was actually slower than some of my colleagues to  
7 want to go for this therapy. But I think that her  
8 liver tests -- she had kind of a marked abnormalities  
9 of her liver test at that time. I was basically  
10 worried that she was starting to show signs of  
11 accelerated liver disease.

12           And her -- since then her liver tests have  
13 normalized. And I -- but anyway, at that time that was  
14 a concern. We weren't making any progress. She was  
15 stuck in terms of her ability to take in things. And  
16 it was -- she was in and out of the hospital. We were  
17 having lots of troubles.

18           So there are a few things that we changed at  
19 the time. But the biggest one since then has been  
20 basically adding the growth hormone. So I don't  
21 know -- I think she's a different baby now, different  
22 child now than she was before, and that could just be a  
23 maturity process, it could just be that she's gradually  
24 been able to, you know, adapt from the feedings or  
25 could be, you know, or it could be due to this.

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1           That's why we do these kind of trials is to  
2   know for sure what it is. I would say that at the end  
3   of that year period I don't think there is any -- in my  
4   mind at that point, particularly given what -- the  
5   progress she's made so far, I would think at that point  
6   there would be diminishing returns because we're  
7   getting at the point now where she taking in -- it  
8   won't be that much more. But she could take in more  
9   enteral feedings where that whole -- that process may  
10  hopefully sustain itself. The feeding itself  
11  stimulates the G.I. tract to adapt.

12           THE COURT: Okay.

13           DR. JACKSON: And whoever -- the people, you  
14  know -- I think that, you know, whoever provided the  
15  growth hormone to date -- I think I.H.C. has been doing  
16  that, you know, they've been quite generous. So...

17           THE COURT: Okay, thank you. I'm going to  
18  swear Mrs. Peterson in and then you will be able to ask  
19  some questions but since this is on the same track I  
20  just want to ask her about the changes.

21           MR. GATZEMEIER: I have some questions about  
22  his testimony.

23           THE COURT: Right.

24           MR. GATZEMEIER: Going to swear both of them  
25  at the same time?

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1 THE COURT: I'd just like to get comments on  
2 that one area and then you can ask them both questions.

3 Will you raise your right hand, please?

4 HEIDI PETERSON,  
5 appearing as a witness on behalf of the  
6 Petitioner, having been first duly sworn,  
7 testified as follows:

8 DIRECT TESTIMONY

9 THE COURT: Your name for the record.

10 MS. PETERSON: My name's Heidi Peterson and  
11 I'm Markelle Frei-Peterson's aunt.

12 THE COURT: Okay. I was just going to ask  
13 and I'll probably want you to testify later, but just  
14 if you wanted to comment on Dr. Jackson's remarks about  
15 how she had improved since the hormone therapy.

16 MS. PETERSON: Markelle used to stool up to a  
17 thousand cc's of stool a day and now we're down to  
18 between three and four hundred cc's of stool a day. I  
19 have upped her feedings from -- the maximum we used to  
20 get three months ago -- we're on our third month of  
21 growth hormone this month -- the maximum we got to in  
22 her tube feedings was 15 cc's an hour. And that was  
23 with turning her on and off through the night. Now I'm  
24 up to 21 cc's an hour.

25 We are doing feeding therapy through a speech

1 therapist. She eats with her mouth every meal that we  
2 eat. We're teaching her how to drink juices and that  
3 kind of thing. So I mean it's a lot.

4 THE COURT: Okay. Do you have any questions  
5 you want to ask Miss Peterson now? Okay.

6 Then I'll go back to Dr. Jackson. And before  
7 I finish questioning you then Health Care Financing has  
8 the right to cross-examine so they're going to ask some  
9 questions. Then I'm going to have them put on their  
10 case. You will be able to cross-examine them, ask any  
11 questions you'd like to ask of them. And then at the  
12 end if you'd like to provide any rebuttal evidence and  
13 both sides can summarize. Okay?

14 WILLIAM DANIEL JACKSON, M.D.,  
15 appearing as a witness on behalf of the  
16 Petitioner, having been previously duly sworn,  
17 testified further as follows:

18 DIRECT TESTIMONY (CONTINUING)

19 THE COURT: Dr. Jackson, since I need to  
20 consider this in my decision and I'm bound by the Utah  
21 Administrative Code, could you just go over the medical  
22 necessity role and state why or why not, why you think  
23 that Markelle Frei-Peterson needs this? And I'm just  
24 going to read it and let you address it. And then you  
25 can add anything else you want. Then we'll have both

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1 your findings and questions.

2 It says a service is medically necessary if  
3 it's reasonably calculated to prevent, diagnose or cure  
4 conditions in the recipient that endanger life, cause  
5 suffering or pain, cause physical deformity or  
6 malfunction, or threaten to cause a handicap. Do you  
7 want to take that one on first? That's the first part.

8 DR. JACKSON: Well, from my biased  
9 perspective I feel like it's reasonably calculated to  
10 use this agent and the goal would be to basically  
11 prevent premature death, reduce -- or improve quality  
12 of life by reducing dependence on total parenteral  
13 nutrition, and increasing her chances of becoming  
14 independent of that by being able to eat and consume  
15 foods normally.

16 Avoid the future suffering of -- well, future  
17 and things that she's already encountered of central  
18 line infections, complications of central venous  
19 catheters to provide the total parenteral nutrition.  
20 Including infection and dislodgement and vascular  
21 thrombosis. And finally to prevent chronic liver  
22 disease that plagues so many patients that are on  
23 chronic TPN, with the possibility of requirement for a  
24 liver transplantation.

25 THE COURT: Okay. And then the second part:

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1 There is no other equally effective course of treatment  
2 available or suitable for the recipient requesting this  
3 service which is more conservative or substantially  
4 less costly. Could you address that too?

5 DR. JACKSON: There's no -- the alternative  
6 basically is to do what we've done before which is to  
7 try to encourage feedings and give time.

8 THE COURT: Has that worked?

9 DR. JACKSON: To my -- in my estimation it  
10 hadn't worked. We were stalemated and it wasn't  
11 working. And my experience has been that patients with  
12 severe short bowel that she has, that have been on TPN  
13 as long as she had, with the struggles that she had had  
14 did not have a good prognosis. In other words had a --  
15 were destined to be TPN dependent for a long -- we see  
16 many babies in situations like this who have progressed  
17 on to get liver disease.

18 I have one patient who has a similar  
19 situation where she lost -- she basically had somewhat  
20 less bowel than Markelle has, but ended up progressing  
21 on and she ended up getting a liver and small bowel  
22 transplant. We have others that have gone on to get  
23 liver transplants. We have others that have basically  
24 because they haven't been able to adapt their G.I.  
25 tracts have not been counted for liver transplants and

1 so they just died.

2 So that's -- I guess in the life of a  
3 pediatric enterologist an infant with short bowel  
4 syndrome that's dependent on total parenteral nutrition  
5 who can't adapt their G.I. tract is -- has a very high  
6 likelihood of progressing on to end stage liver  
7 disease, cirrhosis and the complications related to  
8 that.

9 So in some ways I guess that's probably what  
10 powers our urgency and interest in wanting to do things  
11 like this. And maybe put a product on line before it's  
12 gone through the randomized -- called the randomized  
13 controlled type of trials, the large ones.

14 THE COURT: Okay.

15 DR. JACKSON: So anyway, I would say that the  
16 customary standard therapy that we've used for this has  
17 not worked. Or at least has a very low probability of  
18 working. And the only alternative that has any  
19 credibility and has quite a few -- you know, has an  
20 accumulating number of people working on it and  
21 publishing in it, is this combination of growth hormone  
22 therapy, glutamine, which in this case is provided in  
23 the Vivonex, which is the formula which she's getting,  
24 and a relatively high carbohydrate diet. Those are the  
25 things that we have data on.

1 THE COURT: Okay. Is there anything else  
2 you'd like to add at this time or should I let Health  
3 Care Financing ask their questions?

4 DR. JACKSON: I think that our -- I can admit  
5 up front that the indications are not in your code for  
6 using it this way. The area is -- does have  
7 controversy as with any new therapy, and there is a  
8 possibility that this could be disproved. And there  
9 have been other times when medicine has gone down the  
10 wrong path and thought they were -- had a therapy that  
11 was helpful but it turned out not to be true.

12 Or there's some other element that they  
13 weren't quite right on, they didn't know the dose, or  
14 the timing, or the combinations weren't exactly right.  
15 So all those kinds of things are things that can be  
16 granted. However, the relationship between the patient  
17 and this physician at least in terms of background,  
18 training, and the colleagues that I've consulted and  
19 worked with has been -- have basically led me to  
20 advocate the use of this therapy. And at least in my  
21 judgement and tying together the benefits outweigh the  
22 risks and the costs.

23 THE COURT: Okay.

24 DR. JACKSON: The costs if it's successful  
25 will be much, much less than the alternative.

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1 THE COURT: Okay, thank you. Dr. Hylen, do  
2 you have questions for Dr. Jackson?

3 DR. HYLEN: Yeah, I have a question.

4 Have you given any patient growth hormone  
5 that clearly prevented liver disease or liver  
6 transplant over the long term?

7 DR. JACKSON: It's a new -- no, it's a new --  
8 for us, our particular group here, it's a new approach.  
9 We have probably -- Dr. Book has two patients that are  
10 receiving it. I have one other patient that's  
11 receiving it. And they're our most difficult patients.  
12 So they're desperate situations actually for those  
13 patients. And Dr. Book's impression, albeit anecdotal,  
14 is that those patients have shown some improvement  
15 since being started on it.

16 These are, you know, these are rightfully  
17 labeled and disparaged as anecdotes and that's where we  
18 are. The only stronger data I can have that would  
19 justify doing this are those from the people who have  
20 published in the field from Mayo Clinic and from --  
21 particularly from Brigham and Women's Hospital in  
22 Boston.

23 THE COURT: Okay. Have those articles  
24 already been submitted?

25 DR. JACKSON: Several of those articles have

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1    been submitted.  There's been some recent ones in  
2    October '97 and there's some others.  You know, some of  
3    these come down on the side of -- and there's an  
4    editorial in that same article.  So I could fax those  
5    over to Dr. Hylen.

6                They don't -- they don't in my mind -- they  
7    demonstrate increased -- you know, some measures of  
8    increased absorption and function but over the short  
9    term.  And this one small human study, eight humans in  
10   a crossover study for 21 days, which is a very short  
11   period of time, and these are adults, those ones don't  
12   show morphologic changes.  And there was changes in  
13   what you could see when you looked microscopically at  
14   the bowel.

15               THE COURT:  Well, I'll leave that up to you  
16   if you think that would be helpful then.

17               DR. JACKSON:  It will just be -- I don't  
18   think it strengthens the case over what previous things  
19   I've submitted.  But --

20               THE COURT:  Okay.

21               DR. JACKSON:  It would certainly maybe give  
22   Dr. Hylen more -- I mean since it just says it's more --  
23   it's just a controversial area.

24               THE COURT:  Okay.  Thank you.  I'll give you  
25   10 days if you want to --

1 DR. JACKSON: Okay.

2 THE COURT: -- submit that or even fax that  
3 over to us.

4 DR. JACKSON: Okay.

5 THE COURT: Dr. Hylen?

6 DR. HYLEN: What's the longest that any of  
7 your patients have been on growth hormone for this sort  
8 of problem?

9 DR. JACKSON: I think Dr. Book's -- I think  
10 we're on about six months on one of my other patients,  
11 five months on my other patient. And Dr. Book's  
12 patient is probably greater than that. Probably six or  
13 seven months.

14 DR. HYLEN: One comment you made was that  
15 since she's been on growth hormone that her liver  
16 function tests have normalized. Does that mean that  
17 they're totally normal, and what were they before, and  
18 can you give us more documentation of --

19 DR. JACKSON: Yes, I can. I don't know why  
20 her -- I actually don't know why her liver tests jumped  
21 as they did. But -- and they have -- my feeling is  
22 that if I look back I think they jumped up and  
23 normalized independent of growth hormones. In other  
24 words I think by September they had come back down.  
25 And I think --

1 DR. HYLEN: What --

2 DR. JACKSON: Growth hormone was initiated in  
3 December. So I don't know that -- I have the data  
4 right here. They weren't completely normal then but  
5 they had come back down some.

6 THE COURT: Doctor, do you want to come up --  
7 can you hear Dr. Hylen okay?

8 DR. HYLEN: Yeah, he can hear me.

9 DR. JACKSON: He's in the distance but I can  
10 hear him.

11 THE COURT: Okay. All right.

12 DR. HYLEN: Anyway, we would like  
13 quantification of the date she was started on growth  
14 hormone and what her liver function tests were before  
15 and subsequent to the -- through the whole time period  
16 what her liver functions did.

17 DR. JACKSON: Okay. I think --

18 DR. HYLEN: Because it's hard for us to  
19 comment on some of the things that you're saying growth  
20 hormone's going to do when we don't have --

21 DR. JACKSON: I don't -- I don't really -- I  
22 think that growth hormone did not -- in my mind I  
23 don't think growth hormone caused the normalization of  
24 these liver tests.

25 DR. HYLEN: Okay.

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1 DR. JACKSON: I don't think that it did that.  
2 I think that was an acute -- I don't know what caused  
3 that exactly. We didn't do a liver biopsy. Her  
4 transaminases went up into the several hundreds without  
5 much cholestasis. And her GGT went up a little bit.  
6 And that's basically what one of our concerns was, that  
7 she was going to start showing us some liver disease,  
8 which is something we always had worried about.

9 But by the time that the growth hormone was  
10 begun I think those numbers had come back, had started  
11 to come back down. In fact we have some normal, you  
12 know, as early as September, we have pretty much near  
13 normal levels. The GGT remained slightly high off and  
14 on during that period of time.

15 But I'm not claiming that the growth hormone  
16 normalized liver functions. Its role in my mind is in  
17 stimulating adaptation of the G.I. tract and improving  
18 her tolerance of enteral feedings that could set up a --  
19 set the stage for continued adaptation. And the more  
20 enteral feedings she can get the more protection her  
21 liver has. Our kids that can be fed somewhat enterally  
22 have a much lower incidence of progressing on to liver  
23 disease, even if it's partial feedings. In other words  
24 not 100 percent.

25 But those that can't like she was before, as

1 Ms. Peterson commented on, when she was really having  
2 difficulty even tolerating 15 cc's an hour, that's a  
3 tablespoon an hour of an elemental formula, that's --  
4 that was problematic. That meant her G.I. tract was  
5 not able to be fed and the risk there was of her liver  
6 not getting the appropriate stimulation that it likes  
7 to get to keep it from developing liver disease.

8 THE COURT: Okay. With that additional  
9 information from Dr. Jackson, Dr. Hylen, would that  
10 still be helpful, that information?

11 DR. HYLEN: I think we still need some  
12 quantification.

13 DR. JACKSON: I'll put that together, okay.  
14 I'll put it together in a flow sheet.

15 DR. HYLEN: The other thing that I think  
16 makes it sort of difficult here at the hearing is not  
17 having the articles and the editorial.

18 DR. JACKSON: I sent all of those articles  
19 over back in June and I just have some of these other  
20 recent ones. One's as recent as October.

21 MR. GATZEMEIER: Those recent ones would be  
22 valuable.

23 DR. HYLEN: We don't have the recent things.

24 DR. JACKSON: Right.

25 DR. HYLEN: So I think it's hard for us to

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1 comment without seeing those. What additional articles  
2 are you going to send us I think is what we'd like to  
3 know?

4 DR. JACKSON: I could send you an article  
5 from Gastroenterology, 1997 October. I could send you  
6 a recent search on short bowel and growth hormone use  
7 that has the literature summarized from '93. And I  
8 have, you know, the previous articles that I'd sent  
9 over that I could put together and send again.

10 THE COURT: Okay, that would be very helpful.

11 DR. JACKSON: There's an editorial on this  
12 one article that's published by the Mayo Clinic. It'll  
13 give you a perspective. You know, it obviously does  
14 not come down saying that everybody should do this.

15 THE COURT: Okay. Well, what I would  
16 probably like to do after Health Care Financing has had  
17 an opportunity to review all that is maybe continue the  
18 hearing briefly by telephone just so you can -- they  
19 can ask you questions and vice versa. Do you have any  
20 other questions right now?

21 DR. HYLEN: I don't, no.

22 THE COURT: Mr. Gatzemeier?

23 MR. GATZEMEIER: Yes. First of all, Dr.  
24 Jackson -- well, first of all I want to know if you've  
25 read your contract with the University of Utah, the

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1 fine print. I understand the University of Utah has in  
2 fine print that nobody up there can use the word "cold  
3 fusion."

4 DR. JACKSON: That's right.

5 MR. GATZEMEIER: Anyway, the concern I have  
6 is that the reason we refused this was not on medical  
7 necessity.

8 THE COURT: I need to swear you in, too, now  
9 that you're presenting your case.

10 MR. GATZEMEIER: We're just cross-examining.

11 THE COURT: You were cross-examining but --  
12 okay.

13 MR. GATZEMEIER: I'm just asking him some  
14 questions.

15 THE COURT: Okay.

16 MR. GATZEMEIER: You can swear me whenever  
17 you want.

18 THE COURT: No, whenever you're ready.

19 MR. GATZEMEIER: Or we can not swear, we can  
20 attest.

21 THE COURT: Whenever you're ready to present  
22 your case we'll swear you in. If you're  
23 cross-examining go ahead.

24 MR. GATZEMEIER: Okay. Dr. Jackson, the  
25 reason that was given for the state denying this was

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1 not medical necessity, it was on experimental. Now, as  
2 I understand your testimony you indicated that this  
3 practice was still considered experimental?

4 DR. JACKSON: I think there's a lot of  
5 therapies that we use that are rightfully considered  
6 experimental which in terms of -- if you think of it in  
7 terms of data being accumulated and evaluating the  
8 efficacy, the appropriate dosage, the appropriate  
9 indications, things like that. And this one  
10 particularly as early a therapy as this is, as young a  
11 therapy I guess as this is would definitely I think  
12 have to be considered that.

13 In my -- the strict interpretation of  
14 experimental in my mind would be is she on an  
15 experimental protocol of like one patient in a study.  
16 And I guess I don't consider it that. I consider it  
17 more of a situation of taking a therapy that's been --  
18 that is in use, that is new, that is not 100 percent  
19 validated and may very well have certain subjects,  
20 certain patients in which it works in and certain  
21 patients that it doesn't. That stuff is all being  
22 worked out.

23 And so I see this more as just a decision in  
24 the -- I guess -- I don't know whether you call it the  
25 art of medicine but it's the idea of taking data, what

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1 data is available, and a desperate clinical situation  
2 and adding up pluses and minuses and trying to come to  
3 a judgment. And that judgment could be deemed  
4 erroneous by peers or other people, but on the other  
5 hand there are a number of different peers and  
6 superiors to me who agree with trying this kind of  
7 therapy, so they have been my guide.

8 So I see it in that sense as more of a  
9 medical judgment. I think that's what -- I think  
10 that's what's interesting about this whole process here  
11 is how do you decide, based on the rules and  
12 regulations and your charge to take care of lots of  
13 people with that pool of money, what's the best way to  
14 spend that money? Is this a gamble? Is this, you  
15 know, is this foolishness that should not be supported?  
16 And I think that just comes down to where you make it.

17 If I'm her physician my judgment is that I  
18 would like to try this. I have a certain idea of how  
19 to use it. We don't have all the information or  
20 details and we often don't in making practice decisions  
21 and making clinical decisions, we often don't. We  
22 don't know that this indeed is what cured the patient  
23 or this indeed is what did anything. A lot of times we  
24 just claim credit for things that would have gotten  
25 better anyway.

1           You look at antibiotic use for ear infections  
2 or for all around -- I mean huge expenditures of money  
3 on therapies that are given to people who would get  
4 better anyway. There's a lot of therapies like that  
5 that are out there. And I'm weighing this against a  
6 therapy that you do pay for, that is approved for  
7 non-life threatening short stature related to  
8 idiopathic growth hormone deficiency, and I'm comparing  
9 that to paying for that for a child who has a  
10 life-threatening problem in which some people, and  
11 people that have worked hard and have produced some  
12 evidence in favor of it, suggest that that can be  
13 beneficial.

14           The data in pediatrics is later, much later  
15 than the data in adults in this case, which is often  
16 the case. And so we had that other issue from  
17 pediatrics where we apply things -- there are many  
18 drugs that are used that have never been verified or  
19 proved in pediatrics. You look through the PDR or any  
20 of the drug reference groups for most of the  
21 medications that we use it says pediatric indications  
22 and use have not been established. That's just a fact  
23 of life for practicing pediatrics.

24           And part of it is that the society has not  
25 deemed it necessary to study children in that regard.

1 It's expensive to do that and there's concerns about  
2 the well being of children in those situations. So  
3 what's happened to pediatricians is they have to take  
4 those drugs that aren't approved for pediatrics and use  
5 them. And there's a very, very long tradition of doing  
6 that, both for good and for bad for children.

7 So I guess I fit myself within that tradition  
8 of making a physician's decision weighing the evidence.  
9 And obviously I'm at the mercy of the court for looking  
10 at the letter of the law and making a decision that  
11 way, as is Markelle. So I would -- what I was  
12 proposing was a self-limited, short-term use of this  
13 within the reason -- you know, the reasonable use of  
14 this drug as it has been used with patients that have  
15 growth hormone deficiency to see if it's going to make  
16 a difference.

17 And are we validated by what's happened in  
18 the last three months by her being treated? Well, it  
19 certainly hasn't gone the other -- hasn't gone the  
20 wrong direction, and she seems to have made some  
21 progress. So that does not prove anything. I don't  
22 think there's anything you could write an article about  
23 or it'd be a very dubious case report. I don't know  
24 what kind of a case report that would be at this point.  
25 But it was not done within an experimental protocol.



1 It would be something -- it's not the kind of thing  
2 that I would deem purely an experiment that way. It's  
3 more of a medical just judgment decision based on a  
4 certain amount, perhaps not optimal amount, of data  
5 that's out there.

6 THE COURT: Okay. Any more questions?

7 MR. GATZEMEIER: Yeah. Dr. Jackson, I'm sure  
8 you're aware of the fact that the reasons -- and I  
9 agree 100 percent with what you're saying on -- you  
10 know, you have to use things as you deem appropriate  
11 from a medical perspective to try and treat things.  
12 Unfortunately we are in a situation in Medicaid where  
13 we are governed totally by rules. The federal  
14 government because of some of the inappropriate use of  
15 federal programs in the '40's and '50's have totally  
16 eliminated the ability to utilize things that are  
17 considered experimental predominantly, primarily  
18 because they were used in a poor context previously.

19 And, you know, in the '40's and '50's they  
20 took groups and used experimental procedures which were  
21 not beneficial to the groups but were negative to the  
22 groups. And so when the Medicaid law was written it  
23 basically said you do not use things which are  
24 experimental on any of these groups. That, as most  
25 laws, cuts both ways. Cuts to cut out the

1 inappropriate experimentation, but it also eliminates  
2 the ability to experiment with things that could in  
3 fact be beneficial.

4 And that is one of our concerns, is that even  
5 though procedures and things may be considered  
6 beneficial -- and we don't know. You know, we just had  
7 this situation with Phen-Phen where everybody thought  
8 we had a wonderful miracle thing. But the fact is we  
9 are limited to doing things which are proven or  
10 considered proven, recognizing Phen-Phen was a  
11 non-label use.

12 DR. HYLEN: No, it was an off-label.

13 MR. GATZEMEIER: All right. But it was  
14 approved by the FDA for that purpose.

15 DR. HYLEN: No.

16 MR. GATZEMEIER: Wasn't it?

17 THE COURT: Well, that's not relevant, let's  
18 not get into that.

19 MR. GATZEMEIER: Either way. The fact is  
20 this is an off-label use as we understand it of this  
21 drug and the fact is because it's an off-label use it's  
22 considered experimental to us and we have a real  
23 difficulty dealing with both the federal regulations  
24 and the state regulations. Do you have any  
25 information, doctor, that shows that this drug has been

1 approved by either the FDA or the drug manufacturer for  
2 on-label use for this purpose?

3 DR. JACKSON: No, no, I don't think so. Not  
4 in the -- as far as I know it's not. There might be an  
5 IND, you know, for the people that are doing -- are  
6 using it in a research setting. There has to be. But  
7 as far as I know it's not approved as an extended --  
8 you know, as an indication for this.

9 MR. GATZEMEIER: Okay. That's --

10 THE COURT: Any other questions?

11 Okay. Duane Park has a question.

12 MR. PARK: Just one question, doctor. Before  
13 you started the supplemental use of the growth hormone  
14 did you do a blood level to determine what the normal  
15 circulation was?

16 DR. JACKSON: Yes, I did, actually. I  
17 checked IGF-1 which is a marker for that. And she has  
18 normal levels of IGF-1. And that's not -- as I  
19 understand the information I have, literature, that's  
20 not -- that would be expected. They don't have low --  
21 they don't have those kind of indications. In other  
22 words she doesn't have growth hormone deficiency. The  
23 use of growth hormone came out of observations that in  
24 resection growth hormone levels go up. And the  
25 products that that stimulates that stimulate growth --

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1 THE COURT: Excuse me, doctor, I have to flip  
2 the tape. I'm sorry.

3 (Whereupon, the hearing was briefly  
4 interrupted to begin Side 2 of Tape 1.)

5 THE COURT: Okay.

6 DR. JACKSON: Basically the fact that your  
7 growth hormone levels are normal does not necessarily --  
8 does not mean -- that's not the reason that the growth --  
9 why the growth hormone is being used. It's higher than  
10 normal levels of growth hormone are observed in  
11 patients that have lost small bowel, and the idea that  
12 they stimulate growth factor production in the body,  
13 including epidermal growth factors, things like that  
14 that work on the lining of the intestine to stimulate  
15 growth.

16 And those are -- the other -- another  
17 experimental line has been in animals that have  
18 excessive growth, have tumors that express growth  
19 hormone, excessive growth hormone, have hyperplasia of  
20 their small bowel. And so the idea basically is that  
21 if you give excessive growth hormone it induces  
22 transcription of the genes for all these growth factors  
23 and stimulates growth of the small bowel.

24 So basically the goal here is to use it as a  
25 pharmacologic agent rather than a replacement agent.

1    Though the indications for using growth hormones for  
2    people of short stature is one based on replacement of  
3    something that is missing. In this case it's being  
4    used in the lines of a pharmacologic agent to actually  
5    stimulate the kind of growth factors that would be  
6    required to try to make the small bowel develop and  
7    grow more.

8               THE COURT: Sort of like a catalyst?

9               DR. JACKSON: No, it would be more actually  
10   as a growth hormone, as something that you would -- I  
11   mean, I guess Schwarzenegger could use it. But it's  
12   along those lines of a drug. In other words you're  
13   using it at a higher superphysiologic level.

14              We're not monitoring levels, for example, of  
15   IGF-1 and things like that. Should that be done? I  
16   don't know. That might be an -- some of those things  
17   might be some of the things that people have not --  
18   they've looked at those things in the studies but  
19   they've not used that as a marker for adjusting the  
20   dose. They've just taken pretty much a standard dose.  
21   There's a lower dose that someone has used, much lower  
22   than what we're using, and so there's some  
23   experimentation. There's some people trying different  
24   doses.

25              THE COURT: Okay. Any other questions?

1 MR. GATZEMEIER: Yeah. Doctor, you mentioned  
2 that --

3 THE COURT: This is Steve Gatzemeier for the  
4 record.

5 MR. GATZEMEIER: Yes, I'm sorry.

6 You mentioned that Markelle is receiving  
7 growth hormone at this point. Who's supplying that,  
8 how is that happening?

9 THE COURT: I believe he testified he didn't  
10 know. But do you know, doctor?

11 DR. JACKSON: I think I.H.C. is doing it.  
12 Julie Rich would know. I think I.H.C.

13 MS. PETERSON: Primary Children's funds is  
14 supplying that for us.

15 DR. JACKSON: Oh, Primary Children's --

16 MS. PETERSON: Primary Children's pennies,  
17 their charity is providing the funds right now.

18 THE COURT: That was Heidi Peterson.

19 Anything else?

20 Did you have anyone else you wanted to  
21 testify for you on Markelle Frei's condition that would  
22 be relevant or has the doctor pretty much covered  
23 everything?

24 MS. RICH: Well, I was case manager for a  
25 brief time with Markelle. I'm Julie Rich. And I'd

1 just like to say that what Heidi has seen at home, if  
2 you look at Markelle as a holistic person that we want  
3 to make developmental milestones and progress then we  
4 need to support her in this. The fact that she was  
5 having so much stool output it made it difficult for  
6 her to meet any of her milestones or progress at all.  
7 It's made it a lot easier to care for her. And it  
8 makes it easier for us to even look at decreasing  
9 nursing hours in the home.

10 THE COURT: Okay. Do you solemnly swear or  
11 affirm that the testimony that you have just given and  
12 may be about to give is the truth, the whole truth, and  
13 nothing but the truth?

14 MS. RICH: Yes.

15 THE COURT: And your name?

16 MS. RICH: My name's Juliana Rich.

17 THE COURT: Okay. And was there anything  
18 that you wanted, either of you...

19 MS. SMITH: I'm Abby Smith.

20 THE COURT: Okay. Raise your right hand,  
21 please.

22 ABBY SMITH,  
23 appearing as a witness, having been first duly  
24 sworn, testified as follows:

25 THE COURT: Your name for the record?

1 MS. SMITH: Abby Smith.

2 THE COURT: Okay.

3 MS. SMITH: I'm from I.H.C. Access. We don't  
4 provide anything in the way of drugs for any Medicaid  
5 patients so we would really not be able to do anything  
6 for Markelle.

7 THE COURT: Okay.

8 MR. GATZEMEIER: Were you able to hear that,  
9 doctor?

10 DR. JACKSON: I lost her after she said "We  
11 are not able to provide anything but..."

12 MS. SMITH: Medicaid provides all of the  
13 drugs for I.H.C. Access patients. So we are not  
14 allowed to provide monies for drugs.

15 MR. GATZEMEIER: The pharmacy portion of the  
16 Medicaid program is not funded through I.H.C. Access.  
17 They're being paid for other services but the actual  
18 expenditures of the pharmacy comes directly from the  
19 state.

20 THE COURT: Okay, any more questions from  
21 Medicaid --

22 MR. GATZEMEIER: Not at this time. He may  
23 have some questions.

24 THE COURT: Would you like to go ahead and  
25 present --



1 MR. GATZEMEIER: Certainly. Should we swear  
2 all of us at the same time?

3 THE COURT: Yes. I'm going to swear Health  
4 Care Financing in now. And I'm going to point to you  
5 after I administer the oath and if you'll state your  
6 name then for the record.

7 (All witnesses for Health Care Financing  
8 were sworn.)

9 MR. PARK: Yes. Duane Park.

10 DR. HYLEN: I do. John Hylen.

11 MR. GATZEMEIER: Yes. Steve Gatzemeier.

12 MS. NAHLEY: Yes. Penny Nahley.

13 THE COURT: Thank you.

14 PENELOPE NAHLEY,  
15 appearing as a witness on behalf of Health  
16 Care Financing, having been first duly sworn,  
17 testified as follows:

18 EXAMINATION

19 BY MR. GATZEMEIER:

20 Q Okay. Miss Nahley, you were the one who  
21 initially took the action to deny this request. Can  
22 you tell us what process you went by to deny that and  
23 what the rationale was for denying the request?

24 A Well, I went -- I got out the both criterias  
25 to see if she met any of that and she did not meet that

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1 the criteria. I asked for additional documentation  
2 from the physicians knowing that this was not a common  
3 use for the drug according to our criteria. So I had  
4 asked for additional information to be sent and that  
5 was to include any literature they had that would  
6 support the use of this drug. I asked for liver  
7 function tests, her clinical records, what type of TPN  
8 she was on, her entero products, that sort of thing.

9 That all came in and it was reviewed. I  
10 reviewed it. I took a lot of notes on it and then  
11 presented it to the Check Utilization Review Committee  
12 and they reviewed it and agreed that this was not a  
13 typical use for this drug, that it was an experimental  
14 and we denied it.

15 Q Okay. When you say you took it to the Check  
16 Utilization Review Committee can you tell us what the  
17 constitution of that committee is.

18 A It's made up of physicians and nurses.

19 Q Okay. I believe there's also a social worker  
20 or a check portion of it?

21 A I believe she is -- she's a social worker and  
22 then there's the consultants. We have OTPT  
23 consultants.

24 Q Okay. And that committee reviewed this  
25 request and determined that it was denied. What was

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1 the rationale again?

2 A It was to be denied that the documentation  
3 indicated it was an experimental procedure.

4 Q Okay. You also indicated, Miss Nahley, that  
5 you looked at the criteria for growth hormones and it  
6 did not meet the criteria. Specifically what criteria  
7 did it not meet?

8 A She did not have a documented failure of  
9 growth due to an endogenous growth hormone secretions.  
10 Or she did not have insufficiency due to kidney  
11 failure.

12 Q Okay. Now, the doctor has already testified  
13 that this isn't really the rationale for providing this  
14 drug, however this is the rationale and the  
15 documentation that the state uses to determine whether  
16 the drug should be prior authorized. Can you tell us  
17 where this is found, what this comes from?

18 A Where this criteria comes --

19 Q Yes.

20 A This comes from our pharmacy provider manual.

21 Q Okay. And the pharmacy provider manual  
22 outlines the state's policy related to particular drugs  
23 or utilization of --

24 A Yes.

25 Q Drug types?

1           A     Yes.

2           THE COURT:   Are you going to be submitting  
3     that into evidence?

4           MR. GATZEMEIER:   Yes, we will.

5           THE COURT:   Do you have any objection to  
6     that, Dr. Jackson?

7           DR. JACKSON:   Oh, no.

8           THE COURT:   Okay.

9           Q     (By Mr. Gatzemeier)   Okay.   So you looked at  
10    the information, you issued a denial letter, you got a  
11    request for reconsideration.   Was there any additional  
12    information that you looked at following that denial?

13          A     I'm not really sure how that came.   I believe  
14    in with the hearing request there were some other  
15    documentation on studies that have been done.   And so  
16    that was looked at --

17          Q     You did review that information?

18          A     -- at that time.   Uh-huh.

19          Q     Did that change at all your position?

20          A     No, it's definitely stated in there that  
21    these were small groups and that it was study groups  
22    that were being done.   Still didn't meet our criteria.  
23    It still was experimental.

24          Q     Okay.   What is the documentation or the  
25    justification for the denial on experimental?   In the

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1 denial letter you have a citation. Can you tell us  
2 where that came from?

3 A Let me just find it real quick. Okay, that's  
4 Utah Administrative Code R414-10-6, Physician's Covered  
5 Services. And it states, "Experimental or medically  
6 unproven physician services or procedures are excluded  
7 from coverage."

8 MR. GATZEMEIER: Okay. That's all the  
9 questions I have. Are there any questions of Miss  
10 Nahley?

11 THE COURT: Do you have any questions for  
12 Miss Nahley, Dr. Jackson?

13 DR. JACKSON: No, that's okay. Thank you.

14 THE COURT: Okay. Are you going to be  
15 submitting those --

16 MR. GATZEMEIER: Yes. Well, that is part of  
17 the denial letter --

18 THE COURT: Oh, that's part of the -- okay,  
19 that will be Respondent's --

20 MR. GATZEMEIER: -- that you already have.

21 THE COURT: Oh, it's part of the record  
22 already?

23 MR. GATZEMEIER: Yes.

24 THE COURT: Okay.

25 MR. GATZEMEIER: Okay. Then we'd like to

1 call Dr. Hylen.

2 THE COURT: Okay. Dr. Hylen, want to be  
3 sworn?

4 MR. GATZEMEIER: Well, we'd like to call  
5 Duane Park. Duane, you've been sworn in. You might  
6 want to get up close to a microphone.

7 DUANE PARK,  
8 appearing as a witness for Health Care  
9 Financing, having been first duly sworn,  
10 testified as follows:

11 EXAMINATION

12 BY MR. GATZEMEIER:

13 Q Can you tell us what your credentials are?

14 A I'm a registered pharmacist and have a  
15 master's in health administration. My job is to  
16 coordinate and develop the drug utilization review  
17 process for the state of Utah, which is mandated by the  
18 over laws of 1990, '93, and more recently in the  
19 Reconciliation Act of 1997.

20 MR. GATZEMEIER: Can you hear him okay,  
21 doctor?

22 DR. JACKSON: Yes, thank you.

23 MR. GATZEMEIER: Okay.

24 Q (By Mr. Gatzemeier) Mr. Park, in your  
25 capacity with the state are you familiar with the Drug

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1 Utilization Review Board?

2 A Very familiar with it.

3 Q Can you tell us what that board is and who  
4 constitutes it?

5 A This is a review board composed of  
6 physicians, pharmacists, one advocate for clients or  
7 patients, and one advocate for the drug manufacturers'  
8 organization called Pharma, and also one dentist. It's  
9 a 12-member board as defined by law what the membership  
10 will be derived from. So the numbers are set for the  
11 number of physicians, pharmacists, one dentist, one  
12 advocate, and one manufacturer representative.

13 Q Okay. What is the purpose of that board?

14 A This board is to do drug review and  
15 utilization. Their job is to see that the drugs used  
16 by Medicaid are in fact used according to the law and  
17 in a cost effective and patient effective manner.

18 Q Okay. Has that board at all looked at the  
19 possibility of -- you've heard testimony by Dr. Jackson  
20 that this particular drug that we're looking at is  
21 basically an off-label use. It's a new use of the drug  
22 other than what the drug was originally identified for.  
23 Has the drug utilization review board ever looked at  
24 the possibility of utilizing drugs for off-label use?

25 A They have. Growth hormone was placed on

1 prior approval through the action of the DUR board.  
2 They have recently passed a policy on off-label use.  
3 That was independent of the recent Reconciliation Act.  
4 That use recognized label use, listed unlabel use, and  
5 unlisted uses that would fall into the experimental  
6 area.

7 MR. GATZEMEIER: Okay. We do have a copy of  
8 the notes and the action of that board which we would  
9 like to submit --

10 THE COURT: Do you have any objection to  
11 that, Dr. Jackson?

12 DR. JACKSON: Oh, no.

13 THE COURT: Okay. What number? Is that  
14 Respondent's Exhibit 1?

15 MR. GATZEMEIER: Are we at 1 now?  
16 Respondent's Exhibit 1.

17 THE COURT: Okay, it was part of the record  
18 already.

19 MR. GATZEMEIER: This was not, Respondent's  
20 Exhibit 1 just came in. The other was part of the  
21 record.

22 THE COURT: Okay, it's admitted.

23 (Whereupon, Respondent's Exhibit 1 was  
24 received into evidence.)

25 Q (By Mr. Gatzemeier) All right. Mr. Park,

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1 based on the actions of that board and as I understand  
2 it you are the Department of Health staff to that  
3 board; is that correct?

4 A That is correct.

5 Q Okay. Based on the actions of that board and  
6 the drug that we've been talking about this morning how  
7 would use of that drug fall within the adopted policy  
8 of that board?

9 A This policy was developed to address a  
10 mechanism for dealing with drugs just such as growth  
11 hormone that have enormously broad application. It  
12 recognizes that the current technology and information  
13 that's coming out so rapidly has yet to be codified and  
14 put into approved or FDA reviewed status. So it's  
15 merely a policy that gives physicians like you, Dr.  
16 Jackson, a mechanism to go to the board and request  
17 that this particular drug be considered for -- by the  
18 board for coverage for a select one-on-one patient.

19 Q Okay. Based on that action of the board is  
20 the current requested use of the recombinant human  
21 growth hormone that we're talking about in this hearing  
22 covered -- would it be covered under Medicaid  
23 currently?

24 A No, it would have to be -- the determination  
25 would have to come from the DUR board, your peers, for

1 this specific client.

2 MR. GATZEMEIER: And I do think that that is  
3 an important note, Dr. Jackson. That board does meet  
4 monthly. What our position would be currently, and  
5 this is kind of -- I guess it's kind of testimony.  
6 Currently is that the drug is not covered but that  
7 board does have the ability to say a drug will be  
8 covered for a specific purpose, which in this case it  
9 would seem that that might be something that you would  
10 want to take to that board and say, "Can this drug be  
11 approved for this purpose?"

12 Recognizing we also have the capability  
13 through this hearing process to review that, but, you  
14 know, to preclude situations like this from happening  
15 in the future if the board says that is a covered  
16 Medicaid process we would not have to be in the hearing  
17 process to review it.

18 THE COURT: Would the board be reviewing the  
19 use in that way for just this particular patient or for  
20 all similar --

21 THE WITNESS: So far they have only used this  
22 policy one time. It was for a particular patient.

23 THE COURT: For a particular patient.

24 THE WITNESS: For a singular use of a drug.

25 THE COURT: So that is a possibility should --

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1 THE WITNESS: Uninvestigated possibility at  
2 this point, yes.

3 THE COURT: Okay. Should the --

4 DR. HYLEN: I think they also could take a  
5 class of patients for unlabeled. So I think it's  
6 either way.

7 THE COURT: Okay. Thank you for that  
8 clarification.

9 DR. JACKSON: Could I ask a question?

10 THE COURT: Yes.

11 DR. JACKSON: What is DUR? Utilization  
12 Review?

13 THE WITNESS: Drug Utilization Review Board.

14 DR. JACKSON: Thank you.

15 MR. GATZEMEIER: You do have a representative  
16 from the University of Utah -- actually I think it's  
17 the School of Pharmacy -- that is on that board.

18 THE WITNESS: That's correct. Dr. Lynda  
19 Oderda from the College of Pharmacy serves on the  
20 board. We also have Dr. Hare from the College of  
21 Medicine who serves on the board.

22 THE COURT: Okay. Should he not prevail at  
23 this hearing can you give him any more information on  
24 how to approach that?

25 THE WITNESS: If the policy was sent to him

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1 he could see that there is an avenue that he can  
2 explore which would be very similar to this one. He  
3 would provide all the current articles he has to the  
4 board for their review and then they would determine  
5 whether it's covered or not.

6 MR. GATZEMEIER: Could you see that a copy of  
7 that is sent to him so that he will have that avenue  
8 available to him?

9 THE WITNESS: May I have your fax number,  
10 doctor?

11 MR. GATZEMEIER: We have the information. We  
12 can give it to you afterward.

13 THE COURT: Okay. Do you have any other  
14 questions for Mr. Park, Dr. Jackson?

15 DR. JACKSON: No, thank you.

16 MR. GATZEMEIER: I was mistaken. We  
17 apparently don't. So if we have that information we  
18 can send it to him.

19 THE COURT: Okay. Apparently they do need  
20 your fax number.

21 DR. JACKSON: It's 588-2375.

22 THE COURT: Okay. Was there anything else  
23 that...

24 MR. GATZEMEIER: Yes we'd like to call Dr.  
25 Hylen.

1 THE COURT: Dr. Hylen is going to testify  
2 now. Thank you, Mr. Park.

3 THE COURT: You've already been sworn,  
4 doctor.

5 DR. HYLEN: Yes, I have.

6 JOHN HYLEN, M.D.,  
7 appearing as a witness on behalf of Health  
8 Care Financing, having been first duly sworn,  
9 testified as follows:

10 EXAMINATION

11 BY MR. GATZEMEIER:

12 Q Okay, Dr. Hylen, you've reviewed the  
13 situation related to this case?

14 A Yes, I have.

15 Q Okay. Can you tell us what your findings  
16 are?

17 A Maybe we should start with my credentials.

18 Q Okay. Can you tell us what your credentials  
19 are?

20 A Yes, I have a doctorate in medicine, and a  
21 master's of public health, and I'm board certified in  
22 internal medicine, cardiovascular medicine, and  
23 geriatric medicine.

24 Q Okay. Can you tell us what your finding and  
25 conclusions were related to this case?

1           A       Well, I think one of the things that concerns  
2 me is that this is an area where the Drug Utilization  
3 Review Committee by federal law has been set up to have  
4 controls over off-label use. And so I think that it's  
5 important that they be involved in any decision that  
6 would open this up. I think I have concern that  
7 they're going to approve the use of this drug in this  
8 case since their judgment has to be not only based on  
9 the findings of this case but also a review of the  
10 literature. And I think Dr. Jackson has testified that  
11 growth hormone for this use could be disapproved, which  
12 to me sounds like that it hasn't been proven yet that  
13 it's effective in preventing liver disease and  
14 preventing the need for liver transplants.

15                   And the other thing I think we have to be  
16 concerned about, what are the toxicities. You know, if  
17 you're going to use this for more than a year what are  
18 the toxicities for children.

19                   So I think there's several things that are of  
20 concern in this case. One certainly is expenses. It's  
21 an expensive medication. I have concerns about whether  
22 the side effects and also if it is not documented to  
23 prevent liver disease, progression of liver disease and  
24 liver transplantation, if this is only a medication  
25 that promotes feeding then are there other more

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1 cost-effective ways to get the child or infant to eat.  
2 So I think there are a lot of unanswered questions.

3 THE COURT: The biggest one I have is is it  
4 Health Care Financing's contention that I don't have  
5 the jurisdiction to -- if I were to pay -- to say this  
6 should be paid for in this case because of the DUR?  
7 I'm --

8 MR. GATZEMEIER: No, no, no. It's Health  
9 Care Financing's --

10 THE COURT: Otherwise it shouldn't have come  
11 this far to me.

12 MR. GATZEMEIER: No, it's Health Care  
13 Financing's contention that there is a -- there is an  
14 administrative process set up to establish these. The  
15 hearing process is also an administrative process which  
16 has been set up. I don't know that they have to work  
17 against each other. I think that the mechanism is such  
18 that one could utilize the other.

19 THE COURT: I'm just concerned about judicial  
20 efficiency and wasting everybody's, potentially wasting  
21 everyone's time.

22 DR. HYLEN: I don't have the answer to that.  
23 Certainly administrative hearings have been around a  
24 lot longer than the DUR Committee. But the federal  
25 government did set up and mandate, I mean, who's there,

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1 and you will function, and you will control the  
2 utilization of what medications are used and how  
3 they're used amongst Medicaid clients. And so...

4 And the other thing is that I think is very  
5 pertinent to the court is that the DUR has addressed  
6 unlabeled uses and has set up mechanisms for approval  
7 both of for individual patients and for classes of  
8 patients that they can set up guidelines so that -- so  
9 that it's not an impossibility to receive medications  
10 on it for unlabeled uses.

11 THE COURT: Uh-huh. Okay, thank you. Do you  
12 have questions for Dr. Hylen, Dr. Jackson?

13 DR. JACKSON: No. I just reiterate that it's  
14 not -- the growth hormone's indication for this  
15 petition is not to try to make Markelle eat simply as  
16 an appetite stimulant or anything like that. It's  
17 really specifically to get her to reduce her dependence  
18 or eliminate her dependence on parenteral nutrition.  
19 And that's the principal reason and...

20 DR. HYLEN: And I would agree with that.

21 MR. GATZEMEIER: And we would all agree with  
22 that. And that's basically the reason I think the  
23 state has taken for saying this is not covered. Growth  
24 hormone according to the state provider manual, the  
25 drug criteria manual, is utilized -- there's two



1 groups. Both of them are growth failure. We all  
2 recognize that is what the primary or the initial  
3 rationale for utilizing this drug was. This is a  
4 different approach to utilizing the drug. It's not  
5 covered in policy as far as this is one of the things  
6 we can approve. So until we get some change of policy,  
7 which is what the DUR would address --

8 DR. JACKSON: I understand that was the  
9 motivation for the hearing, otherwise it would have  
10 been pretty simple.

11 THE COURT: That's exactly what I was talking  
12 about a couple of minutes ago. You know, if I don't  
13 have the jurisdiction to do this it should have just  
14 gone to the DUR Board. But apparently I believe I do  
15 have jurisdiction to make the ruling independent of the  
16 DUR Board. I think they're two separate administrative  
17 processes.

18 UNIDENTIFIED FEMALE SPEAKER: Were we  
19 notified about the DUR before we came this far?

20 THE COURT: No.

21 MR. GATZEMEIER: No.

22 THE COURT: And I wasn't aware how that  
23 process worked either.

24 MR. GATZEMEIER: And that's one of the things  
25 we wanted to flush out in here is what processes there

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1 were, what other mechanisms and options there were.

2 UNIDENTIFIED FEMALE SPEAKER: And this is an  
3 avenue we could have taken months ago?

4 MR. GATZEMEIER: Yeah. Now, they just  
5 addressed the issue of off-label drug use policy  
6 November 13th. So they have been --

7 DR. HYLEN: Well, they've been addressing it  
8 over a long period of time, but this particular policy  
9 came out. But they've been looking at that issues for  
10 a long --

11 UNIDENTIFIED FEMALE SPEAKER: So our first  
12 denial we could have started this avenue? If we would  
13 have been notified about this process we could have  
14 started?

15 MR. GATZEMEIER: Right.

16 UNIDENTIFIED FEMALE SPEAKER: Okay.

17 THE COURT: I'd just like to encourage you,  
18 Dr. Jackson, to get any other information you can in to  
19 us and would five business days --

20 DR. JACKSON: Sure. I'll just have them just  
21 fax it to you and Dr. Hylen.

22 THE COURT: And, Dr. Hylen, how long would it  
23 take you to review that?

24 DR. HYLEN: Well, since they're going to have  
25 more current data I think we probably should do the

1 same. But that shouldn't take long.

2 THE COURT: What I'd like then is both sides  
3 to exchange --

4 DR. JACKSON: I'll send the search that I  
5 have and I have copies of those articles.

6 THE COURT: Then I'd like to ask Dr. Hylen to  
7 send his -- the results of his research to you.  
8 Hopefully we don't have to have --

9 DR. JACKSON: Sure. We may have the same --

10 THE COURT: -- another hearing. If you'd  
11 like to, you know, comment in writing -- you know, I  
12 don't know if it's going to do any good to have another  
13 continuation of the hearing where we discuss the  
14 literature. I think, you know, if Dr. Hylen decides  
15 that -- based on this literature that it should be  
16 approved then that's fine. We know we wouldn't have to  
17 go further in the hearing. Otherwise I think I will  
18 just make a decision on all the documents that are  
19 submitted, and the evidence in the record, and the  
20 testimony.

21 DR. JACKSON: I think that's fine. We have a  
22 point of closure.

23 THE COURT: Yes.

24 UNIDENTIFIED FEMALE SPEAKER: I have a  
25 question.

1 THE COURT: Yes.

2 UNIDENTIFIED FEMALE SPEAKER: In this  
3 information can it be provided from pharmacy and also  
4 from Dr. Jackson or my insurance how much Markelle,  
5 where we're talking about cost efficiency, how much it  
6 would cost today for the growth hormone, how much she  
7 costs to live for her TPN, her nutrition, my nursing,  
8 and all of that so that the cost efficiency can be  
9 determined in that way also?

10 THE COURT: Yes.

11 UNIDENTIFIED FEMALE SPEAKER: Because in the  
12 long run if this does help her that would eliminate a  
13 big cost every month.

14 THE COURT: Okay.

15 UNIDENTIFIED FEMALE SPEAKER: So could that  
16 be included someplace?

17 THE COURT: Uh-huh. Do you know how long  
18 that would take --

19 UNIDENTIFIED FEMALE SPEAKER: We have figures  
20 and I know myself I called pharmacies to self pay for  
21 the growth hormone.

22 THE COURT: Would five business days be  
23 sufficient? If you have any trouble with that time  
24 period let me know. If you'll submit a copy of that to  
25 the court --

1 UNIDENTIFIED FEMALE SPEAKER: Okay.

2 THE COURT: And also to Health Care Financing  
3 so Dr. --

4 UNIDENTIFIED SPEAKER: Yes.

5 MR. GATZEMEIER: One question. We need to  
6 clarify that it's our position that one does not  
7 preclude the other. This growth hormone is an  
8 experimental process. Theoretically it could lead to  
9 elimination of the other costs but there is no cause  
10 and effect proved right now. We're saying we will try  
11 this and see if it can reduce these costs. But trying  
12 this does not necessarily -- it's not given that we  
13 would reduce the other costs by doing the growth  
14 hormone.

15 THE COURT: Understood. But I -- yeah, I can  
16 give the evidence the weight that I determine that it  
17 should have based on what it is.

18 MR. GATZEMEIER: We would also -- it would  
19 probably be advantageous if when we're giving this  
20 information to Dr. Jackson if we send him a copy of  
21 this Respondent's Exhibit 1.

22 THE COURT: Respondent's Exhibit 1, okay.  
23 You can fax that right after the hearing. Is there  
24 anything else?

25 DR. JACKSON: Not from my side.

1 THE COURT: Is there anything else from  
2 Health Care Financing?

3 MR. GATZEMEIER: No, I think that's --

4 THE COURT: Okay, thank you very much for  
5 your time, Dr. Jackson.

6 DR. JACKSON: Thank you.

7 THE COURT: Thank you all.

8 DR. JACKSON: Goodbye.

9 THE COURT: Goodbye.

10 (Whereupon, the proceedings were  
11 concluded for the day.)

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1 STATE OF UTAH )  
2 : ss.  
3 COUNTY OF SALT LAKE )

4 I, Jane G. Saville, Certified Shorthand  
5 Reporter and Notary Public for the State of Utah,  
6 residing in Salt Lake County, certify:

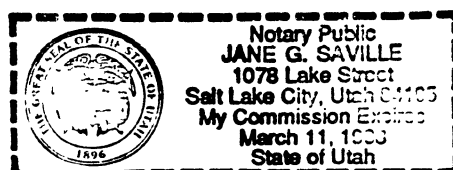
7 That the foregoing reporter's transcript of  
8 audiotaped proceedings were stenographically prepared  
9 by me upon listening to audio tape labeled "Markelle  
10 Frei-Peterson" provided to me by the Utah Department of  
11 Health;

12 That the foregoing reporter's transcript of  
13 audio taped proceedings represents a complete  
14 transcription of my stenographic notes so taken;

15 I further certify that I am neither counsel  
16 for nor related to any party to said action, nor in  
17 anywise interested in the outcome thereof;

18 In witness whereof, I have subscribed my name  
19 and affixed my seal this 1<sup>st</sup> day of March  
20 1998.

21  
22   
23 JANE G. SAVILLE, CSR and NOTARY PUBLIC



## OFF-LABEL USES

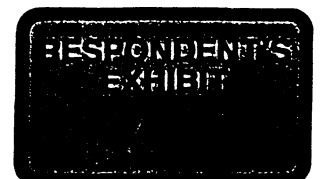
Utah restricts the covered drug products on the open formulary to uses approved and documented by the officially recognized compendia [OBRA 1993, section 1927 (d) (6)]. The designated compendia are:

1. package insert, FDA approved uses
2. American Hospital Formulary Service Drug Information (AHFS)
3. American Medical Association Drug Evaluation (AMADE)
4. United States Pharmacopeia Drug Information Drug Information (USP- DI)
5. DRUGDEX

The DUR Board may approve an unlisted off-labeled use for a given drug if the off labeled use meets the following criteria.

1. Use must be diagnosis specific as defined by an ICD9 code (s).
2. Off-labeled use must be supported by one major multi-site study or three smaller studies published in JAMA, NEJM, Lancet or specialty peer review medical journals such as Journal of Cardiology. Articles must be current - within five years.
3. Off-labeled use must have a defined dosage regimen.
4. Off-labeled use must have a defined duration of treatment.
5. The off-labeled use shows clear and significant clinical or economic advantage over existing approved drug regimens.

The UMA, Utah based Group Practices or Utah based prescribers may have the option of petitioning the DUR Board for coverage for an unlisted off-labeled use of a given drug. The petitioner(s) must schedule an appearance before the Board to present the case for the petitioned drug. Petitioners must provide documentation including one published major multi-cite study or a minimum of three recent (five years) articles from **JAMA, NEJM, Lancet or peer review specialty medical journals such as the Journal of Cardiology**, supporting the petition's position. The documentation must be submitted six weeks in advance of the scheduled DUR Meeting.





## Addendum D

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Short Bowel Rehabilitation Program: A Unique Approach  
Including Glutamine, Growth Hormone and Special Diet

*D. Wilmore, Boston*

The short bowel syndrome is a lethal disease which lacks an effective low-cost method of treatment. Because the bowel can hypertrophy following resection, we have evaluated therapy which will enhance future compensation of the residual bowel following enterectomy. A variety of animal studies have demonstrated the trophic effects of growth hormone (GH), glutamine (GLN) and dietary fiber in enhancing intestinal growth and absorption of nutrients from the gastrointestinal tract. To evaluate this effect in humans, we initially studied 15 TPN-dependent short-bowel patients over 3-4 weeks in the Clinical Research Center; the first week served as a control period and during the next 1-3 weeks the specific treatment was administered and evaluated. Throughout the study, food of known composition was provided and all stool was collected and analyzed to determine absorption across the remaining bowel. The effect of a high-carbohydrate, low-fat diet (DIET), GLN and GH administered alone or in combination with the other therapies (GH+GLN+DIET) was evaluated. While both GH and GLN demonstrated some independent effects, these studies indicated improvement in absorption of protein by 39% accompanied by a 33% decrease in stool output with the combination therapy. Because of the clinical improvement which occurred with the GH+GLN+DIET, the study was expanded to 47 adults (25 men, 22 women) with the short bowel syndrome, dependent on TPN for  $6 \pm 1$  years. The average age was  $46 \pm 2$  years and the average jejunal-ileal length was  $50 \pm 7$  cm (median 35 cm) in those with all or a portion of colon and  $102 \pm 24$  cm (median 102 cm) in those with no colon. After 28 days of therapy, the patients were discharged on only GLN + DIET. Forty percent of the group remain off TPN and an additional 40% have reduced their TPN requirements, with the longest follow-up being over 5 years. In addition to the adults, 12 children have been treated to date and these patients have shown enhanced growth velocity and improved absorption.

This approach offers a potential method for providing cost effective rehabilitation of surgical patients who have the short bowel syndrome or other complex problems of the gastrointestinal tract. This therapeutic combination may also be useful to enhance bowel function in patients with other gastrointestinal diseases or to consider in those patients where gastrointestinal disease or its treatment prevents a full growth potential.



## A New Treatment Option for Patients with Short Bowel Syndrome: Bowel Rehabilitation with Growth Hormone, Glutamine, and a Modified Diet

Theresa A. Byrne, DSc, RD, CNSD; Barbara Browning, BSN, CRNI; Natalie Tu, RD, CNSD; Douglas W. Wilmore, MD

### Introduction

Short bowel syndrome (SBS) is a disorder characterized by the signs, symptoms, and metabolic alterations that occur due to the loss of functional absorptive surface area of the gastrointestinal tract. The patient presents with diarrhea, dehydration, electrolyte disturbances, malabsorption and progressive malnutrition. SBS is usually the result of extensive small-bowel resection following intestinal infarction due to mesenteric vascular disease, intestinal volvulus, trauma, malignancy, congenital abnormalities, or complications of Crohn's disease. Less often the defect is functional, rather than anatomical, as in patients with radiation enteritis or active Crohn's disease.

The severity of this disorder depends upon the length, location, and health of the remaining bowel and the degree to which the remnant bowel adapts following intestinal resection. The minimal length of small bowel required to maintain enteral autonomy is 50–70 cm of jejunum-ileum (if the colon is left intact) or 110–150 cm if the resec-

tion is associated with a colectomy. If less bowel remains or if the remnant bowel is severely diseased or damaged, dependence upon total parenteral nutrition (TPN) is usually permanent. In some individuals, bowel adaptation may occur with time, and TPN is needed for only 6–24 months. Maximal bowel adaptation is achieved within 1–2 years following resection. However, if the patient is still dependent on TPN at this time in spite of optimal medical and nutrition management, it is unlikely that the bowel will undergo sufficient adaptation to support the individual. In these cases, dependence on parenteral nutrition is usually permanent (1–3) (Table 1).

### Contributions and Limitations of Long-term TPN

The first comprehensive report of small-bowel resection in humans was published by Haymond in 1935 (4). From his analysis of 257 patients, he concluded that resections of greater than 50 percent of the small bowel were associated with metabolic complications and a poor outcome. The

overall operative mortality was 10 percent and only 20 percent of patients survived more than 1 year. With time, developments of new diagnostic techniques and advances in intraoperative management and for prompt surgical intervention improved operative survival. It was the demonstration in 1961 that weight gain, growth, and development could be achieved if all nutrients were administered by TPN that has had the most dramatic influence on the survival of patients undergoing massive intestinal resection. Shortly thereafter, the concept of home care evolved, and it became possible to provide TPN in the home. As a result of these developments, it has been estimated that approximately 70 percent of patients with SBS are discharged from the hospital and a similar number are alive one year later (6). By

(Continued on p. 2)

### PEARL

*"One of the greatest pains of human nature is the pain of a new idea."*

Walter Bagehot (1826–1897)  
English economist

**Table 1: Primary Factors Determining Long-term Dependence on TPN**

#### Inadequate bowel length

- ≤ 50–70 cm of jejunum-ileum with colon
- ≤ 110–150 cm of jejunum-ileum with no colon

#### Incomplete bowel adaptation

not maximized 1–2 years following resection

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TPN's dramatic impact on patient survival, this form of therapy quickly became the standard approach to the care and management of patients with severe SBS.

Although long-term parenteral nutrition is a life-sustaining therapy for these individuals, the complications and extraordinary costs are now recognized. The complications include hepatic dysfunction (7), progressive renal insufficiency (8), bone demineralization (9), numerous nutrient deficiencies (10, 11) and catheter sepsis (12). Patients receiving home TPN are hospitalized on average twice a year, usually for septicemia. In addition, the cost of home-administered TPN is now estimated to be approximately \$100,000 per patient year (12). Because of the expense, many patients remain on medical disability even though the majority want to return to daily activities, including work. Socialization and rehabilitation are often suboptimal. As the patient remains dependent upon TPN, the quality of life often deteriorates, and two-thirds of the population report problems such as the loss of friends, failure to find employment, and depression (13).

### Treatment Options

Because of the risk, complications, limitations, and costs associated with long-term TPN, researchers have explored alternative therapeutic options aimed at reducing or eliminating long-term parenteral nutrient requirements. Surgical procedures to lengthen short intestines and/or slow intestinal transit have resulted in relatively poor clinical outcomes (14). Successful cases of intestinal transplantation have been reported; however, this form of therapy remains experimental and is associated with significant morbidity and mortality and tremendous costs (\$500,000 per transplant and \$20,000 per patient year for medical follow-up and immunosuppressive medications) (15). There is also concern about the potential development of lymphoproliferative disease (eg, lymphomas) in transplanted bowel seg-

ments; this problem is only now addressed by a variety of researchers. Others have explored the use of bowel rehabilitation, which involves the administration of specific growth factors, nutrients, and/or enteral feedings to enhance the normal physiological adaptation/compensation of the bowel.

### BOWEL REHABILITATION

#### Intestinal Adaptation in Short Bowel Syndrome

One of the most intriguing aspects of SBS is the gradual improvement in symptoms following intestinal transplantation. Bowel adaptation, first described by Flint in 1912 (16), is associated with a decrease in diarrhea and malabsorption and an increase in tolerance of enteral feedings with time. The process is characterized by elongation and dilation of the remnant bowel, an increase in villus height, crypt depth, cell proliferation, and increased secretory activity. Although the precise mechanisms that account for these adaptations are not known, similar changes can be observed when one administers various enteral factors (eg, growth hormone, insulin-like growth factor-1 [IGF-1]), or exposure of the mucosa to specific nutrients (eg, glutamine, short-chain fatty acids) and from the various factors brought into play by the presence of enteral feedings (eg, enteric hormones, pancreatic-biliary secretions). Together these trophic stimuli stimulate the remnant bowel to adapt (hyperplasia) (17). In addition, the composition of the diet can greatly influence the ability of both the small and large bowel to compensate following extensive intestinal resection.

#### Growth Hormone and the Intestinal Tract

The exogenous administration of growth hormone (GH) or its analogs has been shown to influence bowel adaptation by enhancing mucosal growth and hyperplasia following extensive intestinal resection in animals (18, 19). Christensen and colleagues have

that GH administration increases colonic mass (20); an effect that may enhance the reservoir function of the colon. The exogenous administration of IGF-1, which is regulated by GH, has been shown to enhance bowel hyperplasia and hypertrophy in rats following extensive jejuno-ileal resection (21). Others have demonstrated that IGF-1 induces ornithine decarboxylase (22, 23), the rate-limiting enzyme in the synthesis of polyamines (substances that are necessary for normal cellular growth and differentiation). While the inhibition of ornithine decarboxylase activity suppresses DNA synthesis and results in the complete absence of intestinal adaptation following resection (24), the intraileal infusion of IGF-1 has been shown to increase polyamine synthesis and produce a significant trophic effect on the gastrointestinal mucosa (25).

In addition to the morphologic effects of GH and IGF-1 on the bowel, exogenous GH exerts specific functional effects. Growth hormone increases water and sodium transport in the small intestine and in the colon (26, 27) and appears to regulate intestinal amino acid absorption in several animal models (28). More recently, others (29) have demonstrated that the exogenous administration of GH increases amino acid transport in the human jejunum and ileum.

### Glutamine and the Intestinal Tract

Like GH, glutamine (GLN) exerts important morphologic and functional effects on bowel. Glutamine is a major fuel source for both the enterocytes and the colonocytes (30) and is necessary for the maintenance of intestinal structure, in both normal and stress states. In animals, infusion of glutamine markedly reduces the concentration of blood GLN; simultaneously diarrhea, villous atrophy, mucosal ulcerations, and intestinal necrosis results (31). In vitro studies demonstrate that the addition of GLN to an incubation medium stimulates crypt-cell proliferation in healthy human

ileum, proximal, colon, and rectosigmoid colon (32). Animal studies have documented that the addition of GLN to standard amino acid solutions prevents the villous atrophy associated with the provision of TPN in the absence of enteral feedings (33–36). In hospitalized patients unable to take adequate enteral nutrition, the addition of GLN to standard TPN solutions has been shown to prevent TPN-induced gut permeability (37). Enteral (rather than parenteral) GLN has also been shown to induce trophic or regenerative effects on the bowel (38,39).

Glutamine is also now recognized as a required substrate following extensive small-bowel resection in both animals (40) and humans (41). Intravenous GLN supplementation has been shown to accelerate post-resection hyperplasia following massive intestinal resection in several animal models (42,43).

Enteral GLN also appears to play an important role in maximizing bowel function by influencing nutrient absorption. The luminal (or enteral) administration of GLN enhances glucose absorption (44), an effect that was not observed when GLN was administered intravenously. Others have described the ability of enteral GLN to enhance sodium absorption in various models of experimentally induced diarrhea (45–48). The administration of oral GLN has also recently been shown to increase circulating levels of GH in humans (49), an effect that could indirectly contribute to important trophic and functional effects within the resected bowel.

### The Role of Diet

Enteral nutrition is essential to the process of bowel adaptation. Intestinal adaptive hyperplasia does not occur in the absence of enteral feeding — even when the necessary calories are given via the intravenous route (50). The intestinal mucosa of parenterally fed animals becomes hypoplastic and hypofunctional (51). Levy et al (52) provide evidence that the provision of

luminal nutrients during the adaptive phase of SBS increases the likelihood of enteral autonomy in patients who would otherwise be dependent. Although some advocate elemental or peptide-based formulas to facilitate absorption, Levy et al suggest that polymeric diets are equally or more effective in SBS patients during the early rehabilitative period. The hyperosmolality of some of these solutions is thought to contribute to diarrhea and limit delivery of adequate calories. However, these concerns may be unfounded, for there are no prospective, randomized studies which prospectively, randomly assign patients with very short segment small bowel to the various (elemental, elemental, polymeric, etc.) formulas and systematically evaluate the effect on nutrient absorption and long-term TPN dependence.

In addition to the role of enteral nutrition in stimulating the process of intestinal adaptation during the postoperative period, specific dietary recommendations are often instituted to further assist the bowel in coping with the limited surface area by minimizing nutrient malabsorption. Although some clinicians favor the continued use of liquid formulas during the long-term nutrition management, most patients are successfully transitioned to solid foods. The optimal composition of these diets depends on the length and location of the resected functional small bowel and the extent of colon.

Although estimates of adult small intestinal length vary from 300 to 600 cm (or about 365–600 cm) (53), animal intubation studies have shown that absorption of carbohydrate, amino acids, and simple fatty acids begins in the duodenum and is complete by 100 cm of jejunum (55). The major inefficiency in absorption is in the uptake of triglyceride in the proximal intestine is also the major area for the absorption of ir

(Continued on

cium, and water-soluble vitamins. If the jejunum is removed, the ileum adapts and assumes its absorptive function. However, there are functions that are unique to the ileum; they include the absorption of vitamin B12 and bile salts. In addition, the ileum has a marked effect on slowing transit. When less than 100 cm of ileum is resected, watery choleraic diarrhea with little or no steatorrhea often results. When more than 100 cm of ileum is resected, bile salt loss in the stool can be considerable (56).

The presence of unabsorbed bile salts can alter the tonicity of the luminal contents and produce a secretory state within the colon. Consequently, there are fewer bile salts available in the jejunum, which limits the absorption of fats and fat-soluble vitamins, resulting in steatorrhea. The unabsorbed free fatty acids bind with calcium, magnesium, and zinc to form insoluble intraluminal soaps. The formation of unabsorbable calcium soaps prevents intraluminal calcium from binding to dietary oxalates. The unbound oxalates pass to the colon, where they are reabsorbed and subsequently excreted in the urine. This state of hyperoxaluria, particularly when associated with a state of marginal hydration and decreased renal perfusion, renders the patient more prone to the development of calcium-oxalate nephrolithiasis. An additional factor influencing calcium absorption is the reduction in serum 25-hydroxy vitamin D levels, which is related in part to the loss of ileal surface area and the associated malabsorption of fat-soluble vitamins. The suboptimal levels of calcium and vitamin D are thought to contribute to the osteopenia and osteomalacia of the SBS (9,57).

Thus, for patients who have undergone extensive ileal resections (with or without jejunal resection), the restriction of fat is thought to minimize steatorrhea, reduce the excessive loss of divalent cations and associated complications, and if the colon is present,

diminish the bile salts that can induce secretory diarrhea. Others have suggested that the absorptive capabilities for high-fat and high-carbohydrate diets (58) are similar in patients with SBS, and argue that restriction of dietary fat deprives these patients of important calories (58,59). However, because the majority of patients in these studies did not have colons, such recommendations cannot be applied when the colon remains in continuity with the remnant small bowel.

For patients with colons, low-fat, high-carbohydrate diets aid in the compensatory response following resection. The anaerobic bacterial metabolism of carbohydrates (fibers and proteins) that either resist digestion or escape absorption in the upper intestinal tract result in the production of short-chain fatty acids (acetate, propionate, and butyrate), hydrogen gas, carbon dioxide, methane, and water. The short-chain fatty acids (SCFA), the major byproducts of bacterial fermentation, are readily absorbed by the colonic mucosa and utilized for energy (60). Thus, some of the carbohydrate calories that would have otherwise been lost because of upper-intestinal tract malabsorption can be salvaged by this process (61). Under normal circumstances, it has been estimated that the absorption of short-chain fatty acids from the colon provides 5 to 10 percent of daily energy requirements (62). For patients with short bowel syndrome, Nordgaard et al demonstrated that a change to a 60 percent high-carbohydrate, 20 percent low-fat diet diminished the fecal loss of calories, compared with a diet with the reversed ratios (63). The percentages of calories absorbed were significantly increased on the high-carbohydrate diet (69%) compared to the high-fat diet (49%). For patients without colons, the percentage of absorbed energy was similar with both the high-carbohydrate and a high-fat diet. In addition, the authors noted that intake of either diet (high-fat or high-carbohydrate) did not sig-

nificantly affect the daily total of stool or jejunostomy output or total fecal nitrogen content. They suggest that dietary manipulation alone could not adequately provide independence from parenteral infusions that provide not only adequate calories but other important nutrients and necessary fluid.

## CLINICAL TRIALS

Because of the stimulatory effect of GH and GLN on bowel structure and function, it was hypothesized that these substances could enhance nutrient absorption and thereby eliminate or reduce TPN requirements when alone or in combination with a diet designed to enhance bowel compensation in patients with severe SBS.

Preliminary human studies evaluating the effect on nutrient absorption of GH, GLN, or a high-carbohydrate modified oral diet alone produced only minor biochemical changes (65). Subsequently, their combined administration (GH + GLN + Diet) was evaluated in a small group of SBS patients ( $n = 8$ ) that were far beyond the limits of maximal adaptation ( $6 \pm 1$  years from the time of resection) and with jejunal-ileal lengths (mean = 37 cm with colonic remnant) that classed them as individuals who would be dependent on TPN for life. All patients were admitted to a metabolic ward for 28 days; the first week served as a control period when nutrition (enteral, parenteral) and medical management simulated their usual home therapy. Thereafter, exogenous GH, supplemental IV, oral GLN, and a modified high-carbohydrate, fiber-containing diet were administered. The efficiency of net nutrient absorption (percent absorbed) for total calories, protein, fat, carbohydrate, water, and sodium was calculated from the measured nutrient intake and stool losses.

Following three weeks of treatment with GH, GLN, and the modified diet, total caloric absorption increased from  $60.1 \pm 6.0$  to  $74.3 \pm 5.0$  percent ( $P < 0.003$ ), protein absorption from

**Table 2. Effects of GH+GLN+Diet on TPN requirements.**

<b>Patient characteristics</b>	
Sex	25 men, 22 women
Age	46 ± 2 years
Years on TPN	6 ± 1
Jejunum-ileal length	50 ± 7 cm (median = 35 cm) with colon, n=43 102 ± 24 cm (median = 102 cm) with no colon, n =4
<b>Results</b>	
Off TPN	n = 19 (40%)
Reduced TPN	n = 19 (40%)
No Change in TPN Requirements	n = 9 (20%)

**Table 3. TPN requirements and selected indices of nutritional status before and after treatment with GH+GLN+Diet.**

	Before GH+GLN+Diet	After* GH+GLN+Diet
TPN volume (L/week)	11 ± 1	7 ± 1 +
TPN calories (kcal/week)	8,816 ± 941	5,201 ± 880 #
TPN protein (gms/week)	434 ± 27	230 ± 33 +
Body weight (pounds)	132 ± 4	130 ± 4
Serum albumin (gm/dL)	3.7 ± 0.1	3.8 ± 0.1

Values represent the Mean ± SEM.

\* After = 10 ± 1 months following treatment.

+ =  $p \leq 0.0001$ , # =  $p \leq 0.001$  vs before treatment.

4.8 to 63.0 ± 5.4 percent ( $p \leq 0.006$ ), and carbohydrate absorption from 60.0 ± 9.8 to 81.5 ± 5.3 percent ( $p \leq 0.02$ ). Fat absorption did not change (61.0 ± 5.3 to 60.3 ± 7.9 percent,  $p = \text{NS}$ ), and appeared to be adversely affected by the intake of soluble fiber. Water and sodium absorption increased from 45.7 ± 6.7 to 65.0 ± 7.3 percent ( $p \leq 0.002$ ) and from 49.0 ± 9.8 to 69.6 ± 6.5 percent ( $p \leq 0.04$ ), respectively. These absorptive changes resulted in a 33 percent decrease in stool output (1,783 ± 414 g/day control period vs 1,308 ± 404 g/day by the third week of treatment,  $p \leq 0.05$ ).

Thus, the combined administration of GH, GLN and a modified diet significantly enhanced the ability to absorb calories, protein, carbohydrates, water and sodium from the remnant bowel following massive intestinal resection. These changes occurred in a group of patients that had previously failed to adapt to the provision of

enteral nutrients.

Because of the positive effects of GH+GLN+Diet on nutrient absorption, a subsequent study was conducted to determine whether GH+GLN+Diet could eliminate or reduce TPN requirements in patients with severe SBS (65). Forty-seven adult patients who were also far beyond the period of maximal adaptation and had jejunum-ileal lengths that would classify them as individuals who would be dependent upon TPN for life were studied (Table 2). All patients received exogenous GH, supplemental IV and/or oral GLN and a high-carbohydrate, modified oral diet for a minimum of 26 days. Thereafter, GH was discontinued and patients were discharged home on supplemental oral GLN and the modified diet.

The administration of GH+GLN+Diet markedly altered TPN requirements. With an average follow-up of 1 year (range 5 months to 5 years), 40 percent

of the group remain off TPN and another 40 percent have reduced TPN requirement (Table 2). 20 percent of the patients experienced no significant change in TPN requirements (65).

Thirty-one of the patients participated in a prospective study to evaluate the effects of this treatment on specific TPN requirement selected indices of nutritional status ± 1 months following discharge (3). The significant decrease in calories, protein and fluid requirements allowed patients to eliminate TPN days per week (in turn decreased TPN-related costs). Despite these significant reductions in TPN requirements, body weight, serum albumin concentration and electrolytes were adequately maintained. Additional long-term studies have also indicated that serum electrolytes and renal and liver function have remained stable following treatment.

### Summary

These data suggest that treatment with GH+GLN+Diet offers an alternative to long-term TPN for some patients with severe SBS. Prospective, randomized trials are underway to determine whether use of only one of the treatment modalities (GH, GLN or the high-carbohydrate diet) will produce equivalent results to the combined treatment.

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(Continued on next page)

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# A New Treatment for Patients with Short-Bowel Syndrome

## Growth Hormone, Glutamine, and a Modified Diet

Theresa A. Byrne, M.S., R.D., Rebecca L. Persinger, M.S., R.D., Lorrie S. Young, M.S., R.D., Thomas R. Ziegler, M.D., and Douglas W. Wilmore, M.D.

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### Objective

The purpose of this study was to initially determine if growth hormone or nutrients, given alone or together, could enhance absorption from the remnant small bowel after massive intestinal resection. If clinical improvement were observed, this therapy would then be used to treat patients with the short-bowel syndrome over the long term.

### Summary Background Data

Patients who undergo extensive resection of the gastrointestinal tract frequently develop malabsorption and require long-term parenteral nutrition. The authors hypothesized that the administration of growth factors and/or nutrients could enhance further compensation of the remnant intestine and thereby improve absorption. Specifically, animal studies have shown that there is enhanced cellularity with the administration of growth hormone (GH) or glutamine (GLN), or a fiber-containing diet.

### Methods

Initially, 17 studies were performed in 15 total parenteral nutrition (TPN)-dependent short-bowel patients over 3 to 4 weeks in the clinical research center; the first week served as a control period, and during the next 1 to 3 weeks, the specific treatment was administered and evaluated. Throughout the study, food of known composition was provided and all stool was collected and analyzed to determine absorption across the remaining bowel. The effect of a high-carbohydrate, low-fat diet (DIET), the amino acid glutamine (GLN) and growth hormone (GH) administered alone or in combination with the other therapies (GH + GLN + DIET) was evaluated. The treatment was expanded to 47 adults (25 men, 22 women) with the short-bowel syndrome, dependent on TPN for  $6 \pm 1$  years. The average age was  $46 \pm 2$  years, and the average jejunal-ileal length was  $50 \pm 7$  cm (median 35 cm) in those with all or a portion of colon and  $102 \pm 24$  cm (median 102 cm) in those with no colon. After 28 days of therapy, the patients were discharged on only GLN + DIET.

### Results

The initial balance studies indicated improvement in absorption of protein by 39% accompanied by a 33% decrease in stool output with the GH + GLN + DIET. In the long-term study, 40% of the group remain off TPN and an additional 40% have reduced their TPN requirements, with follow-up averaging a year and the longest being over 5 years.

## Conclusion

GH + GLN + DIET offers a potential method for providing cost-effective rehabilitation of surgical patients who have the short-bowel syndrome or other complex problems of the gastrointestinal tract. This therapeutic combination also may be useful to enhance bowel function in patients with other gastrointestinal diseases and those requiring extensive intestinal operations, including transplantation.

Intestinal resection is a commonly performed operation that is usually without complications. Occasionally, however, removal of large segments of the small bowel with or without a portion of the colon is necessary because of thrombosis of a mesenteric vessel, progressive inflammatory disease, major abdominal injury, or the presence of congenital abnormalities. These operative procedures result in short-bowel syndrome, a disorder characterized by an intestinal absorptive surface area that is insufficient to support the host. This intestinal loss results in malabsorption of fluid, electrolytes, and other essential nutrients; severe diarrhea; dehydration; and progressive malnutrition.<sup>1</sup>

Surgeons have long been aware of the ability of the small bowel to compensate after massive intestinal resection. This response, first described by Flint<sup>2</sup> in 1912 and later characterized in greater detail by many others,<sup>3-5</sup> is accompanied by elongation and dilation of the remnant bowel and hypertrophy of the intestinal villi, resulting in a greater absorptive surface area and prolonged transit time. With bowel compensation, absorption of enteral nutrients is gradually enhanced and diarrhea and malabsorption are reduced<sup>6</sup>; occasionally the clinical problems resolve. Although this adaptive response may support normal hydration and nutrition in individuals with resection of up to 80% of the small bowel, patients with less than 50 to 70 cm of jejunum-ileum (approximately 1½–2½ ft) with an intact duodenum and a portion of colon in continuity usually require total parenteral nutrition (TPN) for life.<sup>1,7</sup> Other factors, such as normal structure and function of other gastrointestinal organs, health of the intestinal mucosa, the presence and length of the remaining colon, and the age of the individual, also determine the ability of a patient to adapt and become independent of parenteral support.

Although TPN is regarded as lifesaving to patients af-

ter massive bowel resection,<sup>8</sup> data emerging over the past 20 years have detailed both short- and long-term complication rates of this therapy,<sup>9-11</sup> described the effect of nightly infusions on the disruption of a normal lifestyle,<sup>12</sup> and quantitated the costs associated with the therapy.<sup>13</sup> All of these factors have limited more comprehensive rehabilitation and shortened longevity, and investigators are now seeking alternative methods of care for this group of patients. Reconstructive procedures on the remnant bowel and intestinal transplantation are areas of special interest to surgeons working in this field.

This report provides details of the evolution of a treatment program that enhances absorption of nutrients from the remnant bowel through the use of growth factors and specialized nutrients. Absorption has been enhanced by using a combination of therapeutic agents, and this approach has now been applied to a larger group of patients with short-bowel syndrome to reduce or eliminate the need for TPN for prolonged periods.

## MATERIALS AND METHODS

### Absorption Studies

#### Patients

Seventeen studies were performed in 15 patients (7 women, 8 men; mean age, 44 years; range, 24–68 years) with severe short-bowel syndrome. All patients had previously undergone extensive bowel resection for traumatic mesenteric infarction, or inflammatory bowel disease with or without colonic resection. The average length of jejunum-ileum in the group, as determined from operative reports and confirmed by perioperative radiographs, was 54 cm (range, 8–120 cm) in the 12 patients with a portion of colon in continuity and 60 cm (range, 40–100 cm) in those without a colon. All patients were chronically dependent on specialized nutritional support. The patients were ambulatory, clinically stable, and did not demonstrate evidence of infection or active inflammatory bowel disease. In addition, they had no extradiaphragmatic organ failure, were free of cancer and diabetes, and did not have a history of cancer for the past 5 years. All patients were able to tolerate an *ad libitum* oral diet; however, without parenteral support they were unable to adequately maintain hydration and/or nutritional status. The protocol was approved by the Brigham and

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Women's Hospital's Committee for the Protection of Human Subjects from Research Risks, and informed consent was obtained from all subjects.

### Study Design

The patients were admitted to the Clinical Research Center of the Brigham and Women's Hospital for a 21 to 35 day stay. For the patients receiving a high-carbohydrate low-fat (HCLF) diet alone or diet plus growth hormone plus glutamine, the first week served as a control period during which time the patients' nutritional (parenteral feedings, tube feedings, and *ad libitum* oral intake) and medical management (antidiarrheal agents, etc.) simulated their usual home therapy. The patients were instructed to consume the quantity and type of foods and beverages that best represented their usual eating habits and food preferences. Only foods and beverages of known nutrient composition were provided. Meals and snacks were made available six times per day and beverages were readily available on an *ad lib* basis. During the control period, the infusions of parenteral nutrients and fluid volumes were matched to those prescribed by the patient's physician.

During the remaining 3 weeks, these patients received a diet high in complex carbohydrates and low in fat but nearly isocaloric and isonitrogenous to that which the patient received during the control period. The diet was targeted to provide approximately 60% of total calories from carbohydrate, 20% from fat, and 20% from protein. Calories and protein were divided into six feedings and provided as meals or snacks throughout the day. Near-isotonic fluids containing glucose and sodium (Gatorade, The Gatorade Company, Chicago, IL, and Pedialyte, Ross Laboratories, Columbus, OH) replaced both hypo-osmolar and hyperosmolar fluids and served as the primary source of enteral hydration.

Two of these 10 patients received the modified diet (HCLF diet) only. The remaining eight patients received recombinant methionyl growth hormone (Protropin, Genentech, Inc., San Francisco, CA) at a dose of 0.14 mg/kg/day by parenteral administration. They also received supplemental parenteral and/or enteral L-glutamine (given as an average dose of 0.6 g/kg/day (Ajinomoto USA, Raleigh, NC).

The seven additional studies examined the effects of administering glutamine alone or growth hormone alone. The patients received a fixed diet throughout the entire 21 to 28 day period, which involved foods of their choice on a 2-day rotational schedule. After the first week, either glutamine or growth hormone was provided as described above and the diet continued. Intravenous feedings, fluid volume, calories, and protein were maintained at a constant level of intake throughout the entire study period.

During all investigations, all enteral intake and stool output was weighed and the nitrogen, water, and sodium contents determined. Enteral nutrient balance and absorption were then calculated from the measured enteral intake and stool losses. Body weight was recorded daily. Blood samples were analyzed biweekly to monitor the response to therapy and to adjust electrolytes added to the parenteral solution.

### Determination of Nutrient Intake

All food and fluid was weighed and prepared by the Clinical Research Center's metabolic kitchen. The total daily intake of protein, calories, carbohydrate, fat, sodium, and water (including the water content of all foods and beverages) was determined by a computer program (GCRC Diet Planner, Version 2.03, Clinical Study Center, University of California, San Francisco, CA), which translated the gram weight of intake into nutrient composition. For foods not analyzed or available on the computer program, nutrient values were determined by referring to Handbook 8<sup>14</sup> or other standards.<sup>15</sup> On random days of the study, duplicate patient trays were prepared and analyzed to confirm the nitrogen, fat, and sodium content of the diet.

### Measurement of Nutrient Losses

All stool was collected for consecutive 24-hour periods between 7:30 A.M. and 7:30 A.M. beginning on the morning after admission and continuing until completion of the study. Samples were prepared frozen at -20 C and analyzed for water, nitrogen, sodium, and, in selected patients, fat and calories as previously described.<sup>16</sup> Body weight was recorded each morning to the nearest 0.1 kg using a leveled platform scale (model SR2MI01, Acme Scale, Oakland, CA). All blood chemical and urine analyses were determined using standard hospital analytical techniques.

### Calculations of Nutrient Absorption

The absorption of nitrogen and sodium was calculated by subtracting the quantity of the substance present in the stool from the enteral intake for each 24-hour period. Stool output was the mean of the 24-hour measurements for each week. Because nutrient intake was constant, nutrient absorption of sodium and nitrogen was calculated by subtracting the balance of the final study week from the first or control week. This was expressed as a percentage change in absorption by dividing this difference by the control value and multiplying it by 100. The percentage change in stool weight (output) was calculated in a similar manner.

Table 1. PATIENT CHARACTERISTICS AND RESPONSES TO THERAPY

Patient No.	Gender	Age (yr)	Cause of Resection	Jejunum-Ileum (cm)	ICV (+/-)	Colon Rectum	TPN (yr)	Discharge TPN	Current TPN
1	M	44	SMA thrombosis	0	-	TDR	5	Off	Reduced
2	F	40	Small bowel volvulus	0	-	TDR	4	Reduced	Reduced
3	M	29	Small bowel volvulus	0	-	TDR	13	Reduced	No change
4	F	44	Small bowel volvulus	8	+	TDR	13	No change	Reduced
5	M	47	SMA thrombosis	8	-	TDR	3	Reduced	Reduced
6	F	42	Small bowel volvulus	10	-	TDR	10	Off	No change
7	F	42	Small bowel volvulus	15	-	All	3	Reduced	No change
8	F	31	Trauma to SMA	15	-	TDR	1.5	Off	Off
9	M	48	SMA thrombosis	20	-	TDR	5	Off	Reduced
10	M	19	Malrotation	20	-	All	15	Off	Off
11	M	68	Crohn's disease	20	+	All	1	Off	Off
12	F	34	Venous ectatic disease	24	-	DR	7	No change	No change
13	M	27	Trauma	30	-	TDR	3	Off	Reduced
14	M	54	SMA thrombosis	30	-	TDR	13	Off	Off
15	F	57	Small bowel obstruction secondary to adhesions	30	+	AT	4	Off	Reduced
16	F	34	Mesenteric infarction	30	+	All	8	Reduced	Reduced
17	F	58	Portal vein thrombosis	30	-	TDR	0.6	Off	Off
18	F	50	SMA thrombosis	30	+	All	1	Off	Off
19	F	30	SMA thrombosis	30	-	TDR	6	Off	Off
20	M	71	SMA thrombosis	30	-	TDR	11*	Off	Off
21	M	47	SMA thrombosis	30	-	TDR	7	Off	Off
22	F	45	Trauma	35	-	TDR	11	Reduced	No change
23	M	44	Volvulus	40	+	All	7	Off	Off
24	M	28	Small bowel volvulus	43	-	TDR	2	Off	Off
25	F	42	Small bowel obstruction secondary to adhesions	43	-	TDR	1	Off	Off
26	M	61	Mesenteric infarction	45	-	None	4.4	No change	No change
27	M	65	SMA thrombosis	46	-	TDR	2	Reduced	No change
28	F	44	Multiple resections secondary to adhesions	46	+	AT	9	Off	Off
29	F	65	Crohn's disease	53	-	TDR	5	Reduced	Reduced
30	M	70	SMA thrombosis	58	+	TDR	9	No change	Reduced
31	M	40	Crohn's disease	60	+	All	8	No change	Reduced
32	M	54	Volvulus	67	+	All	2	Reduced	Reduced
33	M	26	Crohn's disease	75	-	TDR	3	Off	Reduced
34	M	51	Crohn's disease	75	-	TDR	10	Reduced	Reduced
35	M	57	SMA thrombosis	76	-	TDR	0.3	Off	Off
36	F	46	Crohn's disease	80	-	TDR	1	Off	Off
37	F	55	Mesenteric infarction	83	-	TDR	14	Reduced	No change
38	F	46	Crohn's disease	90	-	TDR	9	Reduced	Reduced
39	F	38	Congenital malrotation	91	+	All	10	Off	Off
40	M	76	Small bowel obstruction secondary to adhesions	91	-	None	6	Reduced	Reduced
41	F	34	Crohn's disease	100	-	TDR	6	Off	Off
42	M	48	Volvulus	100	+	All	3	Off	Off
43	F	54	Crohn's disease	112	-	None	7	No change	No change
44	M	24	Crohn's disease	122	-	DCR	9	Off	Reduced
45	M	70	Crohn's disease	137	-	TDR	10	Reduced	Reduced
46	F	30	Crohn's disease	159	-	None	8	Off	Off
47	M	53	Small bowel obstruction secondary to adhesions	240	+	TDR	5	Off	Reduced

TDR = transverse and descending colon and rectum; TPN = total parenteral nutrition; DCR = descending colon and rectum; AT = ascending and transverse colon; + = with ileal cecal valve; - = without ileal cecal valve; SMA = superior mesenteric artery.

\* Received TPN and intermittent tube feedings during this time.

## Bowel Rehabilitation

### Patients

This portion of the clinical investigation was performed at the Brigham and Women's Hospital Boston Massachusetts, and at the Nutritional Restart Center Hopkinton, Massachusetts, the latter a low-cost unit for adults and children with severe malabsorptive disorders. Study protocols were approved by the Brigham and Women's Hospital's Committee for the Protection of Human Subjects from Research Risks, and informed consent was obtained.

Forty-seven adult patients with short-bowel syndrome (25 men, 22 women, age 46 years [range, 19–76 years]) were admitted for study. The clinical characteristics and primary diagnoses of the patients are given in Table 1. All patients had undergone extensive small-bowel resection with or without colonic resection. Combined jejunoileal length of the 43 patients with a colonic remnant was  $50 \text{ cm} \pm 7 \text{ cm}$ . For the four patients with no colon, the combined jejunoileal length averaged  $102 \text{ cm} \pm 24 \text{ cm}$ . Most patients ( $n = 39$ ) were referred for rehabilitative therapy while they received TPN. This group, on average, had received intravenous feedings for  $6 \text{ years} \pm 1 \text{ year}$ . Some patients ( $n = 8$ ) were referred because of lack of central venous access and progressive malnutrition. Seven patients in this category were treated without the use of TPN. On admission, all patients were clinically stable and without evidence of infection. Patients with diabetes mellitus, cancer within 5 years of treatment, clinically active inflammatory bowel disease, symptomatic strictures or bowel adhesions, or severe gastrointestinal dysmotility that precluded oral intake were excluded from study. This series represents a group of patients studied in a consecutive manner with no other exclusions.

### Method of Treatment

On the morning after the day of admission, a baseline assessment of the patient's nutritional and hydration status was performed. Weight was recorded to the nearest 0.1 kg, whole-body bioelectrical resistance (ohms) was measured by a plethysmograph (model 101A, RJL Systems, Mt Clemens, MI), and the readings were used to calculate body water as described previously.<sup>17</sup> In a subgroup of 31 patients followed prospectively, blood was obtained to determine concentrations of selected nutrients (vitamins, trace elements, and essential fatty acids) and indicators of organ function using standard analytical techniques. Urine was collected to determine 24-hour volume and creatinine excretion.

Thereafter, recombinant growth hormone was administered by subcutaneous injection at a dose ranging from 0.03 to 0.14 mg/kg/day (average dose of  $0.11 \text{ mg} \pm 0.01$

mg/kg/day). Supplemental glutamine was provided by both the parenteral and enteral routes. As stool output decreased, TPN (including the quantity of intravenous glutamine) was reduced. Parenteral glutamine dose averaged  $0.16 \pm 0.02 \text{ g/kg/day}$ . Because it was not possible to determine the proportion of enteral glutamine that was absorbed, a standard daily dose of 30 g was administered (5 g of enteral glutamine powder were mixed with a hypotonic, cold beverage and taken six times per day).

In addition to growth hormone and glutamine, all patients underwent extensive diet modification and nutritional education.<sup>16</sup> The quantity and frequency of TPN administered was gradually reduced as enteral intake and 24-hour urine volumes increased and stool output decreased. Blood was drawn biweekly to monitor serum electrolyte concentrations.

In all but three of the persons studied, body weight, total body resistance, intravenous fluid volume and calories, enteral fluid volume and calories, and stool and urine volumes were measured daily. The mean of the first 3 days (baseline) was compared with the mean of the last 3 days of treatment (discharge) to evaluate the effect of 4 weeks of therapy.

On completion of the 26-day protocol, growth hormone was discontinued and the patients were discharged home on oral glutamine (30 g/day) and the modified oral diet. The parenteral nutrient prescription on discharge was individualized for each patient, based on the individual's overall response to treatment with growth hormone plus glutamine plus HCLF diet. For those patients whose baseline nutritional assessment indicated an essential fatty acid deficiency, parenteral lipid emulsions were prescribed. Parenteral and/or enteral vitamin, trace element, and electrolyte supplements were prescribed at dosages to correct nutrient deficiencies identified during the baseline assessment and to maintain normal serum concentrations.

Follow-up data were collected at regular intervals and compared with the baseline data in the group of 31 patients entered into the prospective protocol. This evaluation included TPN requirements (days of infusion per week, volume of fluid per week, intravenous protein and calories administered per week), serum albumin concentration, and body weight. Cost of pretreatment intravenous feedings and current TPN requirements were calculated using Medicare reimbursement rates.<sup>18</sup>

At discharge, patients were classified into one of three categories based on their response to treatment: off, reduced, and no change. *Off* was defined as a patient who was removed from TPN at the end of therapy. In addition, patients who were referred for central line placement and received this treatment and were discharged without the need for TPN were placed in this group. However, several of these patients occasionally received

**Table 2. SODIUM AND PROTEIN INTAKE AND BALANCE, AND STOOL WEIGHT DURING SPECIFIC TREATMENT PROTOCOLS**

	Control Period			Final Week of Treatment Period			% Change with Treatment
	Oral Intake (g/day)	Intestinal Balance (g/day)	Stool Weight (g/day)	Oral Intake (g/day)	Intestinal Balance (g/day)	Stool Weight (g/day)	
Diet (n = 2)			1117 ± 332			1334 ± 508	+16.3 ± 10.5
Sodium	4.26 ± 0.49	+2.24 ± 0.60		4.66 ± 0.82	+2.46 ± 0.60		+10.6 ± 3.2
Protein	135.2 ± 24.8	+99.0 ± 12.8		117.5 ± 19.6	+79.4 ± 3.8		-19.0 ± 6.7
GLN (n = 3)			1953 ± 231			2197 ± 669	+8.5 ± 20.3
Sodium	3.27 ± 1.40	+1.25 ± 1.06		4.88 ± 0.84	+1.11 ± 0.86		+35.3 ± 34.9
Protein	64.2 ± 11.7	+30.9 ± 11.8		68.3 ± 10.2	+30.5 ± 11.9		+1.2 ± 14.5
GH (n = 4)			2268 ± 437			1872 ± 351	-12.9 ± 11.4
Sodium	4.52 ± 0.89	+2.77 ± 0.05		5.77 ± 1.16	+4.45 ± 0.02		+60.8 ± 3.5
Protein	118.2 ± 8.3	+70.6 ± 7.3		110.5 ± 14.8	+73.2 ± 11.0		+6.4 ± 16.5
GH + GLN + DIET (n = 8)			1783 ± 418			1308 ± 408	-33.1 ± 10.3
Sodium	3.48 ± 0.56	+1.51 ± 0.68		3.73 ± 0.50	+2.55 ± 0.36		+37.1 ± 40.8
Protein	88.6 ± 18.8	+45.3 ± 12.3		86.7 ± 15.3	+54.2 ± 10.7		+38.8 ± 13.8

Values are mean ± SEM.

+ = improved protein or sodium absorption; - = decreased stool loss.

\* Different from other treatment groups,  $p < 0.05$ .

specific nutrients intravenously to treat a deficiency. In addition, these patients may have required occasional hydration fluid. Patients who continued to receive similar amounts of TPN when compared with baseline were considered unaffected by therapy. This was confirmed by analyzing costs, which also demonstrated *no change*. Patients who were classified as *reduced* were those who had a decrease in their TPN requirements and also experienced a cost reduction.

## STATISTICAL ANALYSIS

Data were analyzed using standard statistical software (Statview No. 512, Abacus Concepts, Inc., Berkeley, CA, on a Macintosh SE personal computer, Apple Computer, Cupertino, CA). For normally distributed data, the paired Student's *t* test was used to determine differences between the control period and the last week of the treatment period. For nonnormally distributed data, the Wilcoxon signed rank test was used. Analysis of variance was used to identify between-group differences. Simple and multiple linear regression analyses were used to identify which variables significantly influenced response to therapy. A probability value of less than or equal to 0.05 was considered statistically significant. Results are expressed as mean ± SEM.

## RESULTS

### Absorption Studies

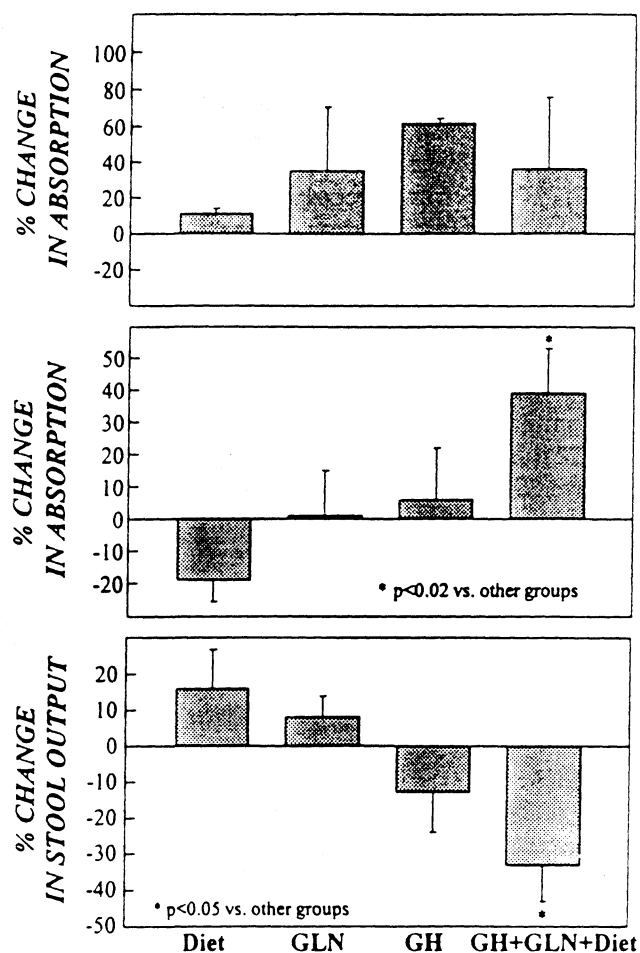
All patients were clinically stable throughout the study period. Weight gain over the 3 to 4 weeks of study was

gradual and averaged approximately 1 kg/week. The oral dietary intake remained relatively constant throughout the study. The patients consumed about 2800 kcal/day and 100 g protein/day by the enteral route, although there were large variations among individuals due to food intolerances and preferences (calories ranged from a group average of 1800–3700 kcal/day, and protein intake ranged from 64–135 g/day).

With diet modification only, sodium and protein absorption did not change significantly, and stool output increased slightly compared with the control period (Table 2). When glutamine was added to a fixed standard diet, sodium absorption was slightly enhanced (approximately 35%, not significant), and protein absorption and stool volume were likewise unaffected. Administration of growth hormone alone also tended to improve sodium absorption and somewhat enhanced protein uptake but reduced stool output slightly. With the administration of all three treatment components (growth hormone plus glutamine plus diet) there was a 37% increase in sodium absorption (not significant) and a 38% improvement in protein absorption ( $p < 0.02$ ). Stool loss decreased by about one third ( $p < 0.05$ ) (Fig. 1). This decrease in stool output was accompanied by a reduction in the frequency of bowel movements and often a change in stool character from liquid to semiformal.

### Response to Four Weeks of Therapy

All subjects entered into the protocol were able to complete the treatment program, and there were no



**Figure 1.** The effect of HCLF diet, glutamine, growth hormone, and growth hormone plus glutamine plus HCLF diet on absorption of (top panel) sodium, (middle panel) protein, and (bottom panel) stool output. An increase in absorption above the 0 balance line indicates enhanced uptake; a negative change indicates decreased absorption. A negative change in stool output indicates a reduction in stool volume.

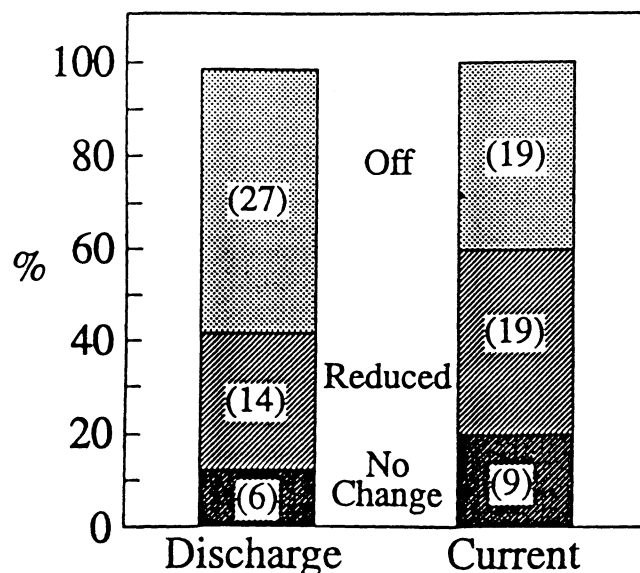
dropouts. The major side effect of the treatment was fluid retention, manifested by peripheral edema and arthralgia, which varied depending on growth hormone dose. This problem was attenuated by limiting fluid intake, reducing the growth hormone dose, or administering diuretics. In this group of 47 patients, 15 febrile episodes occurred; many were attributable to upper respiratory tract infections, and these individuals were treated symptomatically. Patients diagnosed by culture with bacterial infections (urinary tract, sinusitis, catheter sepsis) were treated with specific antibiotics.

For the group, the 4 weeks of therapy resulted in weight gain, an increase in intake of enteral calories and fluid, maintenance of urine output, and diminished need for intravenous fluid and nutrients (Table 3). These responses were variable, however; at the end of the treatment period, 27 of the 47 patients (57%) did not require TPN, 14 (30%) had reduced TPN requirements, and 6 (13%) required ap-

proximately the same quantity of parenteral support as was necessary at the start of therapy. For each subgroup, the changes in absorption of nutrients and fluid during the 4-week treatment period are shown in Table 3. An examination of the characteristics of the subjects in each group revealed that the patients who could not be weaned from TPN were slightly older ( $p = 0.02$ ) and had Crohn's disease as the cause of resection ( $p = 0.04$ ) compared with the other patients who were weaned from or received reduced intravenous nutrition (Table 4). In addition, the patients who failed the therapy (no change) initially had larger stool output ( $p < 0.002$ ) than the other two groups (Table 3). There was no significant difference in bowel length among the three groups.

### Evaluation of Long-Term Effect

The length of follow-up for all patients has been between 5 months and 5 years. During this time, most of the patients have been cared for by their primary care physicians and the nutritional support team located in their immediate geographic area. Nutritional compliance was constantly reinforced and hydration state evaluated by frequent telephone interviews between ourselves and the patients. This information was conveyed to the primary care and home care providers, who likewise emphasized the nutritional plan. We cared for and followed directly a smaller group of patients who lived in the New England area. Over the past 18 months, 31 patients have been entered into a prospective study to



**Figure 2.** The TPN status of patients after discharge after 28 days of treatment and approximately 1 year after treatment. "Off" indicates no TPN, "Reduced" indicates less than what was initially given, and "No Change" indicates similar volume and calories to those initially administered.



Table 3. THE EFFECTS OF FOUR WEEKS OF GH + GLN + DIET TREATMENT ON WEIGHT, RESISTANCE, AND SOME INPUT AND OUTPUT MEASUREMENTS

	Entire Group (n = 44)*			Off (n = 25)			Reduced (n = 13)			No Change (n = 6)		
	Baseline	Discharge	p	Baseline	Discharge	p	Baseline	Discharge	p	Baseline	Discharge	p
Weight (kg)	58.4 ± 1.6	61.4 ± 1.6	0.0001	56.0 ± 1.8	59.5 ± 1.8	0.0001	62.8 ± 3.7	64.7 ± 3.9	0.016	58.8 ± 3.0	62.4 ± 3.5	0.06
Resistance (Ω)	581 ± 18	500 ± 17	0.0001	600 ± 25	496 ± 22	0.0001	559 ± 36	503 ± 35	0.007	548 ± 37	510 ± 41	NS
Oral calories (kcal/day)	2212 ± 144	2568 ± 139	0.003	2356 ± 226	2853 ± 192	0.004	1913 ± 165	2139 ± 215	0.27	2261 ± 282	2308 ± 275	NS
Oral fluid (mL/day)	2892 ± 156	3158 ± 153	0.03	3073 ± 230	3288 ± 220	0.19	2507 ± 238	2966 ± 248	0.032	2970 ± 324	3027 ± 398	NS
IV calories (kcal/day)	1358 ± 115	539 ± 108	0.0001	1284 ± 180	120 ± 60	0.0001	1440 ± 192	890 ± 202	0.003	1429 ± 204	1525 ± 232	NS
IV fluid (mL/day)	1525 ± 165	827 ± 167	0.0001	1210 ± 189	264 ± 115	0.0001	1781 ± 309	1277 ± 272	0.029	2283 ± 534	2200 ± 617	NS
Urine output (mL/day)	1705 ± 132	1814 ± 113	NS	1663 ± 183	1815 ± 156	0.25	1846 ± 269	1877 ± 227	NS	1572 ± 197	1671 ± 200	NS
Stool output (mL/day)	2078 ± 205	1749 ± 214	0.006	1806 ± 246	1336 ± 204	0.005	1902 ± 275	1911 ± 314	NS	3590 ± 726	3118 ± 1004	NS

Values are mean ± SEM.

NS = not significant.

\* Complete data unavailable for three subjects: one who reduced IV feedings and two others who were removed

evaluate periodically the effect of the therapy on long term nutritional intake, route of feeding, costs, and nutritional status.

Eight of the 27 patients who had had TPN discontinued eventually experienced increased requirement for TPN. This occurred because of recurrence of disease in three patients (e.g., recurrence of active inflammatory bowel disease), dietary noncompliance in three patients, and inappropriate removal from TPN by the care team in two patients. With follow-up at 1 year, 40% of the group were off TPN, 40% received a reduced TPN prescription, and the remaining 20% of the patients received TPN similar to their initial pretreatment requirement (Fig. 2). At this time of follow-up (approximately 1 year), body weight and serum albumin concentration were well maintained, despite the reduction of intravenous calories and protein (Fig. 3, Table 5).

For the 31 patients followed prospectively, we could estimate the cost savings that occurred with decreased use of TPN. In those patients weaned from TPN, the annual savings was \$102,270/year, and those with reduced TPN volume, calories, and protein saved approximately \$25,338/year (Table 4). If one assumes that all patients would have received TPN for the coming year, applying these savings to the entire group in the proportion shown at 1 year (see Fig. 2), the money saved for TPN alone would equal \$2,310,396/year, or about \$49,157/patient/year.

## DISCUSSION

The treatment of patients with loss of large segment of the intestinal tract has evolved rapidly over the past 30 years. In the early 1960s, it was common to simply close the abdomen of a patient after laparotomy if extensive bowel loss was identified, because no treatment was available after massive intestinal resection. The development of TPN provided a method for stabilization and support of these patients with the hope that adaptation of the remnant bowel would occur over time. Although this has occurred in many patients who have had adequate lengths of remaining small bowel, it has not been the case in many other persons with inadequate small intestine. It has been estimated that about 10,000 to 20,000 patients with short-bowel syndrome in the United States are now at home being maintained on intravenous feedings.<sup>13</sup> That these persons can be maintained out of the hospital over the long term is a remarkable accomplishment, and it should be realized that patients with short-bowel syndrome served as the stimulus for the growth of a new health service industry—home care—which has facilitated this process. However, the long-term experience with home TPN now reveals that a variety of short- and long-term complications occur including repeated episodes of catheter sepsis, nutri-

Table 4. CHARACTERISTICS OF PATIENTS IN GROUPS

	Off	Reduced	No Change
n	27	14	6
Age (yr)	43 ± 3	51 ± 4	50 ± 6
Gender (male:female)	15:12	7:7	3:3
Jejunum-ileum length (cm)			
With colon (mean)	53 ± 10 (n = 26)	49 ± 11 (n = 11)	38 ± 13 (n = 4)
(median)	30	46	41
Without colon	159 (n = 1)	91 (n = 1)	78 (n = 2)
Years of TPN	5 ± 1	7 ± 1	8 ± 1

Values are mean ± SEM.

TPN = total parenteral nutrition.

tional deficiencies, progressive failure of the liver and kidneys, and severe osteoporosis. These problems, associated with the compromised lifestyle and major costs (about \$100,000/year for the TPN alone), have resulted in other initiatives to solve the problems of patients with short-bowel syndrome. Surgeons are evaluating the effects of bowel reconstruction<sup>19</sup> and intestinal transplantation<sup>20</sup> in this group of patients.

In the past 10 years, however, several important experimental developments have contributed to the evolution of the approach presented in this report. First, it was discovered that glutamine was the major nutrient for the bowel. Providing parenteral feedings that contained this amino acid supported mucosal growth under a variety of conditions,<sup>21</sup> including mucosal hypertrophy that occurred after extensive small-bowel resection.<sup>22</sup> Other studies have documented improved bowel function, including absorption, when L-glutamine was provided by parenteral<sup>23</sup> and/or enteral feedings.<sup>24</sup>

Second, both animal and human studies have demonstrated that growth hormone, now available in recombinant form, stimulates intestinal growth<sup>25</sup> and enhances transport of nutrients across the small bowel.<sup>26</sup> Although we observed few significant clinical effects when these

agents were administered alone, under the conditions of our study, enhanced absorption was observed when the agents were given together. Animal studies have revealed a molecular basis for this proliferative response using combined agents.<sup>27</sup>

The issue of optimizing dietary intake is more controversial, and investigators have differed in their preference for a low-fat<sup>28</sup> or a high-fat (unmodified) diet.<sup>29</sup> Absorption was maximized by providing a diet that contained 20% to 25% fat, similar to recent recommendations by others.<sup>28</sup> However, for these patients with very short segments of jejunum-ileum, we were unable to document major effects of diet alone. The exception to this finding occurred when a patient consumed a high-fat intake (>40% of total calories) during the control period and was then placed on a 20% fat diet during the treatment period. In addition, we have found that many patients were sensitive to lactose and also increased their stool output and complained of bloating with the ingestion of simple sugars (fructose and glucose). We therefore have provided a diet tailored to the individual but that provides about 60% of calories as complex carbohydrates, 20% as protein, and the remainder as fat. This is provided as six feedings given throughout the day, with nutrients distributed into three meals and three snacks. Vitamins and minerals are supplemented by the oral route. Hydrogen-blocking drugs were often helpful to diminish gastric secretion; in contrast, we have observed little benefit with the administration of somatostatin analogues, even in the patients with high stool losses.

In this clinical trial, each subject served as his or her own control. This approach was chosen because of the large variation among subjects in terms of bowel disease, length of remnant bowel, and volume of stool lost. We found that it was possible to wean a large proportion of these patients from TPN using this combined therapeutic approach; another sizable segment of this group was able to reduce their weekly TPN requirements, thus giv-

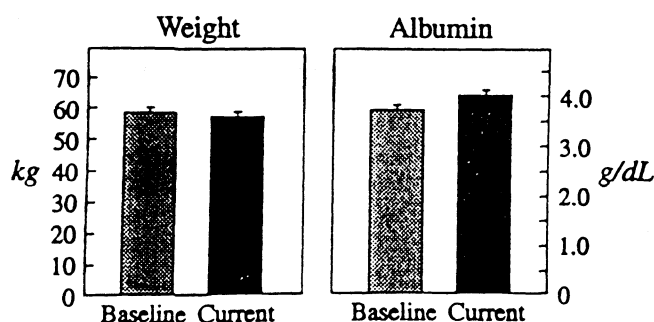


Figure 3. Body weight and albumin at baseline and currently at approximately 1 year.

**Table 5. CHANGES IN TPN REQUIREMENTS, ANNUAL COSTS, AND NUTRITIONAL INDICES BEFORE TREATMENT AND AT THE PRESENT TIME**

	Off (n = 7)			Reduced (n = 16)			No Change (n = 8)	
	Baseline	Current	p	Baseline	Current	p	Baseline	Current
TPN days/wk	6 ± 1	0	0.0001	6 ± 0	4 ± 0	0.0001	6 ± 1	6 ± 1
TPN volume/wk (L)	12 ± 2	0	0.002	12 ± 1	7 ± 1	0.0006	11 ± 2	10 ± 2
TPN protein/wk (g)	387 ± 80	0	0.003	476 ± 32	259 ± 28	0.0001	392 ± 15	375 ± 72
TPN calories/wk (kcal)	9451 ± 2909	0	0.018	9188 ± 1088	5744 ± 950	0.0001	7518 ± 1719	8665 ± 1953
Annual costs (\$/yr)	102,270	0	0.0002	107,143 ± 7117	81,805 ± 7081	0.0003	95,227 ± 12,271	107,911 ± 13,182
Weight (kg)	57.7 ± 3.6	54.0 ± 2.7	NS	59.5 ± 2.7	60.4 ± 2.7	NS	62.7 ± 4.5	60.4 ± 4.5
Albumin (g/dL)	3.8 ± 0.1	3.9 ± 0.1	NS	3.6 ± 0.1	3.8 ± 0.1	0.1	3.6 ± 0.1	3.6 ± 0.2

Values are mean ± SEM.

TPN = total parenteral nutrition; NS = not significant.

ing them nights off from infusion. Body weight and serum albumin, major indicators of nutritional status, were stabilized over the follow-up period, which averaged 1 year. This series represents the largest group of adult patients with short-bowel syndrome studied to date by a single group of investigators, and additional multicenter trials are in progress involving both adults and children to evaluate the effect of this approach in randomized trials.

It could be argued that the patient's response to growth hormone plus glutamine plus HCLF diet occurred because special attention was given to provide the appropriate diet or that specific nutrients were provided to satisfy deficiencies or because the investigators have a sophisticated understanding of the underlying fluid, electrolyte, and nutritional derangements that occur in this group of patients. Although this is possible, we believe our initial study in the Clinical Research Center indicates that this combination of therapeutic agents, coupled with sound nutritional and physiologic management, resulted in the responses observed—the ability to take patients off or keep them off TPN or reduce their requirements in more than 80% of this population. Numerous patients were referred to us after failure to respond to growth hormone or glutamine administered by their own physicians, and all of these patients demonstrated decreased stool output when growth hormone plus glutamine plus HCLF diet were administered in combination. In addition, 14 of 21 patients who were discharged without TPN and who have maintained their nutritional state in follow-up had less than 50 cm of jejunum-ileum. This is an important observation, because this length of intestine is consistently regarded as less than the necessary length for adequate absorption and nutritional maintenance by enteral feedings.<sup>1,7</sup>

Not only did the patients respond to 4 weeks of therapy, but also, many were able to maintain this state of

independence during the year after the initial treatment. Our longest-term patient has been independent of TPN for 5 years (patient 8, 15 cm jejunum anastomosed to transverse colon), and during the last year she became pregnant, carried a normal child to term, had a normal delivery, and breast-fed the infant, events that reflect capacity to withstand additional nutritional stress. Others have been free of TPN, but short-term illness has necessitated brief intervals of intravenous support. In the eight persons who were initially weaned from TPN and who eventually required intravenous feedings, about a third were placed back on TPN because of recurrence of their underlying disease; dietary noncompliance was another cause of failure in several other persons. Care plans need to be developed allowing for all of these persons to receive appropriate long-term care to effectively support the patient with short-bowel syndrome through intercurrent illness. For example, several days of intravenous fluid may be necessary during periods of viral gastroenteritis, but with resolution of the illness and adequate hydration, enteral feeding can be started. In addition, some patients may need to be treated with growth hormone plus glutamine plus HCLF diet at appropriate time intervals and/or have diet compliance frequently reinforced by their care providers. Further adaptation may occur with time—we have worked with several patients with large daily stool losses (>3 L/day) who have reduced their stool output in subsequent 12 months after therapy to about one half this volume while the diet and fluid intake have stayed the same or increased.

Physiologic and morphologic changes occur in the bowel after therapy. With treatment, small-bowel hypertrophy, the bowel dilates and elongates, and intestinal transit time becomes prolonged. Colonic absorption is thought to be enhanced via the process of bacterial fermentation. This process stimulates fluid and

electrolyte absorption and salvages both carbohydrate and protein calories, which are malabsorbed by the small bowel remnant.<sup>30</sup> In addition, volatile fatty acids generated in the colon enhance mucosal growth and prolong transit time.<sup>31</sup>

Because the bowel is constantly renewing its surface area, this organ is ideal for modification by administration of selected nutrients and growth factors. Other hormones are also known to exert effects on the bowel, but growth hormone and glutamine are currently approved agents, readily available, safe, and reasonably inexpensive compared with the other therapeutic options. This method of treatment should be evaluated and considered for patients with inflammatory bowel disease, those undergoing intestinal transplantation, and those with dysfunctional loops of distended bowel who require rehabilitation. Various laboratory and clinical observations suggest that these therapeutic agents administered singly or in combination affect intestinal structure and function in a wide variety of conditions. These observations of patients with short-bowel syndrome may demonstrate for the first time that we can use growth factors and nutrients together to enhance the proliferative response of specific tissue and therefore improve function. This concept may have broad applications to support or enhance the growth and function of other organs and thus improve care of patients.

## Acknowledgments

The authors thank Ajinomoto for providing the amino acids and Genentech, Inc., for providing the growth hormone. The authors also thank the nursing staff at the Clinical Research Center, the members of the Laboratory for Surgical Metabolism and Nutrition, and the administration and clinical staff of the Nutritional Restart Center for their interest, support, professionalism, and highest standards of care.

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## Discussion

DR. JOHN L. ROMBEAU (Philadelphia, Pennsylvania). Dr. Wilmore and colleagues and a number of members of this Association have created a very exciting new area of surgical nutrition and metabolism; namely, the area of nutritional pharmacotherapy. This is broadly defined as providing some nutrients that indeed seem to have more pharmacologic effects than nutritional effects per se, in addition to giving some drugs that in turn either enhance nutrient utilization or modify the metabolic environment of the host.

We have been very interested in the effects of the amino acid glutamine on the transplanted small intestine. In a model of transplanted small intestine in the rat, we compared the effects of supplemental glutamine given either intravenously or directly into the graft on small bowel glucose absorption as measured with C-14 labeled glucose. As shown, the addition of glutamine, when compared with an isonitrogenous controlled diet balanced with a mixture of nonessential amino acids, significantly enhanced the ability of the small intestine to absorb glucose nearly equivalent to baseline pretransplant levels.

I have one question for Dr. Wilmore, and this relates to the human short bowel setting. There is very limited information obtained from intestinal biopsies in patients that have suffered from short bowel syndrome. This information shows that the small intestine seems to reach a maximal rate of adaptive hyperplasia somewhere between 2 and 3 years postoperatively.

In Dr. Wilmore's study, 10 of the 19 patients that remained off total parenteral nutrition had been on total parenteral nutrition for periods greater than 3 years. In fact, one of these patients had actually been on total parenteral nutrition for 15 years prior to the usage of this combined therapy.

My question is, what are the mechanisms by which this combined therapy enhances the absorptive function of the remaining gut in an intestine that has already had at least 3 years to adapt endogenously?

DR. PAUL R. SCHLOERB (Kansas City, Kansas). I am as impressed by this paper as I was a quarter of a century ago when Doug Wilmore, working with Dr. Rhoads, Dr. Dudrick, Dr. Vars, and others in Philadelphia, maintained an infant for many, many weeks by total parenteral nutrition for the first time.

When you have reviewed this manuscript, as I have had the privilege of doing, I think you will agree that this kind of study, with careful clinical observations and measurements, could only be carried out in a clinical research center, although it was

not called that at the Brigham when Dr. Francis Moore set up 47 years ago.

One may philosophize, I suppose, to the extent that nature has a way of correcting defects like this. The more weight that is lost, the less nutrients are required.

But it is worth emphasizing as Doug pointed out, that patients with less than 50 cm of jejunum-ileum are almost destined to require total parenteral nutrition. Two thirds of the patients in this category were taken off total parenteral nutrition.

Weight gain to the tune of approximately 1 kg per week was observed in their study. And I have to ask whether this weight was in fact water, because growth hormone does indeed produce fluid retention.

These favorable results are probably due in large measure to the effect of growth hormone, and yet the patients were discharged while not receiving growth hormone. So my question is, what did growth hormone do? What effect did it have that continued beyond the administration of growth hormone?

Whether it is pediatric cardiac surgery, orthotopic liver transplantation, or carcinoma of the pancreas, the best results are obtained by centralized patient care. I think centralization of care applies to this rather unusual circumstance of short-gut syndrome. Dr. Wilmore makes reference to the possibility of multicenter trials, and I wonder if he would share with us some of his plans and ambitions in this regard.

And finally, in terms of centralized care, I wonder, Doug, you would acquaint us a little more with the so-called Nutritional Restart Center, which, from my limited understanding, represents a real boon to patients with short-gut syndrome.

DR. STANLEY J. DUDRICK (Waterbury, Connecticut). I thoroughly enjoyed this impressive paper, which is in an area of great personal clinical and scientific interest to me. I, too, had the opportunity to read the manuscript, which is replete with data that were not able to be presented here in its entirety. Dr. Wilmore did not have time to explain all aspects of the entry criteria and the therapy, and, therefore, I would like to ask him a few questions. To reduce some of the variables, patients with active infection and inflammatory bowel disease, cancer within 5 years of treatment, diabetes mellitus, other extra digestive organ failure, and severe gastrointestinal dysmotility, were excluded. I wonder if the team had any experience treating some of these patients that were excluded from the study? Furthermore, do you have any recommendations for how one might manage patients with those exclusionary comorbid factors?

Regarding your choice of the recombinant hormone, how did you determine the dosage used? Was the final recommended dose arrived at by trial and error? Or did you give growth hormone to the point at which you began to have complications and then back off? Or were you able to discern some optimal dose above which you had no additional beneficial effects? Additionally, what does a course of growth hormone cost?

In measuring body water, did you fractionate the total body water into intracellular and extracellular water? If so, would you share those data with us?

In the paper, you described a pregnant woman with short bowel syndrome who came off the total parenteral nutrition

and eventually completed her pregnancy with delivery of the child, apparently resulting in both a healthy mother and infant. Did you have to reinstitute total parenteral nutrition at any point to support her through this additional stress? Or was she able to sustain her child and herself nutritionally entirely without the total parenteral nutrition?

Lastly, do you have any thoughts about the future use of growth factors, including growth hormone, administered together with nutrient substrates, in the management of the failure of other single organs such as the liver, kidney, pancreas, and brain?

I thank the authors for the opportunity to read and discuss this fine paper, and I thank the Association for the privilege of the floor.

DR. DONALD D. TRUNKEY (Portland, Oregon): Doug, I enjoyed your paper very much. A couple of questions about your no-change group.

You imply that these were patients who had chronic inflammatory bowel disease. I postulate that when you started them in the study, they were probably in remission. My question is, what percent of the protein loss in these patients represents stool white cells? If they did get an exacerbation, did that protein loss increase because of the white cells?

DR. W. GARDNER SMITH (Baltimore, Maryland): A clinical question for Dr. Wilmore. Nowadays, when we explore a patient who has had an acute ischemic event to their intestine, is there ever any indication to do what we used to do in 1965 and simply quit? If there are indications for this course of action, are there parameters that can help us to make that judgment, such as length of viable intestine remaining or the age of the patient?

DR. DOUGLAS W. WILMORE (Closing Discussion): Thank you for the thoughtful questions and clear discussion.

The mechanisms of adaptation clearly appear related to villus hypertrophy and elongation of the remnant bowel. In animals, there is thickening of the muscularis mucosa and transit time becomes prolonged; initially in these patients, it takes approximately 15 minutes to see barium reach the colon from the mouth, but after 4 weeks of treatment, this time is about an hour or so. So simply the prolongation of transit times allows increased nutrient exposure to the absorptive surface area.

Dr. Schloerb, as you know, the weight gain in these patients was in part water and in part protein. The patients lose some of the water as they come off the growth hormone. The enhanced absorption probably continues for a prolonged period of time for several reasons. One, we are giving oral glutamine to maintain the nutrition of the mucosa and maintain cell turnover. But we are also using the colon as an organ for fermentation and nutrient absorption. The unabsorbed carbohydrate and protein that reach the colon are processed by bacteria and the by-products absorbed so that we are converting these individuals to hind-gut ruminants.

Two multicenter trials of this therapy are being performed in adults in the United States and in Europe. There is also a multicenter trial being formed to use the therapy in a group of children.

We care for the patients in a low-cost, assisted-living center where we have designated beds for patients with malabsorption disorders. Patients have their own apartments, but interact with the nurses, dietitians, and physicians on a regular and scheduled basis.

The doses of growth hormone we used were determined from dose-response studies. Growth hormone costs about \$300 per day at this dose. However, growth hormone is going off orphan drug status and will be less expensive in the next year or so as other pharmaceutical companies bring their growth hormone to market.

If we maintain the proportion of patients that we were able to take off total parenteral nutrition at 1 year—that is, 40% off, 40% reduced, and 20% no change—the number of dollars that we save from total parenteral nutrition cost alone is about \$2.3 million a year, or approximately \$50,000 per patient.

Patients who could not be taken off total parenteral nutrition did not have active acute inflammatory disease. Which patients should not be considered for this therapy? This is an issue of debate because some pediatric surgeons feel that babies with congenital lesions and little hope of survival should not be treated. We have not treated patients with cancer or those with known motility disorders. In general, younger patients from 20 to 55 years of age or so who have losses of large segments of bowel are good candidates for rehabilitation. Older patients should still receive the therapy, but may not respond as well, particularly if they have associated heart disease and other comorbid disorders.

Thank you for the opportunity to present this work.

## Growth Hormone, Glutamine, and a Modified Diet Enhance Nutrient Absorption in Patients With Severe Short Bowel Syndrome

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**ABSTRACT.** *Background:* Massive loss of intestinal surface area results in the short bowel syndrome characterized by malabsorption of fluid, electrolytes, and other nutrients. Although the remaining bowel undergoes morphological and functional adaptation, often these changes are inadequate to support the individual by enteral feedings, and parenteral nutrition is required to prevent dehydration, electrolyte disturbances, and malnutrition. Substances such as growth hormone, glutamine, and fiber exert bowel-specific trophic effects and either directly or indirectly influence nutrient absorption. This study was undertaken to determine whether the co-administration of exogenous growth hormone, supplemental glutamine, and a modified fiber-containing diet could enhance nutrient absorption in patients who had undergone massive intestinal resection. *Methods:* Ten patients (5 men, 5 women, aged  $43 \pm 4$  years) with short bowel syndrome were studied  $6 \pm 1$  years after surgical resection. All patients were admitted to the Clinical Research Center for a 28-day period; the first week served as a control period when nutritional (enteral and parenteral) and medical management simulated usual home therapy. Thereafter, eight patients received exogenous growth hormone, supplemental glutamine, and a modified high-carbohydrate, high-fiber diet. Two patients were treated with the modified diet alone. The efficiency of net

nutrient absorption (percent absorbed) for total calories, protein, fat, carbohydrate, water, and sodium was calculated from the measured nutrient intake and stool losses. *Results:* Three weeks of treatment with growth hormone, glutamine, and a modified diet increased total caloric absorption from  $60.1 \pm 6.0\%$  to  $74.3 \pm 5.0\%$  ( $p \leq .003$ ), protein absorption from  $48.8 \pm 4.8\%$  to  $63.0 \pm 5.4\%$  ( $p \leq .006$ ), and carbohydrate absorption from  $60.0 \pm 9.8\%$  to  $81.5 \pm 5.3\%$  ( $p \leq .02$ ). Fat absorption did not change ( $61.0 \pm 5.3\%$  to  $60.3 \pm 7.9\%$ ,  $p = \text{NS}$ ). Water and sodium absorption increased from  $45.7 \pm 6.7\%$  to  $65.0 \pm 7.3\%$  ( $p \leq .002$ ) and from  $49.0 \pm 9.8\%$  to  $69.6 \pm 6.5\%$  ( $p \leq .04$ ), respectively. These absorptive changes resulted in a decrease in stool output ( $1,783 \pm 414$  g/d control period vs  $1,308 \pm 404$  g/d third week of treatment,  $p \leq .05$ ). Treatment with diet alone did not influence nutrient absorption or stool output. *Conclusions:* The combined administration of growth hormone, glutamine, and a modified diet enhanced nutrient absorption from the remnant bowel after massive intestinal resection. These changes occurred in a group of patients that had previously failed to adapt to the provision of enteral nutrients. This therapy may offer an alternative to long-term dependence on total parenteral nutrition for patients with severe short bowel syndrome. (*Journal of Parenteral and Enteral Nutrition* 19:296-302, 1995)

Extensive loss or dysfunction of the intestinal absorptive surface area results in the short bowel syndrome. This symptom complex is characterized by diarrhea, dehydration, electrolyte disturbances, malabsorption, and progressive malnutrition. The severity of this disorder depends upon the length, location, and absorptive function of the remaining bowel and its ability to accommodate the reduced absorptive surface area.<sup>1</sup> The compensatory process may occur for 1 to 2 years before adaptation is maximal and during this period parenteral nutrition is frequently required. In patients with very short segments of jejunum or ileum ( $< 60$  cm), sufficient adaptation of the remnant bowel to support the individual by enteral feedings is unlikely, and dependence on parenteral nutrition may be perma-

nent.<sup>2</sup> Although parenteral nutrition is life-sustaining, it can be associated with debilitating complications, repeated hospitalizations, and significant costs (at least \$75,000 to \$150,000 per patient year).<sup>3</sup>

For the patient with short bowel syndrome, various operative approaches have been employed in attempts to prolong intestinal transit or expand absorptive surface area. Intestinal transplantation has also been proposed as a solution to the problem of intestinal failure. However, these procedures have major limitations,<sup>4,5</sup> and there remains a need for a relatively safe and cost-effective treatment for these patients. We postulated that one such therapeutic approach might be to enhance the normal physiologic process of intestinal adaptation by administering substances that are trophic to the bowel and/or directly or indirectly influence nutrient absorption.

Intestinal growth and adaptation are mediated in part by factors extrinsic to the gastrointestinal tract (eg, growth hormone and thyroxine) and in part by local

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factors brought into play by the provision of enteral feedings (eg, exposure of the mucosa to specific nutrients, pancreatic-biliary secretions, or enteric hormones).<sup>6</sup> The amino acid glutamine is a primary energy source for the gastrointestinal tract;<sup>7</sup> it exerts trophic effects on the bowel<sup>8</sup> and stimulates nutrient absorption.<sup>9,10</sup> Similarly, fiber is a specific component of the diet that may enhance bowel adaptation by promoting bowel growth and cell proliferation<sup>11</sup> by slowing gastrointestinal transit time.<sup>12,13</sup> Although previous pilot studies investigating the effect of growth hormone or glutamine alone on nutrient absorption in patients with short bowel syndrome produced minor biochemical changes, no significant clinical effects were observed. Others studies have shown that simple dietary manipulation (eg, restricting fat or increasing carbohydrate intake) fails to significantly enhance nutrient absorption.<sup>14-16</sup> Because a single treatment modality is unlikely to induce all the adaptive changes that occur within the resected gastrointestinal tract, we hypothesized that the co-administration of trophic substances such as growth hormone and supplemental glutamine in combination with a low-fat, high-carbohydrate, fiber-containing diet would significantly enhance nutrient absorption from the remnant bowel of patients who had undergone massive intestinal resection.

#### METHODS

##### Patients

Ten patients (5 females, 5 males, mean age  $43 \pm 4$  years) with severe short bowel syndrome were admitted to the Clinical Research Center of the Brigham and Women's Hospital, Boston, MA. All patients had undergone extensive small bowel resection with or without colonic resection. The lengths of the remaining gut structures were determined from operative reports and confirmed by perioperative radiographs (Table I). Patients were ambulatory and clinically stable and without evidence of uncontrolled infection or active inflammatory bowel disease. In addition, they had no extradiigestive organ failure, were free of cancer, and did not have a history of cancer. All patients were able to tolerate an *ad libitum* diet; however, without parenteral support they were unable to adequately maintain hydration and/or nutritional status. The protocol was approved by the Hospital's Committee for the Protection of Human Subjects from Research Risks, and informed consent was obtained.

##### Study Design

The patients were admitted to the Clinical Research Center for a 28-day stay. The first week served as a control period during which the patients' nutritional (parenteral and enteral feedings and *ad libitum* oral intake) and medical management (antidiarrheal agents, etc) simulated their usual home therapy. Patients were instructed to consume the quantity and type of foods and beverages that best represented their usual eating habits and food preferences. Only food and beverages of known nutrient composition were provided. Meals and snacks were made available six times per day. Self-selected beverages were made available 24 h/d. The supplemental enteral tube feeding that two patients received at home before admission was provided and administered at the same rate and concentration. During the control period, the infusion of parenteral nutrients and fluid volumes was matched to those that had been prescribed by the patient's primary-care physician before the research protocol. The nutrient solutions were prepared daily in the hospital pharmacy as previously described.<sup>17</sup> Electrolytes were added daily to the nutrient solution in quantities necessary to maintain normal serum concentrations.

During the remaining 3 weeks, all patients received a diet that was high in complex carbohydrates and low in fat, but nearly isocaloric and isonitrogenous to that which the patient received during the

control period. The diet was designed to provide approximately of total calories from carbohydrate, 20% from fat, and 20% protein. Total dietary fiber (defined as the sum of insoluble and soluble fiber) intake increased as complex carbohydrates replaced simple sugars. In addition, a soluble fiber supplement (Apple powder, Solgar, Lynbrook, NY) was added to specific food items tolerated. Calories and protein were distributed into six feedings served throughout the day. Near-isotonic fluids containing glucose and sodium (Gatorade, The Gatorade Company, Chicago, IL, Pedialyte, Ross Laboratories, Columbus, OH) replaced both hypotonic and hypertonic fluids and served as the primary source of enteral hydration. Two of the 10 patients were treated with this modified diet alone (Diet).

In addition to the modified diet, eight patients received recombinant methionyl-growth hormone (Protopin, Genentech Inc, South San Francisco, CA) at a dose of .14 mg/kg per day by parenteral administration. They also received supplemental parenteral enteral L-glutamine (Ajinomoto USA, Raleigh, NC) (GH+GLN+D). During the 3-week treatment period, parenteral protein requirements were provided by administering a commercially available amino acid solution rich in essential amino acids (Renamine, Baxter Health Corporation, McGraw Park, IL) supplemented with crystalline L-glutamine (average parenteral dose = .42 g/kg per day). The glutamine-supplemented amino acid mixture was combined with hypertonic glucose and fat emulsion to provide an isocaloric and isonitrogenous infusion that was comparable to that received during the control period. Vitamin and trace elements were added to the glutamine-rich solution as had been prescribed during the control period and electrolytes continued to be adjusted to maintain normal blood concentrations. For those patients not receiving parenterally infused nutrients, L-glutamine powder was provided enterally at an average dose .63 g/kg per day, which was slightly higher than the parenteral dose because it was assumed that a portion of enterally administered glutamine would be malabsorbed.

Throughout the entire 28-day study period, all enteral intake and stool output were weighed, and the calorie, nitrogen, fat, water, and sodium contents were determined. Nutrient balance and net absorption were then calculated from the measured enteral intake and stool losses. Weight was recorded daily. Twenty-four hour urinary creatinine was measured daily during the control period to identify the degree of skeletal muscle mass depletion. Blood samples were analyzed biweekly to monitor response to therapy.

##### Details of the Study

**Determination of nutrient intake.** All enteral diets were provided by the Clinical Research Center's metabolic kitchen. Over the entire 28-day study period, all administered food was weighed and fluid measured before consumption. The total daily intake of protein, carbohydrate, fat, sodium, and water (including the water content of all food and beverages) was determined by a computer program (GCRC Diet Planner, Version 2.03, Clinical Study Center, University of California, San Francisco, CA), which translated the gram weight of intake into nutrient composition. For food sources not listed in the computer program, nutrient values were determined either from product information or from *Bowes and Church's Food Values Portions Commonly Used*.<sup>18</sup> The nutrient composition of all tube feedings was determined from the manufacturer's specifications. On random days of the study, duplicate patient trays were prepared and food analyses confirmed the nitrogen, fat, and sodium content of the diet.

Daily caloric intake was expressed as the gross energy content of the diet (ie, the heat of combustion) rather than metabolizable energy (heat of combustion minus fecal and urinary calories).<sup>19</sup> The caloric values were then confirmed by actual food analysis determined by bomb calorimetry (Hazelton Laboratories America, Inc., Madison, WI). The total and soluble dietary fiber content of the control and treatment diets was calculated from standard tables.<sup>20,21</sup> Supplemental soluble fiber dose was determined by weighing a preportioned serving at the beginning and the end of each 24-hour study period.

**Measurement of nutrient losses.** All stool was collected for consecutive 24-hour periods between 7:30 AM and 7:30 AM beginning on the morning after admission and continuing until completion of the study. Samples were frozen at  $-20^{\circ}\text{C}$ . At the end of the study, the samples were thawed; liquid stool was blended and known quantities of distilled water added to semi-solid stool before blending. The homogenized stool samples were then analyzed for calories, nitrogen, and fat as previously described.<sup>17</sup> Stool nitrogen (grams) was converted to stool



protein (grams) by multiplying by 6.25. Calories (kcal) derived from stool protein were determined by multiplying the gram quantity of stool protein by 5.65 (23.64 kJ).<sup>18</sup> Stool fat calories (kcal) were determined by multiplying the quantity of stool fat (grams) by 9.35 (39.12 kJ).<sup>18</sup> Stool carbohydrate calories were determined by subtracting the sum of stool protein and fat calories from the total stool calories. The gram quantity of stool carbohydrate was then estimated by dividing stool carbohydrate calories (kcal) by 4.2 (17.57 kJ).<sup>18</sup> The sodium concentration of the stool was determined by use of a flame photometer (Instrumentation Laboratory, Lexington, MA). Stool wet and dry weights were determined by weighing the samples before and after 72 hours of drying in a 90°C oven (Precision Scientific Co, Chicago, IL). Stool water was defined as the difference between the wet and dry weight of the stool.

**Nutritional assessment and patient monitoring.** Body weight was recorded each morning to the nearest .1 kg using a leveled platform scale (model SR2MI01, Acme Scale, Oakland, CA). Ideal body weight was determined from standard tables.<sup>22</sup> All blood chemical and urine analyses were determined using standard hospital analytical techniques. Creatinine height index (CHI) was calculated from the mean 24-hour urinary creatinine excretion rate during the control period. Actual excretion was compared with the expected excretion rate for an individual of similar height, frame size, and sex, and the values were expressed as a percent of the standard.<sup>23</sup> A radioimmunoassay technique was used to determine the plasma concentration of insulin-like growth factor-one (IGF-1).<sup>24</sup>

**Calculations of nutrient absorption.** The net absorption of nitrogen, fat, carbohydrate, calories, sodium, and water was calculated by subtracting the quantity present in the stool from the enteral intake for each 24-hour period. The efficiency of nutrient absorption (percent of intake absorbed) was calculated by dividing the quantity absorbed by nutrient intake and multiplying the result by one hundred. The ability to absorb food weight was determined by subtracting 24-hour stool weight from the total weight of all food and beverages consumed during that 24-hour period. The percent of food weight absorbed was calculated by dividing the quantity absorbed by the total weight of intake and multiplying the result by one hundred.

### Statistical Analysis

Data were analyzed using standard statistical software (StatView No. 512, Abacus Concepts, Inc, Berkeley, CA) on a Macintosh SE personal computer (Apple Computer, Cupertino, CA). Paired Student's *t* tests were used to determine differences between the control period and the final week of study. Non-paired Student's *t* tests were used to identify differences in nutrient intake between the GH+GLN+Diet-treated patients and those treated with the modified Diet alone. Simple linear regression analysis was used to describe the relationship between dependent and independent variables. A *p* value  $\leq .05$  was considered statistically significant. Results are expressed as means  $\pm$  SEM.

### RESULTS

The clinical characteristics of the patients are provided in Table I. The time elapsed since the last surgical resection

averaged  $6 \pm 1$  years. Mean jejunal-ileal length was 37 cm (range 8 to 90 cm) for the GH+GLN+Diet-treated patients. The jejunal-ileal length of the two patients treated with Diet alone ranged from 65 to 120 cm. In all patients the remnant of small intestine was in continuity with the remaining colon. Before admission, six patients received parenteral nutrition at home 6 to 7 d/wk. Two patients (#2 and #7) were unable to receive IV nutrient infusion due to central vein thrombosis and received daily administration of elemental or semi-elemental enteral tube feedings; these patients were severely undernourished when their weight and CHI were compared with healthy individuals (Table I). Two additional patients (#5 and #10) were maintained at home on an oral diet supplemented occasionally with infusion of isotonic fluids and electrolytes to maintain normal hydration and serum electrolyte concentrations; these patients were also less than optimally nourished (Table I).

At the time of admission, body weight was  $87 \pm 49$  of ideal body weight.<sup>22</sup> Creatinine height index was  $79.0 \pm 5.9\%$  of normal.<sup>23</sup> All patients remained clinically stable throughout the study period. Weight gain over the 28-day admission period averaged  $5.4 \pm 1.2$  kg. Blood concentrations of urea nitrogen, creatinine, glucose, aspartate-aminotransferase, alkaline phosphatase, and total bilirubin did not vary significantly throughout the study. Treatment with GH+GLN+Diet resulted in a significant increase in plasma concentration of IGF-1 ( $110 \pm 25$   $\mu$ g/L at baseline to  $478 \pm 112$   $\mu$ g/L by the end of the fourth week, *p*  $\leq .01$ ). Serum concentrations of IGF-1 remained relatively stable for the patients treated with Diet alone ( $152 \pm 7.5$   $\mu$ g/L at baseline to  $184 \pm 23.5$   $\mu$ g/L by the end of the fourth week).

### Nutrient Intake

Average daily enteral intake during the control period and the final week of treatment is provided in Table II. For the GH+GLN+Diet-treated patients, the composition of the enteral diet consumed during the control period consisted of  $51.7 \pm 4.8\%$  of total caloric intake as carbohydrate,  $29.6 \pm 4.3\%$  as fat, and  $18.7 \pm 1.4\%$  as protein. Total dietary fiber intake averaged 1 g per

TABLE I  
Patient characteristics

Patient group	Sex	Age (y)	Diagnosis	Remaining bowel				Nutritional status	
				Years since resection	Jejunum/ileum (cm)	Ileocecal valve	Colon/rectum	Ideal body weight (percent of ideal)	Creatinine height index (percent of normal)
GH + GLN + Diet									
1	M	51	Small bowel volvulus	0.5	65	+	All	74.3	54.5
2	M	68	SMA thrombosis	8	30	—	TDR	69.9	61.9
3	F	44	Crohn's disease	9	90	—	TDR	95.2	89.7
4	F	37	SMA thrombosis	7	30	—	TDR	113.0	100.0
5	F	28	Trauma to SMA	6	15	—	TDR	93.9	90.1
6	F	31	Venous ectatic disease	5	24	—	SCR	89.6	77.7
7	M	45	SMA thrombosis	7	30	—	TDR	77.1	50.7
8	F	42	Small bowel volvulus	11	8	—	TDR	94.3	96.2
Diet									
9	M	52	Small bowel volvulus	1	65	+	All	80.1	75.1
10	M	34	Crohn's disease	5	>120	—	TDR	81.6	100.0

SCR, sigmoid colon and rectum; +, present; -, absent. //

~220 kcal (921 kJ). Soluble fiber provided approximately 20% of total fiber intake. The composition of the baseline enteral intake of the two patients treated with Diet alone was similar to the other patients:  $48.6 \pm 3.4\%$  of total caloric intake from carbohydrate,  $30.1 \pm 2.3\%$  from fat, and  $21.4 \pm 1.0\%$  from protein. Total dietary fiber intake averaged 1 g per ~180 kcal (753 kJ) with soluble fiber providing approximately 19% of total fiber intake. During the control period, food weight, water, and sodium intakes were also similar among all patients.

For the GH+GLN+Diet-treated patients, the percent of total calories derived from carbohydrate increased significantly to provide  $61.3 \pm 4.1\%$  of total caloric intake ( $p \leq .03$  vs the control period); percent fat intake decreased significantly to  $17.9 \pm 3.1\%$  ( $p \leq .01$  vs the control period), and protein intake remained relatively constant at  $20.8 \pm 1.7\%$ . There was a tendency for caloric intake to decrease as dietary fat was replaced with carbohydrate and fiber-containing foods, which provided greater food volume. Total dietary fiber intake increased to provide 1 g of fiber per ~100 kcal ( $p \leq .002$  vs control period). Soluble fiber intake also increased significantly (from 2.47 g/d during the control period to  $5.58 \pm 1.37$  g/d by the fourth week of study,  $p \leq .05$ ) and provided ~24% of the total fiber intake. The composition of the modified enteral intake of the two patients treated with Diet alone was similar to the other patients:  $60.6 \pm .8\%$  carbohydrate,  $20.0 \pm .6\%$  fat, and  $19.4 \pm .3\%$  protein. Both total and soluble fiber intake was similar to that which was consumed by the GH+GLN+Diet-treated patients during their final week of treatment. For all patients, food weight and the mean intakes of water and sodium were well matched to that which was consumed during the control period (Table II).

For the GH+GLN+Diet-treated patients, parenteral nutrition provided  $26 \pm 4$  kcal/kg per day ( $109 \pm 17$  kJ/kg per day) and  $1.2 \pm .2$  g of protein/kg per day during the control period. These values did not differ significantly from the calories or protein infused during the final week of study,  $23 \pm 6$  kcal/kg per day ( $96 \pm 25$  kJ/kg per day) and  $1.1 \pm .2$  g of protein/kg per day. For the patients treated with Diet alone, parenteral nutrition provided  $29 \pm 7$  kcal/kg per day ( $121 \pm 30$  kJ/kg per day) during the control period and  $25 \pm 6$

kcal/kg per day ( $105 \pm 25$  kJ/kg per day) during the final week of treatment. Because the Diet-treated patient tended to consume a greater quantity of enteral protein IV protein was provided at a slightly lower dose than that which was administered to the GH+GLN+Diet-treated patients ( $0.8 \pm .2$  g/kg per day during the control period and  $.7 \pm .2$  g/kg per day during the final week of treatment). Total protein intake (enteral + parenteral) during the control period ( $2.4 \pm .2$  g/kg per day GH+GLN+Diet vs  $2.8$  g/kg per day Diet alone) and the final week of treatment ( $2.4 \pm .2$  g/kg per day GH+GLN+Diet vs  $2.5 \pm .3$  g/kg per day Diet alone) did not differ between the two groups.

### Nutrient Absorption

Stool output of the GH+GLN+Diet-treated patients was  $1,783 \pm 414$  g/d during the control period and decreased to  $1,308 \pm 404$  g/d ( $p \leq .05$ ) during the fourth week of study. This decrease in stool output was associated with significant increases in the ability to absorb food weight ( $p \leq .0001$ ), calories ( $p \leq .003$ ), protein ( $p \leq 0.006$ ) carbohydrate ( $p \leq .02$ ), water ( $p \leq .002$ ), and sodium ( $p \leq .04$ ) (Table III). The efficiency of fat absorption did not change ( $61.0 \pm 5.3\%$  to  $60.3 \pm 7.9\%$ ,  $p = \text{NS}$ ). However, fat absorption was inversely correlated with the change in soluble fiber intake ( $r = .80$ ,  $p \leq .02$ ).

Stool output of the two patients treated with Diet increased from 1,117 to  $329$  to  $1,334 \pm 503$  g/d. Treatment with Diet alone did not influence the ability to absorb food weight, calories, protein, fat, carbohydrate, water, or sodium (Table III).

The percent changes in the efficiency of nutrient absorption from baseline to the final week of study for the GH+GLN+Diet-treated patients are shown in Figures 1 and 2 for the patients treated with Diet alone. The percent changes in stool volumes are also shown.

### DISCUSSION

Upon admission, the patients in this study were unable to maintain adequate hydration or nutritional status with enteral intake and thus required the parenteral administration of nutrients. Body weight was less than optimal and the baseline determination of CHI identified moderate-to-severe skeletal muscle depletion. Although

TABLE II  
Enteral intake

	Control		Week 4	
	GH + GLN + Diet	Diet	GH + GLN + Diet	Diet
Weight (g/d)	$3352 \pm 464$	$3368 \pm 351$	$3540 \pm 414$	$3913 \pm 803$
Calories (kcal/d)*	$2692 \pm 520$	$3553 \pm 483$	$2367 \pm 374$	$3433 \pm 612$
Protein (g/d)	$88.6 \pm 18.6$	$135.2 \pm 24.6$	$86.7 \pm 15.1$	$117.5 \pm 19.4$
Fat (g/d)	$96.1 \pm 26.0$	$115.6 \pm 24.5$	$44.9 \pm 9.3^\dagger$	$73.0 \pm 11.0$
Carbohydrate (g/d)	$307.9 \pm 51.2$	$406.9 \pm 27.5$	$347.0 \pm 54.9$	$497.0 \pm 95.2$
Total fiber (g/d)	$12.42 \pm 1.99$	$19.7 \pm 0.15$	$23.6 \pm 3.5^\ddagger$	$24.7 \pm 5.6$
Soluble fiber (g/d)	$2.47 \pm 0.44$	$3.69 \pm 0.05$	$5.58 \pm 1.37^\S$	$4.35 \pm 0.9$
Water (L/d)	$2.826 \pm 0.392$	$2.439 \pm 0.143$	$2.900 \pm 0.368$	$2.840 \pm 0.366$
Sodium (mEq/d)	$151.4 \pm 24.4$	$185.3 \pm 21.1$	$162.3 \pm 23.4$	$202.7 \pm 35.5$

\*1 kcal = 4.184 kJ.

$^\dagger p \leq .03$  vs control period.

$^\ddagger p \leq .002$  vs control period.

$^\S p \leq .05$  vs control period.

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TABLE III  
Weight and nutrient absorption

	Control		Week 4	
	GH + GLN + Diet (percent absorbed)	Diet (percent absorbed)	GH + GLN + Diet (percent absorbed)	Diet (percent absorbed)
Weight (g/d)	50.6 ± 6.5	66.3 ± 4.9	68.2 ± 7.1*	67.14 ± 6.08
Calories (kcal/d)†	60.1 ± 6.0	84.5 ± 5.0	74.3 ± 5.0‡	81.6 ± 4.25
Protein (g/d)	48.8 ± 4.8	73.9 ± 4.0§	63.0 ± 5.4¶	68.9 ± 8.2
Fat (g/d)	61.0 ± 5.3	91.3 ± 4.2§	60.3 ± 7.9	81.6 ± 10.2
Carbohydrate (g/d)	60.0 ± 9.8	84.8 ± 6.0	81.5 ± 5.3**	85.5 ± 1.2
Water (L/d)	45.7 ± 6.7	57.6 ± 8.4	65.0 ± 7.3††	56.6 ± 11.2
Sodium (mEq/d)‡‡	49.0 ± 9.8	54.9 ± 20.3	69.6 ± 6.5§§	56.7 ± 22.6

\* $p \leq .0001$  vs control period.

†1 kcal = 4.184 kJ.

‡ $p \leq .003$  vs control period.

§ $p \leq .04$  vs GH + GLN + Diet.

¶ $p \leq .006$  vs control period.

\*\* $p \leq .02$  vs control period.

†† $p \leq .002$  vs control period.

‡‡ = 1 mEq = 1 mmol.

§§ $p \leq .04$  vs control period.

patients with the short bowel syndrome are frequently encouraged to increase enteral food intake in an attempt to decrease dependency on parenteral nutrition, the patients in this study had failed to adapt to the provision of enteral nutrients.

The exogenous administration of growth hormone (or its analogue) has been shown to influence bowel adaptation by enhancing mucosal hyperplasia after extensive intestinal resection in animals.<sup>25,26</sup> Growth hormone is also known to increase colonic mass and biomechanical strength;<sup>27</sup> these effects may enhance the reservoir function of the colon or influence peristalsis, thus prolonging transit time. In addition, IGF-1 production, which is regulated by growth hormone, has been shown to enhance bowel hyperplasia and hypertrophy in rats after extensive jejunio-ileal resection.<sup>28</sup> Furthermore, exogenous growth hormone increases water and sodium absorption in the small intestine and in the colon<sup>29</sup> and appears to regulate amino acid absorption.<sup>30</sup>

Glutamine is a primary fuel source for both the enterocytes and the colonocytes and serves as an essential precursor for purine and pyrimidine biosynthesis.<sup>7</sup> Supplemental glutamine has been shown to accelerate postresection hyperplasia,<sup>8</sup> prevent intestinal atrophy in humans receiving parenteral nutrition,<sup>31</sup> and enhance glucose<sup>9</sup> and sodium absorption.<sup>10</sup>

Growth hormone in combination with glutamine may exert an additive effect on bowel morphology and function. IGF-1 induces ornithine decarboxylase,<sup>32</sup> the rate-limiting enzyme in the biosynthesis of polyamines, which play a central role in intestinal cell growth and proliferation.<sup>33</sup> Glutamine is a required substrate for ornithine decarboxylase and an essential precursor for nucleotide biosynthesis. Animal studies have demonstrated that the inhibition of ornithine decarboxylase prevents enhanced cellularity in residual bowel after intestinal resection,<sup>34</sup> whereas glutamine-supplemented nutrition administered in combination with IGF-1 enhances protein deposition in the residual mucosa after small bowel resection compared with trophic effects of glutamine or IGF-1 alone.<sup>35</sup> Furthermore, both growth

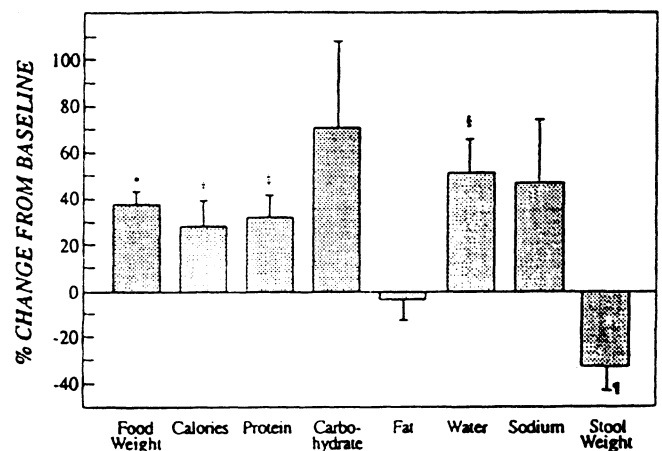


FIG. 1. Changes in the efficiency of nutrient absorption and stool output with growth hormone, glutamine, and diet. Treatment with GH+GLN+Diet produced significant changes in the efficiency of nutrient absorption. These changes resulted in a significant decrease in stool output. \* $p \leq .0003$ , † $p \leq .03$ , ‡ $p \leq .009$ , § $p \leq .008$ , ¶ $p \leq .01$ .

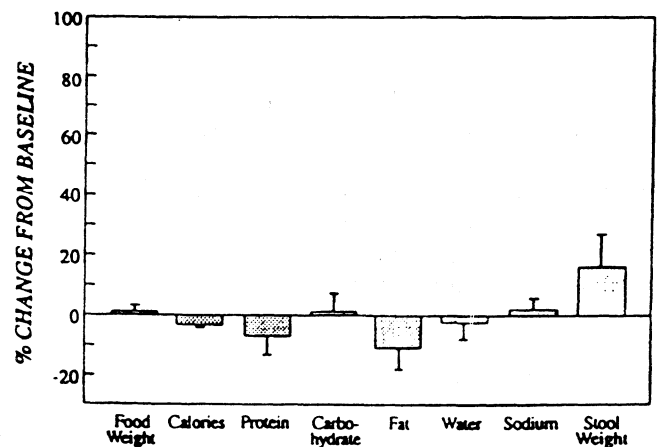


FIG. 2. Changes in the efficiency of nutrient absorption and stool output with diet alone. Treatment with Diet alone produced no change in the

processes that may be enhanced by the provision of bowel-specific fuels such as glutamine.

In addition to growth hormone and glutamine, the patients in this study received a high-carbohydrate, low-fat diet supplemented with fiber. Although controversy exists over the role of diet in the management of the short bowel syndrome, several studies have demonstrated that dietary manipulation (eg, restricting fat) does not significantly influence nutrient absorption.<sup>14-16</sup> These authors argue that clinicians should adopt a more liberal attitude regarding the enteral diets of these patients. Others, however, recommend diets restricted in fat,<sup>36,37</sup> but high in carbohydrate<sup>38</sup> and specific fibers.<sup>39</sup> A recent report has documented that a high-carbohydrate, low-fat diet provided for a 4-day period can decrease the fecal loss of calories in short bowel patients with normal colons.<sup>38</sup>

The rationale for providing an increased carbohydrate or fiber-containing diet to patients with short bowel syndrome is that the malabsorbed carbohydrates and nondigestible fibers pass into the colon, where they can be fermented by bacteria to produce short-chain fatty acids. These organic acids are rapidly absorbed by the colonic mucosa and can be used for energy;<sup>40</sup> thus, some of the carbohydrate calories that would have otherwise been lost because of upper-intestinal malabsorption can be salvaged by this process.<sup>41</sup> Furthermore, short-chain fatty acids are known to enhance sodium and water absorption<sup>42</sup> and exert trophic effects both in the small intestine and in the colon.<sup>43</sup> In addition to their role in the production of short-chain fatty acids, specific soluble fibers have been shown to prolong gastrointestinal transit time<sup>12,13</sup> and elicit stimulatory effects on small and large bowel mucosal growth and cell proliferation.<sup>11,44</sup> Thus, because all patients in our study had colonic remnants, a high-carbohydrate, low-fat diet supplemented with fiber was provided in an attempt to enhance nutrient absorption. However, the provision of this diet without glutamine or growth hormone failed to alter nutrient absorption in two subjects.

Three weeks of combined therapy (GH+GLN+Diet) significantly enhanced calorie, protein, carbohydrate, water, and sodium absorptive efficiency. The effect of this therapy on total caloric absorption was somewhat blunted by the adverse effect of soluble fiber on fat absorption. However, despite the addition of these fermentable soluble fibers and other insoluble fibers that typically increase stool bulk and weight,<sup>45</sup> stool output decreased  $33.0 \pm 10.0\%$  ( $p \leq .01$ ). These adaptive changes were achieved in all GH+GLN+Diet-treated patients, even though seven of the eight individuals had undergone resection 5 to 11 years before participation in the study.

Additional studies are now underway to determine if this therapy can allow for a reduction or an elimination in parenteral nutrient requirements. In addition, a follow-up program is in progress to assess the long-term effects of this therapy on nutritional status, body composition, and liver and kidney function. Additional studies are needed both to determine whether such treatment would exert greater effects shortly after resection and to better define the optimal diet,

particularly the type and quantity of fiber to administer. The use of this therapy in patients with high-output ostomies has not been systematically evaluated and would most likely require further dietary modification.

In summary, the combined administration of exogenous growth hormone, glutamine and a diet high in complex carbohydrates and fiber and low in fat enhanced nutrient absorption from the remnant bowel after major intestinal resection. These functional changes occurred after 3 weeks of therapy in a group of patients who previously failed to adapt to the provision of enteral nutrients. Additional study is needed to determine if this therapy can offer an alternative to long-term dependence on total parenteral nutrition or intestinal transplantation for patients with the severe short bowel syndrome.

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