
Presidential Address

Nutritional Support: Service in Need of New Science*

JOHN L. ROMBEAU, M.D.

From the Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

I have always believed that the best presidential talks were those that challenged, provoked, stimulated, and occasionally angered but nevertheless resulted in further thought and, in some instances, action. Given this personal bias, I have chosen as my subject an issue that has concerned me greatly during the past few years. This issue is that we as a Society have insidiously become a group of technically oriented professionals who are providing the highest level of nutritional support *service* without the highest level of nutritional support *science*. I believe that we do not have the highest level of science because of our failure to adequately support basic nutritional research and well-focused clinical efficacy trials. Because of these concerns I believe that the future of nutritional support as a credible specialty is at risk. I strongly believe that unless there is greater financial support given to, and emphasis placed upon basic nutritional research and the execution of well-controlled, well-focused clinical trials, the future of nutritional support will be relegated to an ancillary service with cookbook treatment algorithms and with neither scientific foundation nor major credibility. My thesis is that an increase in the quality and scope of nutrition research and the acquisition of confirmatory clinical outcome data in specific patient populations will ensure the future of both the scientific foundation of our practice and the professional competence of nutritional support clinicians.

NUTRITIONAL RESEARCH

What is the evidence to support the premise that nutritional research is waning and does this evidence relate to each of our disciplines? The future of any science lies in the ideas, energy, enthusiasm and dedication of its youth. I believe that these qualities are best exemplified in the student members of our disciplines. It concerns me greatly that student interest in nutrition is waning. This is documented by the sharp decrease in the number of A.S.P.E.N. student members as shown in

Figure 1. When compared with 5 years ago the number of student members has decreased by more than 50% and the trend is continuing downward. With regard to physicians, the competition to attract the best and the brightest investigators into nutritional research is becoming increasingly difficult. To use my own specialty of general surgery as an example, during the past decade the emergence of exciting new research advances in organ transplantation, immunology, cardiac physiology, and wound healing, have made it increasingly difficult to attract the would-be investigator into surgical nutrition and metabolism. A further concern relates to decreases in available manpower and reductions in time of training. The time that salaried residents and fellows may allocate to research is becoming increasingly restricted. Because of concerns of too frequent night call schedules and exhaustive clinical work loads, plans are now being drafted to reduce the amount of residency work. Marked regulatory constraints are paradoxically being placed upon residency program directors to decrease the number of trainees concomitant with the proposed reduction in residency work loads. Therefore, I believe that the available physician manpower and potential time for research training will become markedly reduced. To compound these problems, federal support of residency training has also been reduced which threatens to eliminate support of research salaries during residency training.¹ I conclude that more funds will be used to meet clinical needs with less monies available for research.

The quality and quantity of physician training in clinical nutrition is of great concern to me. I strongly believe that greater emphasis must be placed upon the teaching of basic nutritional science. In a recent survey only 23% of clinical nutrition training programs provided a structured basic science educational component.²

There are similar concerns about research opportunities for dietitians. In a recent survey of 424 nutritional support dietitians nearly 80% wanted to spend more time in nutritional research.³ Although 16% of these dietitians had written research proposals, fewer than 10% had their projects approved and/or funded.

Are nutritional support nurses affected similarly? Problems exist in both the areas of sufficient numbers of personnel and adequate fundings. In a recent review of 258 nursing research applications, 65% of proposals funded by private organizations and 59% of intramurally supported projects were limited to \$3000 or less.⁴

Received for publication, May 15, 1989.

Accepted for publication, May 15, 1989.

Reprint requests: John L. Rombeau, M.D., Department of Surgery, Hospital of the University of Pennsylvania, 3400 Spruce Street-4th Floor, Philadelphia, PA 19104.

* Address was delivered at A.S.P.E.N.'s 13th Clinical Congress on February 5, 1989 in Miami Beach, FL.

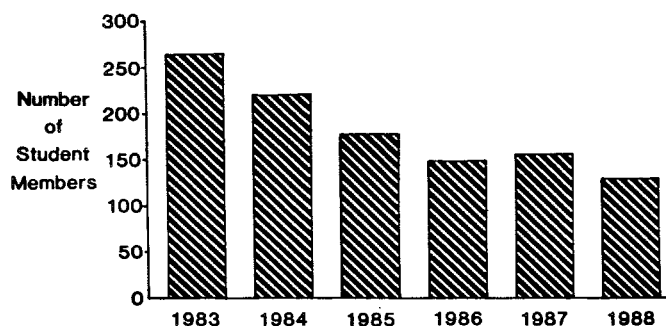


FIG. 1. Chronologic trend in A.S.P.E.N. student membership (Source—A.S.P.E.N. National Office, January 1989).

Hospital pharmacists are acutely aware of their research needs. In his Whitney lecture to the American Society of Hospital Pharmacists entitled "Research the Cornerstone of Pharmacy Practice," Eckel commented "Rather than lament the growth in clinical pharmacy, we need to expand the scientific foundation of clinical practice to ensure continued acceptance of our professional role."⁵

How should the support of nutrition research be increased? I would like to make two recommendations: firstly, major attempts must be made to obtain more monies for young nutritional investigators in each of our disciplines and secondly, new scientific and medical technologies must be integrated into nutrition research.

The principal sources of funding for new nutritional investigators are the National Institute of Health (NIH), United States Department of Agriculture and Industry. The NIH continues to be the largest single supporter of nutritional research in this country comprising 70% of federal expenditures in support of human nutrition research and training.⁶ I encourage all investigators to read the 11th Annual Report of the NIH Program in Biomedical and Behavioral Nutrition Research and Training.⁶ In this report, many opportunities and awards are listed for young nutritional investigators. These awards include the Research Career Development Award, Clinical Investigator Award, Physician Scientist Award and New Investigator Award. Despite the availability of these awards, the number of persons with professional degrees and predoctoral students supported by NIH training grants and fellowships in nutrition has not increased significantly when compared to 10 years ago.⁶ Furthermore, the current nutritional dollars expended as a percentage of total NIH obligations has not significantly increased from 1977.⁶

Industry is a major potential funding source for nutritional research for each of our disciplines. Industry continues to support a large percentage of research activities in many countries as documented in a study from the National Science Foundation comparing percent industrial research expenditures for 1970 and 1984.⁷ As shown in Figure 2, the percentage of industrial research funding is increasing in every country except for the United Kingdom. Despite initial concerns of industrial support of university and institutional based research activities, excellent working relationships now exist in most instances and the *university* as well as industry benefits from these relationships.⁸

The second recommendation to improve nutritional research is to integrate new scientific and medical technologies into nutritional investigations. We are now in the midst of a revolution in molecular and cellular, biotechnology. Examples of these technologies are shown in Table I. Cellular protein activity can be altered and defective enzyme functions repaired using recombinant DNA and protein engineering techniques.⁹ *In vivo* metabolic activity in muscle can be measured noninvasively with ³¹P magnetic resonance spectroscopy.¹⁰ Cells and bacteria can be transformed into factories to produce custom made monoclonal antibodies or valuable hormones and growth factors such as human growth hormone.¹¹ These advances have primarily been made in the past decade and they are now diffusing into nutritional-metabolic investigations.^{12,13} I am not suggesting that all of us should become molecular biologists. However, it is imperative to learn the language and to be familiar with potential applications of molecular biology to nutrition. Clearly these new technologies can be applied to nutritional support research.¹⁴ In our own area of investigation of intestinal fuels and gut adaptation, we have shown that feeding diets with selected fuels such as soluble fiber and short chain fatty acids produces trophic^{15,16} and functional^{17,18} benefits to the intestinal mucosa when compared to diets without these fuels. The question emerges as to how these effects may be mediated? By using techniques such as immunohistochemistry, investigations can now be performed to qualitatively and quantitatively identify those cells that produce enterotrophic hormones such as enteroglucagon.¹⁹ These measurements may partly explain the means by which dietary delivered intestinal fuels mediate gut trophism. I believe that these revolutionary technologies will permeate all aspects of clinical nutrition and thus will have profound

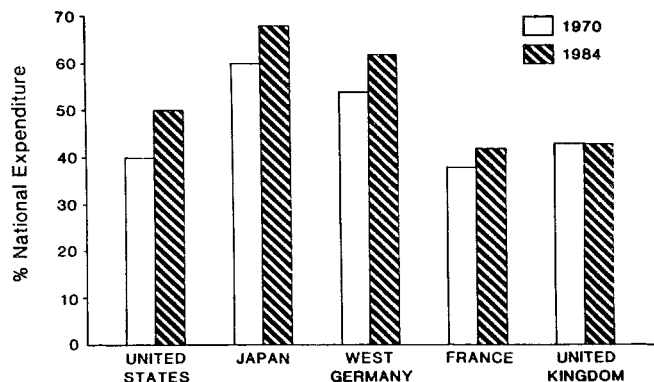


FIG. 2. Proportion of national research expenditure financed by industry in five countries in 1970 and 1984 (National Science Foundation—modified from Ref. 7).

TABLE I
New and improved biotechnologies applicable to nutritional research*

Recombinant DNA
Monoclonal antibodies
Gene synthesis and sequencing
³¹ P NMR spectroscopy
Cell and tissue culture techniques
Fermentative processes
Enzymology

* Amended from Ref. 6.

effects on functions of nutritional support teams during the next decade. The pharmacists will probably be influenced to the greatest extent. Major findings are emerging in the area of nutritional pharmacology that involve the effects of growth factors,²⁰ cytokines,²¹ and nutrient drug manipulations²² to enhance substrate utilization. The nurse will have to learn the actions and side effects of many of these pharmacologic agents which will undoubtedly be administered concurrently with different nutritional regimens. The dietitian must also understand the effects of these adjuvant therapies on nutrient utilization, energy expenditures, nutrient requirements, and recommended dietary allowances during stress and disease. Finally, the physician must have a basic understanding of the rationale, mechanism of actions, indications, and contraindications for these new adjuvant therapies. I believe that these new therapies will result in a shifting of priorities in nutritional care. There will be less emphasis on how to provide appropriate quantities of basic nutrients, and more emphasis on how to modify the metabolic and physiologic environment to the patient's advantage.

CLINICAL OUTCOME DATA

What about the absence of confirmatory clinical outcome data? Gertrude Stein said "A difference to be a difference must *make* a difference." Ms. Stein's comment might be paraphrased by stating that if parenteral and enteral nutrition is to truly make a difference, it must improve clinical outcome. As a clinical nutritionist I am justifiably proud of the thousands of lives that have been saved directly due to nutritional support. For example, when I was a junior surgical resident, the severe short bowel syndrome was 100% fatal. In 1989, directly as the result of nutritional support, these patients are not only alive but they are leading productive lives. However, we must not become complacent with our accomplishments. Interestingly, we are members of a Society based on a highly sophisticated form of medical care at costs exceeding a billion dollars annually, and escalating at a rate of 10 to 12% per year²³ for which there is very little published data to support the premise that nutritional support is a difference that makes a difference. Recently I reviewed the published clinical outcome data relating to perioperative nutritional support.²⁴ This review revealed that only three of 13 published prospective randomized controlled trials of perioperative TPN showed substantive improvement in clinical outcome. In the largest performed trial which is awaiting publication, the Veterans Administration cooperative trial, preliminary results reported to the American College of Surgeons revealed that nonseptic complications were significantly reduced with perioperative TPN, however, septic complications were significantly increased and mortality was not significantly reduced.²⁵ These findings are corroborated in the most recently performed prospective controlled trial of perioperative TPN at the National Cancer Institute.²⁶ A 53% incidence of infections was noted in the total parenteral nutrition (TPN) group compared to 18% in the control group. In the trial design a 20 to 25%

complication rate had been expected in the oral nutrition group. When the results of the first 26 patients were reviewed it was determined that there was only a 7% chance of detecting improvement with TPN even if 200 patients were added to the study.

The results of controlled trials in perioperative enteral nutrition are similar to TPN.²⁴ Only five of 12 prospective randomized controlled trials revealed substantive improvement in clinical outcome.

Those of you who disagree with my remarks and the more avid enthusiasts of generalized nutritional support will cite the inadequate sample sizes and poor research design in many of the published studies; examples of other areas of definitive medical care for which a prospective randomized controlled trial has never been performed such as appendectomy for acute appendicitis; and the ethical and teleologic question of why must we as clinical nutritionists have to justify feeding patients who cannot eat? Despite the reasonable logic and general acceptance of this rationale among nutritional support specialists, I propose that during the next decade this "self-evident" rationale will be unacceptable to hospital administrators and budgetary managers who will insist upon objective evidence to support the use of these expensive therapies.

What is the solution to the lack of confirmatory clinical outcome data? Clearly there is a major need to perform appropriately designed multicenter clinical nutritional trials. I propose that large, heterogeneous studies should not be undertaken. Such studies are enormously expensive and often provide results which are difficult to interpret. I recommend that more focused, carefully designed studies be performed such as the work by Bastow et al.²⁷ This study of 122 malnourished patients showed improved rehabilitation with postoperative enteral nutrition in a very specific group of elderly patients with hip fractures. The rehabilitation time was significantly reduced in very thin patients undergoing supplemental enteral nutrition when compared to a control group which received standard oral nutrition. This type of study can be performed with realistic costs and is clinically meaningful. I would also like to propose that the members of A.S.P.E.N. conduct well-focused studies as described. With the establishment of appropriate data registries such as successfully performed by the Oley Foundation and A.S.P.E.N. under the leadership of Dr. Howard and co-workers,²⁸ computer-networking techniques could identify the locations of selected patients and their respective nutritional support services. In this way nutritional support teams would have the opportunity to provide optimal nutritional care and advance nutritional science by participating in clinical research studies. This is also a means by which sufficient numbers of patients can be accrued to objectively answer many questions relating to therapeutic efficacy. I recommend that a central registry or foundation be established with high-level computer access to ensure the ease of modem entry for every patient started on specialized nutritional support. This will provide important pilot data and better identity problems in specific patient populations. The combined funding sources of government, private foundations and industry should be solicited to cover the costs of this enterprise.

RECOMMENDATIONS TO A.S.P.E.N.

How can A.S.P.E.N. provide better support for nutritional research? A.S.P.E.N. has unequivocally been the national leader in the provision of nutritional support and in clinical nutrition education. However, I believe that we have failed as a Society in adequately recognizing and supporting nutritional research. I submit that a major commitment to nutritional research is the foundation for the future survival of A.S.P.E.N.

I would like to make seven recommendations to A.S.P.E.N. as shown in Table II: (1) A.S.P.E.N. must increase budgetary allotments to nutritional research. With a major financial commitment it will be possible to accomplish the aforementioned goals. (2) A permanent research position should be established on the Board of Directors. This might be accomplished by appointing the Chairman of the Research Committee as a formal member of the Board. (3) The Ph.D. membership of A.S.P.E.N. must be strengthened by soliciting additional Ph.D. members of the American Society of Clinical Nutrition, Federation of the American Societies for Experimental Biology, American Federation of Clinical Research, and other research societies. (4) A basic research award should be established specifically to recognize the interaction between molecular or cellular biology and nutrition support. (5) A.S.P.E.N. should establish a central registry to include data entry for all patients on parenteral and enteral nutrition as discussed previously. (6) Industrial supporters of A.S.P.E.N. should establish research grants for young investigators in nutritional support to include all disciplines. And finally, societal priorities should be significantly altered to acknowledge that the administrative and fiscal investments in nutritional research are an insurance for the continuation of our field as a clinical care specialty.

CONCLUSIONS

The specialty of nutritional support needs to address the problems of reduced numbers of young investigators, the need for integrating new molecular biologic techniques, and the lack of confirmatory clinical outcome data. Unless aggressive strategies with financial risks are undertaken toward solving these problems, it is projected that they will increase during the next decade. If we do not provide optimal science, the future of nutritional support will be relegated to a minor ancillary care service.

It should be emphasized that these problems can be solved. The future of nutritional support as a specialty rests in our ability to improve the quality and scope of

TABLE II
Research recommendations to A.S.P.E.N.

1. Increase research budget
2. Establish research representative to Board of Directors
3. Expand and increase support of Ph.D. membership
4. Establish basic research award for nutrition-molecular biology
5. Create central registry of patients receiving nutritional support
6. Encourage industry to establish research grants for young investigators
7. Recognize importance of research for future viability of nutritional support

nutritional research. There is a major need to redefine nutritional support and nutritional research in view of the advancing technologies in molecular and cellular biology. Plans must be made to adequately design well-controlled trials to examine the effect of nutritional support on clinical outcome *in very specific patient populations*. A.S.P.E.N. must play a major role in supporting and implementing these strategies.

It is my hope that 10 years from now when we start the next century, the 23rd A.S.P.E.N. President will comment on the foresight and wisdom demonstrated by the A.S.P.E.N. membership in 1989 in recognizing the need to provide nutritional support *science with nutritional support service*. Thank you for providing me with the opportunity to have served as your President during 1988.

ACKNOWLEDGMENTS

The author is very grateful for comments from the following reviewers: Barney Sellers, R. Gregg Settle, Douglas W. Wilmore, Lyn Howard, Joel Kopple, Rolando H. Rolandelli, Patrick Twomey, and Peggi Guenter. The secretarial support of Mrs. Phyllis Schultz is gratefully appreciated.

REFERENCES

- Rikkers LF, Bland KI, Kinder BK, et al: Funding of surgical research: the Roles of government and industry. *J Surg Res* 39:208-215, 1985
- Merritt RJ, Heymsfield SB, Howard L, et al: Biennial survey of physician clinical nutrition training programs. *Am J Clin Nutr* 47:911-921, 1988
- Schiller MR: Research activities and interests of dietitians. *JPEN* 12:1-7, 1988
- Strickland OL, Burgess AW, Oberst MT, et al: Private sector support of nursing research. *Nurs Res* 36:253-256, 1987
- Eckel FM: Research—The cornerstone of pharmacy practice. Harvey A.K. Whitney Lecture. *J Hosp Pharm* 42:1717-1723, 1985
- Eleventh Annual Report of The National Institutes of Health Program in Biomedical and Behavioral Nutrition Research and Training. U.S. Department of Health and Human Services, 1988
- Smith R: Is research to be privatized? *Br Med J* 296:185-188, 1988
- Blumenthal D, Gluck M, Seashore K, et al: Industrial support of university research in biotechnology. *Science* 231:242-246, 1986
- Dinarelli CA: An update on human Interleukin-1: From molecular biology to clinical relevance. *J Clin Immunol* 5:287-297, 1985
- Jacobs DO, Maris J, Fried R, et al: *In vivo* 31P nuclear magnetic resonance (NMR) spectroscopy of rat hind limb skeletal muscle during sepsis. *Arch Surg* 116:1425-1428, 1988
- Manson JM, Smith RG, Wilmore DW: Growth hormone stimulates protein synthesis during hypocaloric parenteral nutrition. *Ann Surg* 208:136-142, 1988
- Beutler B, Cerami A: Recombinant Interleukin-1 suppresses lipoprotein lipase activity in 3T3 cells. *J Immunol* 135:3969-3971, 1985
- Flores E, Drabik M, Bistran BR, et al: The acute phase response to human recombinant mediators. *Surg Forum* 37:28-30, 1986
- Gwozdz GP, Meltzer SJ, Knodell RG: Total parenteral nutrition decreases steady-state levels of cytochrome P-450 PCN-E mRNA but does not prevent dexamethasone-induced increases in PCN-E mRNA and enzyme activity. *Clin Res* 37:2368A, 1989
- Koruda MJ, Rolandelli RH, Settle RG, et al: The effect of a pectin-supplemented elemental diet on intestinal adaptation to massive small bowel resection. *JPEN* 10:343-350, 1986
- Kripke SA, Fox AD, Berman JM, et al: Stimulation of intestinal mucosal growth with intracolonic infusion of short chain fatty acids. *JPEN* 13:109-116, 1989
- Rolandelli RH, Koruda MJ, Settle RG et al: Effects of intraluminal

- infusion of short-chain fatty acids on the healing of colonic anastomosis in the rat. *Surgery* 100:198-203, 1986
18. Zimmaro DM, Rolandelli RH, Koruda MJ, et al: Isotonic tube feeding formula induces liquid stool in normal subjects: reversal by pectin. *JPEN* 13:117-123, 1989
 19. Ghatei MA, Bloom SR: Enteroglucagon in man. IN *Gut Hormones*, vol 2, Bloom SR, Polak JM (eds). Churchill Livingstone, Edinburgh, 1981, pp 332-338
 20. Dahn MS, Lange P, Jacobs LA: Insulin-like growth factor: Production is inhibited in human sepsis. *Arch Surg* 123:1409-1414, 1988
 21. Pomposelli JJ, Flores EA, Bistrian BR: Role of biochemical mediators in clinical nutrition and surgical metabolism. *JPEN* 12:212-218, 1988
 22. Li S, Nussbaum MS, McFadden DW, et al: Addition of glucagon to total parenteral nutrition (TPN) prevents hepatic steatosis in rats. *Surgery* 104:350-357, 1988
 23. Anderson GF, Steinberg MD: DRGs and specialized nutrition support. Prospective payment and nutritional support: The need for reform. *JPEN* 10:3-5, 1986
 24. Rombeau JL, Rolandelli RH, Wilmore DW: Nutritional Support. IN *American College of Surgeon's Care of the Surgical Patient*, Wilmore DW (ed). Scientific American Publishers, New York, 1988, pp 1-39
 25. Buzby GL: Personal communication
 26. Cromack D, Moley J, Pass H, et al: Prospective randomized trial of parenteral nutrition in patients with upper GI cancer and weight loss undergoing surgical treatment. *J Surg Res* (in press)
 27. Bastow MD, Rawlings J, Allison SP: Benefits of supplementary tube feeding after fractured neck of femur: A randomized controlled trial. *Br Med J* 287:1589-1593, 1983
 28. Howard L, Claunch C, Fleming CR, et al: The outcome of Crohn's patients on home parenteral nutrition as shown in 3 years of national registry data. *Gastroenterology* 96:AL19, 1989