ing cross-infection from the anesthesia breathing circuit.

These studies are significant for several reasons. First, they emphasize the importance of the scientific method in the practice of medicine. Garibaldi et al. do not dispute that bacterial filters reduce the movement of airborne bacteria within anesthesia tubing and that bacterial colony counts are invariably lower in tubing sites that are distal to a filter than in those that are proximal. They agree that it is a logical hypothesis that bacterial filters should lower the risk of developing pneumonia. Feeley et al. similarly concede the accuracy of studies which have documented the presence of bacteria on and in anesthesia equipment. However, both have questioned the clinical relevance of these points. They expose their reservations to the next step in the deductive reasoning process, the step which often is neglected in clinical medical practice. They subject a logical hypothesis to the scrutiny of a prospective, controlled trial to determine clinical efficacy. As is often the case, the hypothesis cannot be substantiated.

These studies should also have a significant economic impact on anesthesia practice. We should stop using bacterial filters for breathing circuits until such time when equally well-designed and executed experiments cause us to question the validity of the conclusions of Garibaldi and Feeley. These studies should also cause us to evaluate the other "logical hypotheses" that have led to modifications in our practice. There are many areas that could be examined, but in the category of filters alone, we have accepted to a greater or lesser extent, millipore epidural catheter filters, gas-line filters, and filters for removing microaggregates from transfused blood. Although the value of these devices at first seems obvious, evidence that their use improves patient care is either completely lacking, in the case of the first two devices, or highly debatable, in the case of blood filters. If these devices are not clinically efficacious, then at the least, their use introduces an unnecessary expense into anesthesia practice. At the most, their use may be associated with complications which can be more serious than the disease they are intended to prevent. The best way to avoid such situations is to ensure that the scientific basis of our practice remains strong and that all "logical hypotheses" are adequately tested before they are accepted.

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Total Parenteral Nutrition in the Perioperative Period—A Time for Caution?

The state of nutrition of the surgical patient has long been a subject of discussion among anesthesiologists. Starvation, a "lack of glycogen in the liver", was first suggested by Opie and Alford in 1915 to be responsible for a susceptibility to liver damage in patients exposed to chloroform. Overnutrition by contrast, has been implicated as a major problem in the anesthetized obese patient, but concern has been mainly for physical and mechanical problems, rather than for the accompanying altered metabolism and organ function.

It was not until the early 1970s that surgeons and anesthesiologists began to truly understand the basis of altered metabolism in the starving or undernourished patient, and how anesthesia and trauma might interfere with "caloric homeostasis" in such a patient. Clearly, it was shown that vital tissues could use substrates other than glucose. A large proportion (19.6 per cent) of basal metabolic expenditure is devoted to nourishing the central nervous system. Investigations in humans and animals showed that the brain is able to utilize ketone bodies in addition to glucose. It also became apparent that the myocardium can utilize ketone bodies as metabolic fuel, and that both the myocardium and the liver can utilize free fatty acids. In fact, evidence accumulated

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to show that by raising plasma levels of free fatty acids, starvation lessened rather than enhanced the anesthetic depression of myocardial and hepatic function in experimental animals. The effects of anesthetic agents on metabolic pathways, and particularly on substrate utilization by individual organs, have an important bearing on altered organ function during prolonged anesthesia.

Knowledge of the metabolic needs and altered physiological control processes in the injured patient, has increased rapidly. There have been notable advances in the understanding of the complex endocrine interrelationships governing the use of body fuels following major trauma: e.g., the reversed insulin/glucagon ratio, and the greatly increased caloric and nitrogen requirements. In addition, attention has focused on specific forms of intravenous feeding for patients with burns, renal failure, hepatic failure, myocardial failure, and respiratory failure.

Anesthesiologists are thus supplied with vastly increased information on which to base the management of patients receiving parenteral nutrition, both in the operating room and in the intensive care unit. However, the increasing use of total parenteral nutrition is now coming under clinical scrutiny. The widespread use of this form of therapy has predictably led to unsuspected important complications such as the hyperosmolar, hyperglycemic, non-ketotic coma syndrome; dangerous hypoglycemia following unplanned discontinuation of high concentrations of intravenous glucose; hypophosphatemia; metabolic acidosis; and the technical complications of central intravenous lines. These problems can all be avoided by good management based on an understanding of the basic metabolic background involved in hyperalimentation. A new concern in the use of high concentrations of glucose, infused intravenously in an attempt to supply adequate calories to the undernourished, septic or injured patient, is reported in this issue of Anesthesiology by Askanazi et al. The authors show that the increased CO₂ production resulting from the metabolism of large quantities of glucose in patients with injury or sepsis may result either in the need to initiate artificial ventilation, or in failure to wean the patient from long-term ventilation. This study draws attention to an unsuspected problem in managing patients receiving hyperalimentation in the peroperative period: the relationship of intravenous infused energy sources to the patients' non-protein Respiratory Quotient (RQ) and his respiratory reserve. The only logical approach to avoiding such unrecognized metabolic consequences of parenteral nutrition is to make measurements of energy requirement in the acutely ill patient prior to initiating therapy, and to repeat the measurement of Respiratory Quotient during hyperalimentation.

Recently, there has been an increased interest in the measurement of human energy expenditure. Acute conditions, such as major injury and infection, are associated with weight loss and tissue depletion during hospitalization. The availability of potent nutritional therapy raises many questions regarding energy expenditure and utilization, questions that were never previously involved in the treatment of these patients. Kinney has underlined the fact that no other segment of clinical management shows less concern with achieving a balance between input and output than in the matter of energy. Sophisticated plans of parenteral nutrition, combinations of glucose, fat, and amino acids, are often based on an assumed level of energy expenditure, rather than on actual measurements. It is possible to determine the ratio of carbohydrate, fat, and protein oxidation by measuring O₂ consumption, CO₂ production, and N₂ excretion. The total energy expenditure is the sum of a relatively constant component, the “basal rate”, and of increments produced by physical activity, injury, sepsis, and response to food intake. Thus, the non-protein Respiratory Quotient depends on the type of substrate being metabolized:

\[
1 \text{ glucose } + 6 \text{ O}_2 \xrightarrow{RQ = 1.0} 6 \text{ CO}_2 + 6 \text{ H}_2\text{O} \\
\text{ (Energy yield: 673 kcal)}
\]

\[
1 \text{ palmitate } + 23 \text{ O}_2 \xrightarrow{RQ = 0.7} 16 \text{ CO}_2 + 16 \text{ H}_2\text{O} \\
\text{ (Energy yield: 2398 kcal)}
\]

At the level of the whole organism, substrate distribution is regulated to meet the variable needs of organs and tissues. The main factors which contribute to the selection of fuels by individual organs are: the concentration of the fuel in the plasma resulting from release from stores of triglyceride or glycogen; the entry of the substrate from plasma into tissue which is controlled by hormones (including insulin, glucagon, and epinephrine); and the presence in the tissue of the appropriate enzyme required for the degradation of the substrate or fuel. In the case of the brain, the impressive caloric need is compounded by another biologic fact, the blood-brain barrier. The most significant effect of the blood-brain barrier in fuel metabolism is the exclusion of large molecules from the central nervous system, i.e., either albumin-bound free fatty acids or complex lipids. Thus, only water
soluble substrates, such as glucose and ketoacids, are capable of easily crossing the blood-brain barrier. The bulk of energy for most other tissues and organs is normally provided by lipid-bearing macromolecules.

As far as respiratory function is concerned, it has previously been shown that starvation will blunt the ventilatory response to hypoxia and hypercarbia. However, the other extreme, with high carbohydrate loads in excess of calculated and measured demand, may cause an undesirable increase in CO₂ production. The Respiratory Quotient in these patients may rise well above 1.0 as the excess glucose is converted to fat. Fat synthesis from glucose can incur a Respiratory Quotient as high as 9.0. Because of the problems of overnutrition using high-energy forms of parenteral nutrition, a knowledge of the optimum level of caloric intake assumes a new position of importance. Askanazi et al. suggest a rationale for the use of fat emulsions to supply 50 per cent of the caloric requirements in injured and septic patients requiring hyperalimentation. They point to a significant reduction in CO₂ production and hence in ventilatory requirements with the use of moderate quantities of fat emulsion (oxidized with an RQ of 0.7). While this argument makes excellent metabolic sense, and has indeed been shown to be valid by the measurements reported in this paper, it is necessary to point out that the use of fat emulsions remain controversial in certain situations.

The case for any indiscriminate use of total parenteral nutrition must be carefully reviewed. Apart from the various metabolic implications of the use of this therapy alluded to above, it appears that certain obese subjects may respond to overnutrition in an even more complex way. In addition to the potential problems of the infusion of excess calories in the form of glucose or fat, the implications of intravenous infusions of synthetic crystalline amino acids must also be considered. During the past ten years the brain has also proved to be subject to dietary influence in spite of the blood-brain barrier, which was long thought to isolate it from the rest of the body. Variations in concentrations of choline and amino acids in the plasma can be correlated with fluctuations in the brain's content of neurotransmitters and their precursors. A diet high in carbohydrates and low in proteins stimulates the synthesis of serotonin (an inhibitory neurotransmitter) because its precursor, tryptophan, can enter the brain without competition from other amino acids, most of which are taken up by muscle. On the other hand, infusion of intravenous amino acids into acutely ill patients in incipient renal and hepatic failure, without knowledge of their existing amino acid levels, can lead to alterations in consciousness based on central neurotransmitter changes. It thus seems reasonable to appeal for caution in the use of hyperalimentation in the perioperative period, specifically to appeal for its use by those who are aware of the metabolic implications, and for its use on the basis of measured energy requirements and plasma levels and patterns of the substrates about to be infused.

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