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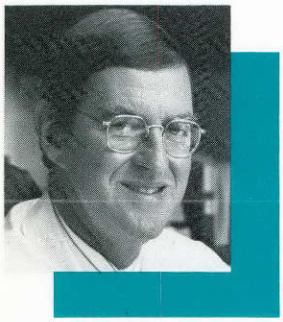
ONCOLOG

Is Malpractice Litigation Undermining Informed Consent?



Lester J. Peters

In a society willing to assume no risk, a good lawyer can turn success into failure. Consider this: Your patient has a potentially fatal cancer. His only hope is aggressive radiotherapy. He goes through the treatment and is cured, but necrosis of the jawbone caused by the radiation leaves him with a permanent disability. He sues you for negligence. Next time you have a similar case, would you suggest the therapy that offers the best chance of cure, knowing that the likely sequelae may land you in court?

Lester Peters, M.D., feels that many physicians having faced that scenario are choosing to treat less aggressively. The unfortunate consequence is that true informed consent is being subverted because physicians are fearful of potential litigation. Physicians are more likely to be sued for a severe, debilitating side effect of aggressive treatment than for the death of a patient, according to Peters, head of the Division of Radiotherapy at the M. D. Anderson Cancer Center.

It sounds irrational, but "it's much easier to convince a jury that a severe treatment side effect is the fault of the doctor than it is to convince them that someone dying of cancer is the fault of the doctor," Peters said. Occasionally, in the process of saving a patient's life, severe normal tissue injury may be unavoidable, and whereas the physician considers the therapy a success, a patient may view the side effect as a failure. And though such cases are few, the specter of malpractice suits is sufficient to make some physicians reevaluate whether to propose aggressive therapy.

Fear of Litigation Should Be Irrelevant

To Peters, this reluctance, though certainly understandable, should be irrelevant in medical decision making because the fundamental concern is curing the patient. Patients must retain the option of choosing the therapy that provides the highest chance of cure, and to do so they must be adequately informed. "No one wants to be sued, but it's not right to avoid it at all costs. You're not doing your current patients a service by cutting down on potentially curative treatment just because someone in the past has sued you," Peters said. "Most cancers require intensive treatment to maximize the chance for cure, so unless the patient specifically desires less aggressive treatment, avoiding the possibility of all severe sequelae should not be the primary concern of the physician. Too little treatment carries the worst possible toxicity: failure to cure the cancer."

No one wants to be sued, but it's not right to avoid it at all costs.

Peters is by no means an advocate of ultraaggressive therapy regardless of outcome. Aggressiveness should be

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weighed against the gravity of the disease and the consequences of inadequate treatment. "If increasing the dose provides a small increase in tumor control but a very great risk of a severe complication (e.g., spinal necrosis), you end up losing more than you gain," he said.

But Peters insists that, at the very least, the patient should be made aware of the relative risks and benefits of the entire spectrum of therapy. "Unless you involve the patient in the decision-making process, you may not be giving him the treatment he really wants," he said. "It's not necessarily true that every patient wants the same intensity of treatment. Some personalities say 'damn the risks; I want the most intensive treatment,' whereas others are afraid of taking that risk. I think we owe it to them to respect those wishes."

Treatment Information Should Be Conveyed in Understandable Terms

Physicians cannot go into all the ramifications of treatment, and explaining the intricacies of clinical and laboratory data may end up only confusing the patient. But Peters insists that, at the very least, the results of relevant research can be briefly presented and easily understood by most patients.

"We don't say, 'your chances of cure are 74% if treated this way and 63% if treated this way.' As far as the individual is concerned, he is either cured or not; he either gets a complication or he doesn't. You can't be 74% cured, so we tell him that with a disease like his about three-quarters of the patients will be cured if they go through the treatment. We can't say whether he's going to be in the fortunate three-quarters, but we can say that a particular treatment will maximize his chances of being cured."

Too little treatment carries the worst possible toxicity: failure to cure the cancer.

As an example of the need for comprehensive patient education, Peters points to his own work in treating head and neck patients with radiotherapy. "It is quite common in the radiotherapy community at large to interrupt radiotherapy half-way through in order to allow acute side effects to resolve, after which treatment is resumed. This is often perceived as necessary because many patients experience a lot of discomfort during treatment. But there is overwhelming evidence that interrupting treatment significantly reduces the chance for cure, because during the rest period the tumor resumes growth. Since the data are so compelling, we feel strongly that treatment should never be interrupted except under extreme conditions."

Peters feels that the key to ensuring that patients continue uninterrupted treatment is to be quite clear as to the discomfort they undoubtedly will have and to inform them of the measures that can be taken to relieve their discomfort. "We also tell them when the pain will reach a plateau, what side effects will heal, and what effects are irreversible. We let them know that we'll give them all the support we can and special foods to make things easier, but they'll have to weather the pain if they want to maximize their chances for cure."

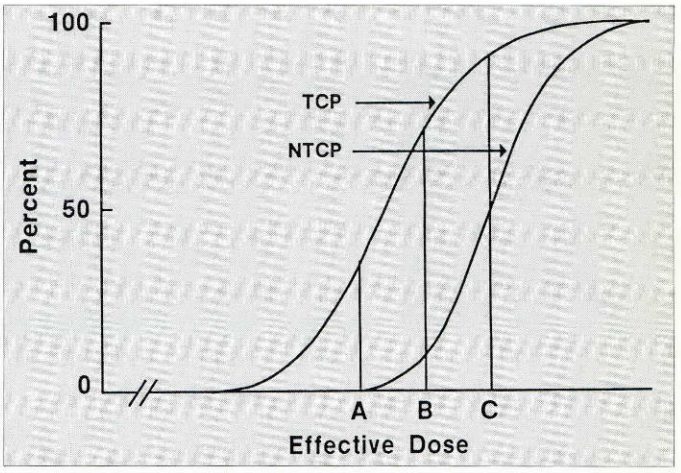


Figure 1. Hypothetical dose-response relationships for tumor control probability (TCP) and normal tissue complication probability (NTCP) to illustrate the concept of "tolerance." The therapeutic ratio is "favorable" in that the TCP curve is displaced to the left of the NTCP curve. Dose A effectively avoids risk of injury to normal tissue, but the probability of tumor control is small. But by accepting a small risk of normal tissue injury, i.e., dose B, the TCP is significantly improved. Further dose increase dose above B might be desirable but is certainly not justified above C, where NTCP increases more rapidly than TCP. Although the phrase "normal tissue tolerance" is widely used, the real limit to radiation therapy is the "tolerance" of a certain risk of injury by an adequately informed patient and his physician.

Awareness of Options Affects Patient's Choice

In general, for consent to be truly "informed," the patient must be apprised of five points, according to Peters: First, the probability of cure (or local control) of the cancer with the proposed treatment. Second, the probability of cure with either less intensive or more intensive regimens. Third, the consequences if the tumor is not controlled. Fourth, the nature of acute side effects, such as intensity, time of onset, and duration, and the available measures to ameliorate them. And fifth, the probability of late treatment-related complications.

The patient should also be apprised of the availability and efficacy of "salvage" therapy in the event that the initial treatment is unsuccessful. If effective salvage therapy is available, the patient may opt for less aggressive initial treatment. Alternatively, if salvage therapy is unavailable or of limited efficacy (as is often the case), most patients will choose to "go for broke" with their initial treatment, Peters said.

"In most cases, when our goal is cure, it's simply illogical to reduce the toxicity of the initial treatment, since the patient may have to face higher morbidity during salvage therapy," Peters said.

The degree to which a physician discusses each of these points is dictated not only by the availability of time and resources but also by the severity of the case. "You have to talk to the patient in great depth when the stakes are extremely high," Peters said. "For instance, a couple of years ago we saw a young patient with a noncancerous tumor in the base of the skull. The tumor had destroyed part of the vertebral column, but there was no way to remove the tumor surgically. Irradiation of the spinal cord was unavoidable, so we had to talk to him and his parents at great length as to where we wanted to aim the treatment and how much of a risk we wanted to take, since it was possible that radiation-induced spinal necrosis would paralyze him. We spent a long time discussing the pros and cons of different levels of treatment before agreeing upon a mutually acceptable point to aim at."

Unless you involve the patient in the decision-making process, you may not be giving him the treatment he really wants.

Physicians Treat Less Aggressively after Lawsuits

Peters' views are not simply based on subjective perception. A staff member of Peters' department, Neil Sherman, M.D., recently conducted an anonymous survey of radiotherapists who had trained or worked at M. D. Anderson at some point during the past 40 years. "He asked how many had been sued—rightly or wrongly, justified or not. He found that by the time the average radiotherapist had been out of training for 20 years, there was about a 50/50 chance of being sued. And of the ones being sued (regardless of outcome), one-third said that they treat people less aggressively now than they did before they were sued."

This reluctance to treat aggressively is not limited to experienced doctors. Peters has found that a defensive attitude is becoming more common among residents in training. "I'm on the examining board for certification in radiation oncology, and I try to present a case to the students to see if they would be prepared to risk a major complication in order to save a patient's life. It's depressing to see how many of them won't take the slightest risk, and when you ask them why, they'll say they don't want to be sued. This attitude is most unfair to the majority of patients who will not sue you but want to get the best available treatment."

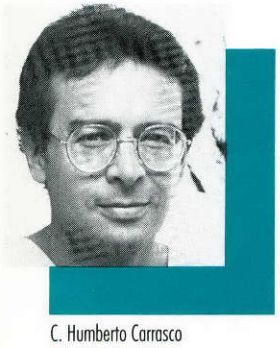
Community Standard of Treatment Intensity Is Lowering

As a result of these changing attitudes, the acceptable level of "standard" treatment is being reduced. Ironically, this reduction may only exacerbate the current excesses of litigation. "When everyone starts acting defensively, the community standard of care, in terms of 'aggressiveness,' gets pushed downward, and so one who is acting reasonably in absolute terms can be judged to be exceeding community standards. This is unfortunate because the question of whether a physician conformed to community standards is often asked when determining negligence. That's a very serious problem. I recently reviewed a case in which a doctor was being sued for a treatment complication. Expert witnesses said that the treatment given would have been perfectly acceptable 10 years ago but did not now meet prevailing standards. What they were really saying was that the standard of taking a modest risk to maximize the chance of cure has changed, and that we live in a society that wants no risk. I don't subscribe to that view at all. If the situation demands taking a risk, then the physician should not be averse to taking it for fear of being sued."

Peters does not know what tack the current situation will take. Reform in the legal system, more specific informed consent legislation, and better education of physicians in training are being discussed. But regardless of whether these measures are taken, the responsibility still rests with the physician. According to Peters, physicians owe it to their patients to describe all options, legal issues notwithstanding. "We have to be bold enough to take some risk if we're going to do the maximum good." ■

Physicians who desire additional information may write Lester J. Peters, M.D., Division of Radiotherapy, Box 97, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, or call (713) 792-3411.

Expandable Stents Provide Relief for Patients with Tumor-compressed Tissue



C. Humberto Carrasco

Symptomatic palliation is an important aspect of treating terminally ill patients. The less energy a patient has to spend battling intense pain, the more energy he or she can devote to friends and family.

For the past several years, M. D. Anderson Cancer Center researchers have been investigating the use of expandable stents in cancer patients to palliate the symptoms caused by compression of various tubular structures. The stent was developed in 1984 by a former M. D. Anderson physician, Cesare Gianturco, M.D., and is made of stainless-steel wire bent in a zig-zag. Using fluoroscopic guidance, the stent is deployed in the desired location through a catheter. In most cases, the stent then expands and eliminates the obstruction (Figure 1).

Many physicians have participated in extensive laboratory investigation of the Gianturco stent at the John S. Dunn Research Foundation Center for Radiological Sciences. The foundation is based in the Department of Diagnostic Radiology and is directed by Kenneth C. Wright, Ph.D. Clinical investigations are being performed by C. Humberto Carrasco, M.D., chief of the Section of Angiography and Interventional Radiology. Carrasco and his colleagues are currently using the stents, primarily in lung cancer patients, to reestablish patency of compressed vena cavas, trachea, bronchi, and bile ducts.

Most patients feel relief immediately after the stent is placed.

Inflammation Is Minor

The stent causes relatively minor inflammatory changes in the tracheobronchial and biliary trees. "The stent elicits mucosal and endothelial proliferation, which eventually covers its struts, essentially incorporating it into the wall of the stented structure. Thus, the risk of clot or debris being deposited on the stent is reduced," Carrasco said. "Another advantage of the Gianturco stent is that it does not occlude the orifices of side branches of stented vessels, bronchi, and bile ducts."

Patients with compression of the vena cava may remain asymptomatic if their collateral circulation is adequate. Unfortunately, in many patients collateral circulation is insufficient, and they develop painful swelling in the parts of the body inadequately drained. In the case of superior vena cava obstruction, increased venous pressure in the brain leads to neurologic impairment. Of the 16 patients with obstruction of the superior or inferior vena cava treated with the Gianturco stent, symptoms were successfully palliated in 12, Carrasco said. "Interestingly, most patients feel relief immediately after the stent is placed."

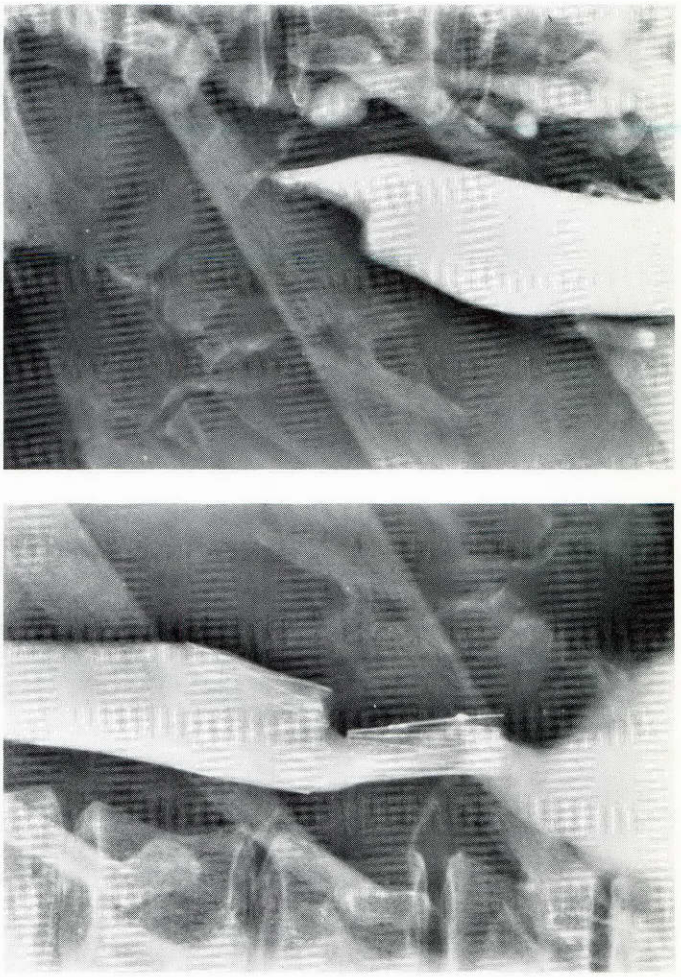


Figure 1. Hepatic segment of the inferior vena cava before (top) and after (bottom) placement of expandable wire "double" stent. The stent was placed after hepatic metastases from a melanoma had completely occluded the vein.

Ten Patients Treated for Tracheobronchial Obstructions

Carrasco has treated 10 patients with tracheobronchial obstructions, six of whom were treated successfully. For the most part, these patients had unresectable or untreatable advanced tumors. "This was a palliative measure, but a very important one," he said. "Compression of the trachea or bronchus makes breathing very difficult, so the stent is very important for the comfort of these patients."

Carrasco is pleased with the approximately 70% (18 of 26) success rate but considers these results only preliminary, since the patient population is still small. Efforts are being focused on why the stent is not always successful. "Our biggest problem may be tumor that has previously been irradiated. Radiotherapy controls the tumor but produces scar tissue," he said. The reduced elasticity of scar tissue requires a stent with more expansile force. "Eventually, we should be able to calculate the expansile force needed in each situation and use a stent that will exert the necessary pressure to reestablish patency."

Because the stent becomes part of the wall, the potential for clotting is very much reduced.

Modified Stents No Longer Migrate

Aside from the few unsuccessful cases, Carrasco said the problems have been few. "Early in our experience, we had one case in which the stent migrated to the heart, where it stayed for five months but did not cause any problems." The stent has since been modified. Barbs have been added, and two stents soldered together are now used in tandem. "We now have much better control, and since that case, no stents have migrated. In general, the stent's benefits far outweigh the risks," Carrasco said.

Timing for stent insertion varies depending on the site. "In patients with impending obstruction of a vena cava, we prefer to insert the stent early. Once the obstruction becomes complete, the resultant blood stasis may result in clotting. Expansion of the compressed segment does not accomplish much since the clot has already blocked blood flow. Thus, the clot has to be dissolved first using thrombolytic agents, which increase the risk of complications. It is much better to insert the stent before occlusion," Carrasco said. Physicians considering referral of a patient for relief of vena cava syndrome should do so as soon as possible. "Waiting will only make symptoms worse," he said.

On the other hand, stenting of the tracheobronchial tree is usually performed when the patient's symptoms become severe. The bronchi usually have to be severely compressed before the patient feels the effects, and irradiation alone may palliate symptoms. Carrasco works closely with his colleagues in thoracic surgery and thoracic oncology, with whom it is decided if stenting is indicated. "Bronchoscopy needs to be performed first to determine the extent of the tumor. If it extends into the lumen, the surgeon has to decide whether laser ablation might reestablish patency. The stent will probably not work if abundant intraluminal tumor is present because it will grow right through the struts. Stents are most effective when obstruction is due to extrinsic compression, and that is determined by bronchoscopy."

It's much better to place the stent before complete occlusion occurs.

Biliary Use Recently Approved

Insertion of biliary stents is performed electively because catheter drainage has to be established first. Recently, the Gianturco stent has been approved by the Food and Drug Administration for use in obstructed bile ducts. The M. D. Anderson experience with the biliary applications of the stent is somewhat limited; it has been more extensively used at Sharp Memorial Hospital in San Diego and in various European countries in a cooperative study. It appears that the stent is more effective in patients with benign biliary strictures than in those who have obstructions caused by tumors.

Other potential uses for the stent include the treatment of unresectable aortic aneurysms, for which preliminary animal studies have been promising. "Aneurysms have a high incidence of rupture. Their primary treatment is surgical, but in patients who are not surgical candidates, the stent would be very useful." ■

Physicians who desire additional information may write C. Humberto Carrasco, M.D., Division of Diagnostic Imaging, Box 57, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, or call (713) 792-8295.

Nutrition continued from page 8

Some studies indicate that nutritional therapy without control of tumor growth actually leads to earlier patient death.

formula for cancer patients. In studies with male Fischer 344 rats with fibrosarcomas or colon tumors, the researchers found that polyamine synthesis increases in cancer cells and that TPN formulas accelerate that synthesis. In the animal studies, they used difluoromethylornithine (DFMO) to selectively inhibit polyamine synthesis in tumor cells and the nonessential amino acid ornithine to prevent the thrombocytopenia associated with the drug. This amino acid, also a polyamine precursor, appeared to selectively stimulate polyamine synthesis in normal cells but did not impede DFMO inhibition of this synthesis in tumor cells (Cancer Research 49:4159, 1989).

You can't tinker with the eight essential amino acids because then the normal tissues don't grow.

Changing the Nonessential Amino Acids

Because arginine seemed to favor tumor cell growth, whereas ornithine does not, Ota and colleagues substituted ornithine for arginine in the TPN solution that might be used in cancer patients. For the ornithine-based formula, "the experimental data show that it does not promote the growth of tumors, and it appears to have a beneficial effect on the intestinal tract," Ota said.

"The problem with the amino acid formulas is that you can't tinker with the eight essential amino acids because then the normal tissues don't grow," Ota explained. However, researchers have some latitude with the five nonessential amino acids in a formula. "We can tinker with those, make adjustments, and not affect normal tissue anabolism. But these changes may affect tumor growth."

Another Formula Uses Glutamine

The gastrointestinal benefit of the other new formula Ota has tried is important because cancer treatment regimens can ravage the stomach lining and cause other gastrointestinal tract problems through irritation or by killing gut flora. In a handful of patients, Ota has tried protecting the gastrointestinal tract by adding the nonessential amino acid glutamine to commercial TPN formulas. The first patient he did this for was a woman with short-gut syndrome. "She was having repeated catheter infections," Ota said. "It looked as if the infections were coming from her intestinal tract and seeding on her catheter. I added the glutamine, which, in theory, helps increase the gut mucosal barrier to bacteria. She hasn't had any infections since."

There has been a great deal of interest in glutamine.

"There has been a great deal of interest in glutamine, which has not been a normal constituent of parenteral formulas," Ota said. "The reason it's important is that glutamine has a trophic effect on the intestinal tract." Trauma patients should benefit from glutamine in their TPN formulas, he said, because it could help protect the gut mucosal barrier. The amino acid also could help patients with ulcerative colitis or Crohn's disease, as well as neonates, who have immature intestinal linings. "It also may be very important to the cancer population, especially those who are receiving chemotherapy, because one of the side effects of chemotherapy is to destroy the lining of the gastrointestinal tract," said Ota. He is working with other M. D. Anderson researchers to design a randomized protocol for testing glutamine's effects on patients.

It's a question of who's going to win out for the nutrients—tumor or normal cells.

Many of the cancer patients who receive TPN have gastrointestinal tumors, Ota noted. And many patients who receive TPN have advanced cancers. His own interest in nutritional support research grew out of concern for his gastrointestinal cancer patients. "I see these problems all the time out on the inpatient floors and in the clinics; metastasis and malnutrition are major problems. Before they come to treatment, a significant number of gastrointestinal cancer patients have a history of weight loss," he added.

"What can we do for these patients? We try to get them on therapy as quickly as possible to control their disease. If you get control of the growth of metastatic cancer, patients will start to do better, to eat and to feel better. You have to get control of the tumor growth. If you don't, even the hyperalimentation doesn't help."

Sometimes TPN represents hope to a terminally ill patient.

Total Parenteral Nutrition Can Be a Double-edged Sword

Ota believes that nutritional support should be just that—support for patients undergoing active therapy. TPN for advanced cancer patients "is a double-edged sword. It's a question of who's going to win out for the nutrients—tumor or normal cells. If you can knock out cancer cells with chemotherapy, surgery, or radiation therapy, the remaining tumor cells don't consume as much of the available nutrients. Then the tide shifts over to the normal tissues," he said. "That's why I don't feel justified in giving patients the TPN formulas unless they are receiving active, ongoing cancer therapy."

Sometimes, though, TPN represents hope to a terminally ill patient. "I have sent patients home on TPN who were terminally ill. To cut them off would mean no hope; they would feel abandoned. But by and large, I am not supportive of sending people home on TPN when they are not on active therapy.

"This specialized area—nutrition [TPN] for the cancer population—is really in its infancy," Ota summed up. "People have searched long and hard for better formulas. But we're just starting to come up with new formulas that address tumor growth and the recovery of the gut mucosal lining." ■

Physicians who desire additional information may write David Ota, M.D., Department of General Surgery, Box 106, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030, or call (713) 792-7216.

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Total Parenteral Nutrition: The Double-edged Sword

David Ota

Nutritional support aimed at sustaining cancer patients often contributes to tumor growth, an M. D. Anderson Cancer Center team has found. After years of laboratory work, these physicians have found what they hope is a solution—a total parenteral nutrition (TPN) preparation based on a new formula they believe will eliminate the cancer cells' advantage in the competition for nutrients. In addition, they believe that the new formula, as well as a further variation on the amino acid feeding solutions, will prevent some drug- or tumor-caused gastrointestinal problems.

"We're trying to develop an amino acid formula that does not stimulate the growth rate of tumors compared with standard commercial formulas," said David Ota, M.D., deputy chairman of the Department of General Surgery. He and his colleagues have developed the first TPN formula specifically for cancer patients; they have applied for a patent and hope the Food and Drug Administration will give the formula investigational new drug status so they can set clinical trials in motion. Until then, the formula cannot be given to patients.

Normal Cells Must Compete with Cancer Cells for Nutrients

"The basic problem [in TPN]," Ota explained, "is that cancer cells and normal cells compete for the same nutrients. If you give someone nutritional therapy, it's a question of who's going to win this competition. Some studies indicate that nutritional therapy without control of tumor growth actually leads to earlier patient death. This means you're feeding the tumor, and it progresses until the patient dies."

Ota, along with Kenji Nishioka, Ph.D., and V. Bruce Grossie, Ph.D., of the Department of General Surgery and Jaffer A. Ajani, M.D., of the Department of Medical Oncology, has tracked the problem of TPN-enhanced tumor growth to the nonessential amino acid and polyamine precursor that many total parenteral solutions are based on—arginine—and applied their findings to designing a

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