therapy who can show an "increased disease-free interval" will live long enough for the second neoplasm to be clinically apparent.

Another, and possibly more biologically intriguing, possibility is that acute myelogenous leukemia is the underlying neoplasm and that Hodgkin's disease is a result of a chronic and effective immunologic reaction on the part of the patient. When this reaction itself becomes the wildly overproliferative reaction called Hodgkin's disease, it requires treatment. This development may occur before complete immunologic control of the underlying leukemia. In a few patients, therefore, after the Hodgkin's disease is controlled, the uncured myelogenous leukemia will become recrudescent. This concept may also explain some of the striking immunoproliferative aspects of Hodgkin's disease that made it generally classified as an infectious or immune disorder for many years.

We are just beginning to be able to observe the natural histories of patients with neoplasia who survive because of more effective modern therapy. Much of what we see may best be described as "accompanying" treatment rather than "induced" by it.

THOMAS C. HALL, M.D.
Pasadena, CA 91101 Tumor Clinic Medical Group

The above letter was referred to the authors of the article in question, one of whom offers the following reply:

To the Editor: Although various conclusions can be drawn from a set of data we thought the conclusion that leukemia is an induced second neoplasm is the one best supported by our data[1] and by those of others.[2,3] In our introduction we raised the question that perhaps the increased incidence of leukemia is merely a result of improved survival. The marked preponderance of acute myeloblastic leukemia in combined-modality-treatment groups and the low incidence in the patients treated with radiation alone[1,3] (none in our study) argue against this point. The irradiation-only patients had survival comparable to that of the combined-modality-treated groups and therefore should have been at similar risk for development of leukemia. As for Dr. Hall's second point, we are unaware of any information that shows that Hodgkin's disease is a "wildly overproliferative reaction," and, in fact, recent data have demonstrated that Reed–Sternberg cells are malignant and appear to be derived from macrophages or closely related cells of the mononuclear phagocytic system.[4]

We certainly agree with Dr. Hall that long-term survivors of neoplastic disease must be closely watched to learn more about both the natural history of the disease and treatment-related phenomena.

C. NORMAN COLEMAN, M.D.
Stanford, CA 94305 Stanford University Medical Center

1. Coleman CN, Williams CJ, Flint A, et al: Hematologic neoplasia in patients treated for Hodgkin's disease. N Engl J Med 297:1249-1252, 1977
2. Chabner BA: Second neoplasm — a complication of cancer chemotherapy. N Engl J Med 297:213-214, 1977
3. Toland DM, Coltman CA: Second malignancies complicating Hodgkin's disease: the Southwest Oncology Experience. Proc Am Assoc Cancer Res/Am Soc Clin Oncol 18:351, 1977
4. Kaplan HS, Gartner S: "Sternberg-Reed" giant cells of Hodgkin's disease: cultivation in vitro, heterotransplantation, and characterization as neoplastic macrophages. Int J Cancer 19:511-525, 1977

LAETRILE

To the Editor: The considerable furor about Laetrile in the lay press, the medical press and numerous government agencies represents a gross misdirection of effort and emphasis. The plain fact is that the effectiveness and toxicity of Laetrile should be of no consequence at all in its use by patients.

During the recent past the concept that the individual adult is, or should be, in complete control of his own body has developed. Thus, women can now decide whether or not to become pregnant; if they become pregnant they can opt for early termination. Our patients must now be given the complete picture of therapy, either medical or surgical — the alternatives, the pros and cons. They are free to accept or reject our recommendations.

With these considerations in mind the Laetrile controversy can be reduced to proper proportion.

We are, or should be, doctors in the classic sense of the word — teachers or instructors. We are not, or should not be, dictators, absolute authorities or enforcers.

If the patient asks about Laetrile we should tell him the truth.

The rest is up to the patient. Neither we as professionals nor any government agency should have the right and power to dictate to the patient what mode of therapy he must follow.

LEO LEWIN, M.D.
Mount Arlington, NJ 07856 90 McGregor Ave.

To the Editor: I am amazed at the lack of understanding in the recent editorials in the *Journal* concerning Laetrile's acceptance and preference in the minds of some patients facing cancer (January 26). Laetrile persists because, unlike conventional chemotherapy and irradiation, which unfortunately sometimes results in opportunistic infections, bleeding, diarrhea, alopecia and a myriad of other side effects, it has yet to do much immediate harm.

Unfortunately, most seasoned oncologists are now watching the exodus of some patients to Laetrile clinics looking for a "cure" and thus bypassing conventional and often lifesaving treatment, and hastening death. Nevertheless, I submit that what is behind the American public favoring the legalization of Laetrile is a protest of medicine's lack of understanding of the real issue here. The Laetrile advocates see it as their hope, their kinsman and their salvation with death so near.

It will only be after medicine addresses itself to man's fear of disability and death that Laetrile will disappear. Next year, it may be a different form of quackery, such as coffee enemas, but as long as it is offered with concern, respect and a thread of hope it will persist.

Gentlemen, stop wasting your money on further study; listen and respond to the screams of your patients as they grapple with their fear of death.

JOHN LOFTUS VERRILLI, M.D.
Seattle, WA 98111 1100 Ninth Ave.

To the Editor: I believe that patients with cancer and the American public are trying to tell us something in their acceptance of Laetrile, and that the Sounding Board articles by Newell and Moertel indicate that we have not yet heard the message. The problem is not one of proving once and for all that Laetrile is worthless in the treatment of cancer; the evidence is already quite abundant. The issue is an emotional, not a scientific one. Patients with cancer have turned to Laetrile because they feel abandoned by their physicians. The proponents of Laetrile offer them hope (although a false one), encouragement and a program of positive action to "treat" their disease. Although the medical profession has made great strides in treating cancer in the last 20 years, there has been very little progress in treating patients with cancer. We have, in large part, ignored the emotional needs of these people for hope, encouragement, support and acceptance. Although the current trend toward treatment of cancer by specialists in regional centers has undoubtedly improved survival, it has also contributed to feelings of alienation and isolation in the patients so treated.

The message seems clear to me. People with cancer, and the American people in general, are saying to the medical profession, "You are not meeting our needs." If we persist in ignoring this message, and continue to concentrate obsessively on trying to prove the inefficacy of Laetrile, patients will simply find another Laetrile, and yet another.

JOHN G. SCOTT, M.D.
Medical University
Charleston, SC 29401 of South Carolina

To the Editor: I should like to comment on Dr. Charles G. Moertel's Sounding Board article, "A Trial of Laetrile Now," in the January 26 issue of the *Journal*.

Dr. Moertel may be right that a carefully conducted trial would convince the medical profession of the worthlessness of Laetrile, but there is little reason to suppose that it would similarly convince the public. The cost of this trial might also be considerable not only in terms of dollars but also in terms of increased suffering on the part of patients treated by Laetrile alone.

Dr. Moertel's fear about legalizing Laetrile is that it would be promoted and exploited. If my original suggestion were followed, it is unlikely that Laetrile would be promoted because it would be illegal to sell Laetrile or to administer Laetrile at anything other than cost. If surcharges were made, the physician who sold or dispensed the drug could be convicted of a felony.

GEORGE CRILE, JR., M.D.
Cleveland, OH 44106 Cleveland Clinic

"SHOTGUN" HEMATINICS

To the Editor: The continued use of "shotgun" hematinics is deplorable. The drug companies supply them because they are prescribed. Too many practitioners apparently believe that the product of a large, prestigious company must have merit.

These combinations are conveniently listed under "Hematinics" in the product classification section of the *Physicians' Desk Reference*. Each physician may make his own decision about which combination of agents is legitimate and which is not.

One manufacturer offers the pious admonition that if the anemia does not respond to his product, "...further exploration of the etiology" of the anemia is in order.

Practitioners who believe that such meretricious practices by drug companies should be discouraged might express themselves with vigor to the appropriate detail men. If doctors refused to see these representatives, the drug companies might get the message even faster.

ROY S. PATTEN, M.D.
MASON TROWBRIDGE, JR., M.D.
Brewer, ME 04412 700 North Main St.

INDOMETHACIN CAUSING PSEUDOTUMOR CEREBRI IN BARTTER'S SYNDROME

To the Editor: Recently, it was suggested that Bartter's syndrome represents overproduction of prostaglandins in the kidney. In support of this hypothesis the treatment of Bartter's syndrome with prostaglandin synthetase inhibitors such as indomethacin was successful.[1,2]

We treated a 10-year-old girl with Bartter's syndrome with indomethacin. There was improvement of clinical symptoms and laboratory data, but pseudotumor cerebri developed.

At the age of one year salt craving developed. She had failure to thrive and occasional attacks of muscle weakness. Bartter's syndrome was diagnosed when she was 2½ years of age on the basis of persistent hypokalemia, increased plasma renin activity, normal blood pressure and subnormal response to exogenous angiotensin II. Spironolactone and potassium salt had been administered since then. Indomethacin in a dosage of 75 mg (5 mg per kilogram per day) was started. Within one week the serum potassium concentration was increased, and muscle weakness was improved, in association with an increase of body weight. Eight weeks after starting the treatment bilateral abducens palsy developed. Choked disk was noted in both ocular fundi. The blood pressure was 92/64 mm Hg. Consciousness was clear. Neurologic examination was normal except for muscle hypotonia. Lumbar puncture showed an opening cerebrospinal fluid pressure of 350 mm of water, but the fluid was normal. Separation of sutures was noted on the skull x-ray film. Computerized tomography suggested a swelling of the brain without evidence of a space-occupying lesion or ventricular dilatation. Since it was suspected that indomethacin might have caused the benign intracranial hypertension, this treatment was interrupted, and intravenous infusion of 10 per cent glycerol was begun. Three weeks later the patient became free from abducens palsy and choked disk.

Therefore, we concluded that water and sodium retention as a result of indomethacin caused pseudotumor cerebri in this case. Although such a report has not been documented previously, it should be kept in mind that indomethacin treatment in Bartter's syndrome may produce pseudotumor cerebri.

HIROSHI KONOMI, M.D.
MASASHI IMAI, M.D.
KENJI NIHEI, M.D.
SHIGEHIKO KAMOSHITA, M.D.
Tochigiken, Japan Jichi Medical School

HIROSHI TADA, M.D.
Tokyo Metropolitan
Tokyo, Japan Tsukiji Maternity Hospital

1. Verberckmoes R, van Damme B, Clement J, et al: Bartter's syndrome with hyperplasia of renomedullary cells: successful treatment with indomethacin. Kidney Int 9:302-307, 1976
2. Fichmann MP, Telfer N, Zia P, et al: Role of prostaglandins in the pathogenesis of Bartter's syndrome. Am J Med 60:785-797, 1976

HYPEROSMOLAR COMA

To the Editor: A large personal experience with hyperosmolar diabetic patients leads me to differ with Feig and McCurdy[1] on some points.

Fulop et al.[2] observed that the state of consciousness in diabetic coma correlates best with the degree of hyperosmolarity and the rapidity with which it develops, and I agree.

Rapid correction of the hyperosmolar state by means of small, frequent doses of regular insulin and large volumes of half-normal multielectrolyte solution[3] has resulted in rapid improvement in the state of consciousness and a mortality rate of less than 1 per cent in ketoacidotic and less than 10 per cent in hyperosmolar, nonketotic patients.

Since beginning to administer potassium and phosphate early in therapy and discontinuing the use of bicarbonate, I no longer see the approximately 10 per cent of patients whose mental state occasionally became further depressed during therapy.

Only one fatal episode of cerebral edema has been seen in a series now approaching 1500 patients, and that was in a young ketoacidotic patient who received bicarbonate and no phosphate.[4]

Meticulous correction of approximately half the fluid deficit in the first four hours and of the remaining deficits plus ongoing losses during the subsequent 20 to 36 hours has resulted in an excellent outcome without "isotonic water intoxication."

ROBERT MATZ, M.D.
Montefiore–North Central
Bronx, NY 10467 Bronx Hospital

1. Feig PU, McCurdy DK: The hypertonic state. N Engl J Med 297:1444-1454, 1977
2. Fulop M, Rosenblatt A, Kreitzer SM, et al: Hyperosmolar nature of diabetic coma. Diabetes 24:594-599, 1975
3. Matz R: Diabetic coma: guidelines in therapy. NY State J Med 74:642-648, 1974
4. Taubin H, Matz R: Cerebral edema, diabetes insipidus and sudden death during the treatment of diabetic ketoacidosis. Diabetes 17:108-109, 1968

The above letter was referred to the authors of the article in question, who offer the following reply:

To the Editor: We agree with Dr. Matz that the state of consciousness in diabetic coma correlates best with the "degree of hyperosmolarity," although we prefer the term "hypertonicity" since the correlation persists even when the contribution of urea is excluded from the calculation.[1] We share the opinion of Fulop et al. that this correlation may reflect the duration of the disorder