SUPPLEMENTARY REPORT BY THE CANCER ADVISORY COUNCIL ON

THE TREATMENT OF CANCER WITH

BETA-CYANOGENETIC GLUCOSIDES

("LAETRILES")

Cancer Advisory Council
State of California
Department of Public Health
1965
Continued study of theoretical considerations concerning the action of Laetrile and the results of treatment of cancer with it was made possible by additional sources of information.

The McNaughton Foundation and the North End Medical Center, both in Montreal, in January 1963 submitted a total of 14 clinical records on patients treated with Laetrile. These were not complete records but were abstracts furnished by the various hospitals in Canada to the McNaughton Foundation. Although the deadline for submission of evidence to the California State Department of Public Health was July 18, 1962, the Cancer Advisory Council decided to examine these records and for this purpose a committee of three physicians highly qualified and actively engaged in the treatment of cancer were appointed from the membership of the Council to review and evaluate these records and to report on them. Each committee member conducted an independent evaluation following which their reports were combined as Section I of a Supplementary Report on Laetrile. Members of this committee were as follows: Dr. Joseph F. Ross, Dr. Thomas S. Nelsen, and Dr. Jesse L. Steinfeld.

The proponents of Laetrile claim that beta-glucuronidase, which is present in abundance both in normal and malignant tissue, is the enzyme involved in the hydrolysis of Laetrile with release of hydrocyanic acid particularly at tumor sites, but since Laetrile or amygdalin, which it is, is a glucoside and therefore presumably subject to enzyme hydrolysis only by beta-glucosidase, additional information from a search of the literature for articles dealing with the presence of the enzyme glucosidase in mammalian tissue conducted, for the Department, by the Crerar Research Library of Chicago was sought. References and further discussion appear in Section II of this Supplementary Report.

A third source of information was a comparative study of the composition and biochemical behavior of Laetrile manufactured in the United States and that manufactured in Canada which was made by investigators from the Pharmaceutical Chemistry Division, Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Ontario and the Research Laboratories, McGill University Surgical Clinic, Montreal General Hospital, Montreal, Quebec.
In the laboratory of the California State Department of Public Health, two varieties of Laetrile supplied by the manufacturers were examined. One of these purported to contain added di-isopropyl ammonium iodide and allegedly in limited use and distribution in the United States did in fact contain 2.5 percent inorganic iodine. This product on recrystallization from boiling acetone developed no crystals whereas the second variety as well as amygdalin did and both showed rather sharp melting points of 210-215° C. It is concluded that the iodine containing variety corresponds to the United States brand available to the Canadian group.

With the permission of the authors and the publisher, the Canadian study, except for the omission of figures depicting the ultraviolet and infrared absorption spectra, the X-ray diffraction patterns and the chemical reactions postulated in the hydrolysis of the United States variety and amygdalin, is reproduced as Section III of this Supplementary Report.

Section I.

Review of Records

Case No. 1, Mrs. A.B., age 51, #628066

Summary:

The abstract of a clinical record shows that a diagnosis of "generalized abdominal carcinomatosis by a basal cell adenocanthoma," primary site not stated, was made on a biopsy specimen taken during laparotomy, although no pathologic report was included. One gram of Laetrile per day for a total of 36 grams was administered between October 25 and November 29, 1962, the date of the final summary and last examination. Blood counts on the same days showed a mild anemia but were otherwise within normal limits. Urinalysis which was normal before treatment was started showed a trace of albumin on November 29.
Results:

There is no follow-up information later than 1 month after treatment was started. There was no change in the blood picture and no information on weight gain. Without objective confirmation, it was stated that previously palpable abdominal masses were smaller and that the patient was "improved."

Impressions:

Reviewer No. 1 - Information inadequate to indicate effect of therapy. Follow-up time inadequate. No objective evidence to support claim of "improvement."

Reviewer No. 2 - This record requires an operative report, pathology report and follow-up information before the evaluation can be made.

Reviewer No. 3 - This is a record only of data in the files of the McNaughton Foundation with none of the original hospital records, and a statement that the patient has palpable abdominal masses which diminished very much in size. A totally inadequate record.

Case No. 2, Mr. H.G., age 58, #62-4693

Summary:

This record shows that a right colectomy and omentectomy performed on September 14, 1962 resulted in a diagnosis of adenocarcinoma of the ascending colon although no pathologic corroboration is included. One gram of Laetrile per day for a total of 38 grams was given pre and postoperatively up to the time of the clinical summary. Blood study before treatment with Laetrile showed a hemoglobin of 8.3 grams, hematocrit of 28.5%, and marked hypochromia and anisocytosis. Fifteen days postoperatively the hemoglobin was 12.2 grams and the hematocrit 40% with no comments regarding red blood cell morphology and on November 27 the hemoglobin and hematocrit were 12.4 grams and 41% respectively. Urinalysis pre and postoperatively were normal.

Results:

There was improvement in the blood picture postoperatively but the physician who last saw the patient on November 29 and who summarized the findings stated that not enough time had elapsed to permit an evaluation of Laetrile effect.

-3-
Case No. 3, Sister M.E., age 71, #1936

Summary:

This record shows that in February, 1958, the patient underwent a surgical procedure which led to a pathologic diagnosis of mucous epithelioma of the breast and was followed by a left mastectomy. The pathologic report is included in the record. On October 9, 1963, the patient reported a weight loss of 25 pounds and subsequently hemorrhaging until November 30, 1962, from site unspecified. A chest X-ray on October 10, 1962 revealed numerous pulmonary condensations compatible with metastatic neoplasm. The hemoglobin at this time was 11 grams and red blood cells 3.6 million and an urinalysis was reported normal. On October 24 one gram of Laetrile three times weekly was started but was increased to one gram per day on November 20th. The latter dosage continued to the date of the clinical summary, December 23, for a total dosage of 51 grams over a two months' period.

Results:

After two months' observation it is stated that the results are satisfactory after Laetrile therapy, that the patient sleeps well and has a good appetite but no objective evidence of benefit is included.

Impressions:

Reviewer No. 1 - Record totally inadequate to permit evaluation of effect.

Reviewer No. 2 - No evaluation possible from this record.

Reviewer No. 3 - This is a patient with stated cancer of the left breast although the pathologic diagnosis report we have
is mucous epithelioma of the breast. It is undetermined here whether this patient has had radiotherapy to the breast or any hormonal therapy so that she has not received standard forms of therapy and the only benefit claimed is cessation of hemorrhaging, but we have no details as to where the hemorrhages were from, nor any data on what happened to the presumed pulmonary metastases, nor do we really have an adequate histologic diagnosis. From the description a totally unsatisfactory case.

Case No. 4, Mr. R.K., age 45, #3163

Summary:

The record shows that the patient was hospitalized on October 27, 1962 because of a painless, firm, freely movable 2.5 cm mass in the left supraclavicular area and a weight loss of 15 pounds during the past four to five weeks. On August 30 cervical lymph nodes were excised and a pathologic diagnosis of reticulum cell lymphosarcoma was made. The actual pathologic report is not shown. Between September 14 and October 17, 1962 the patient received 3,000 r to the left supraclavicular region. Chest X-ray was normal. Blood study on November 12, 1962 showed a hemoglobin of 14.8 grams, white cells 7,050 and on December 19 a hemoglobin of 14.5 and white cell count of 7,550. Urinalysis on November 12 showed a trace of albumin. Between November 14 and December 28, the date of the summary, the patient received three grams of Laetrile per week for a total of approximately 13 grams.

Results:

The blood picture showed no change over a period of about six weeks and the record shows that the patient's general health improved, that his appetite became better, he slept well and had more strength, but no objective evidence of benefit is shown.

Impressions:

Reviewer No. 1 - Record totally inadequate to permit evaluation of any effect of therapy.

Reviewer No. 2 - This patient underwent surgery (diagnostic and/or therapeutic?) and radiation therapy in the amount of 3000 r and was asymptomatic at the time of Laetrile administration approximately three months after his X-ray treatment. It is therefore difficult or impossible to evaluate the effect of Laetrile.

Reviewer No. 3 - This patient has lymphosarcoma presumably diagnosed on a biopsy in August 30, 1962 followed by radiotherapy 3000 r to the involved region from September 14 to
October 17, 1962 and started on Laetrile November 4, 1962 at which time he had no pain or no adenopathy, so that, in the absence of any evident disease it is impossible to evaluate a presumed therapeutic agent. This is no test whatsoever.

Case No. 5, Mrs. J.L., age 67, #49732

Summary:

The record shows that a left radical mastectomy was performed on April 21, 1961, resulting in a pathologic report (unsigned) of anaplastic epithelioma (Grade 3) of the breast. There is no indication of any further treatment or observation until October, 1962, when the patient returned because of pains in the lumbar vertebrae and a "very poor state of health." She received 15 grams of Laetrile during a 15-day stay in the hospital. Blood study before the Laetrile treatment revealed a hemoglobin of 11.3 grams, hematocrit of 35\% and white cell count of 4,000. After treatment the hematocrit was still at 35\% but no other values were given. Urinalyses were normal before and after treatment.

Results:

The record indicates that the patient gained eight pounds, that the lumbar pain disappeared after one week and that the patient left the hospital because, in her words -- "I am well and I feel well." No change in blood picture was shown.

Impressions:

Reviewer No. 1 - Record totally inadequate to evaluate therapy.

Reviewer No. 2 - This abstract is completely inadequate; apparently no X-rays were taken. The diagnosis of carcinoma is in question.

Reviewer No. 3 - Patient with a diagnosis of anaplastic epithelioma, Grade 3, of the breast who came in with pain in the lumbar spine and received 15 days treatment with Laetrile at one vial per day and went home saying she is well. Totally inadequate. No documentation of disease when drug therapy initiated.

Case No. 6, Mrs. W.M., age 49, #4012

Summary:

According to the record, biopsy specimens of an ulcerating and bleeding rectal mass were taken in April, 1962. The pathologic diagnosis was squamous cell carcinoma Grade 1.
of perianal gland. There is no indication of further treatment until October 24, 1962 when daily doses of two grams of Laetrile were begun, 1500 mgs. being given intramuscularly and 250 mgs. applied locally twice a day. This dosage continued until November 12, 1962 when it was reduced to 500 mgs. per day until December 10 the date of last examination and of the clinical summary. The total dosage up to December 10 was approximately 52 grams.

On October 29, 1962 a chest X-ray showed no metastases and a cystic area in the skull was thought to be either a diploic blood lake or a metastasis. The final summary indicates that further surgery with resection of 33 cms. of rectosigmoid was performed on November 29, 1962 but the pathologic report indicates a date of November 23, 1962. The pathologic diagnosis on this specimen was mucoepidermoid epithelioma.

During hospitalization the patient received several transfusions. Blood studies on admission showed 6.5 grams of hemoglobin, 2 million red cells and 3,200 white cells. The hematocrit was 17% and the sedimentation rate 53 mm. On December 10 the hemoglobin was 13 grams, red cells 4.1 million, white cells 13,200, the hematocrit was 39% and the sedimentation rate 27 mm. Urinalyses showed many white cells both on admission and on December 10.

Results:

The blood elements had returned to approximately normal levels but several transfusions had been given. X-ray films of the abdomen on November 20 showed less gaseous distension and a liver reduced in size from the observation on October 25; pains in the pelvic and hepatic areas were gone and therapeutic results were reported as "very satisfactory." There were no objective findings to indicate a beneficial effect by Laetrile.

Impressions:

Reviewer No. 1 - No objective evidence of beneficial effect.

Reviewer No. 2 - This patient underwent surgical resection of the carcinoma of the anus and the Laetrile was administered for non-specific symptomatology approximately one month before operation. At best the history and findings are most confusing.

Reviewer No. 3 - This patient has a rectal squamous cell carcinoma, Grade 1, diagnosis made on a biopsy when three pieces of tissue were removed, the largest of which measured 6 millimeters at its greatest diameter. On November 23, 1962 the patient had a large amount of colon removed, measuring 33 cm in length including the recto-sigmoid tumor. Lymph
nodes were not involved by tumor which was called an epidermoid epithelioma on November 23, 1962. There were no pulmonary metastases and this patient was started on Laetrile prior to operation. The claimed effects were a reduction in pain, a very good effect on fetor, and a decrease in tumor from 9 x 6 cm to 6 x 4 cm at the time of surgery one month later. In addition, the patient did receive supportive therapy and blood transfusions so once again there is no clear evidence of effect on tumor. It is impossible to distinguish what is happening here.

Case No. 7, Miss L.P., age 15, #62-4968

Summary:

A diagnosis of renal adenocarcinoma and a surgical procedure on September 24, 1962 were mentioned in the record but there were no pathologic or operative reports. The patient was given one gram of Laetrile daily for eight days pre and postoperatively and then presumably discontinued until October 24 when its administration was resumed. An additional 35 grams may have been given from this date until November 29 when the patient was last seen.

Preoperative blood studies showed a hemoglobin of 10.3 grams, white cells 6,100, hematocrit 30.7% and a sedimentation rate of 20 mm. On October 3 hemoglobin was 12.2 grams, white cells 9,700, and hematocrit 37.5%. On November 27 the hemoglobin was 12.7 grams, white cells 5,500, and hematocrit 38.5%. Urinalysis on one of three occasions showed a trace of albumin. A chest X-ray on November 27 was normal.

Results:

The blood picture was improved after surgery but there is no indication as to whether or not this was due to transfusions or other incidental therapy. The physician seeing the patient on November 29 stated that it was too early to make an evaluation of Laetrile effect.

Impressions:

Reviewer No. 1 - Record totally inadequate to evaluate effectiveness of Laetrile.

Reviewer No. 2 - The records are inadequate for evaluation.

Reviewer No. 3 - It is too early to evaluate effects of therapy.
Case No. 8, Mrs. C.P., age 50, #120-593

Summary:

The record shows that on May 17, 1960 the patient had a radical mastectomy which revealed an anaplastic epithelioma of right breast with axillary metastasis to one of six lymph nodes. Following local recurrence, she was reoperated on November 8, 1960. The pathology reports confirm the clinical diagnoses in both instances and both reports are included. Again in December, 1962, an inoperable, ulcerated, local recurrence was present.

Before beginning Laetrile therapy on October 10, 1962, a blood study revealed a hemoglobin of 12 grams and a white cell count of 5,700. On December 17, 1962, the hemoglobin was still 12 grams, red cells 4.02 million, and white cells 6,350. Urinalyses on October 10 and December 17, 1962 were normal. Chest X-rays on May 3, June 8 and December 13, 1962 were normal and no metastases were evident in X-ray films of the cervical and dorsal spine on December 13.

Laetrile, one gram three times a week, was given between October 10 and December 7, 1962 and thereafter one gram daily. The final summary is undated but presumably the patient was last seen on or about December 13, the date of last X-ray examination and she therefore probably received a total of 36 grams of Laetrile.

Results:

There was no essential change in the results of blood studies. Urinalyses remained normal and no objective evidence of benefit was presented.

Impressions:

Reviewer No. 1 - No objective evidence of therapeutic effect of agent.

Reviewer No. 2 - This is a patient with breast cancer who underwent a conventional mastectomy as therapy followed by a local recurrence in the operative wound. Because of multiple therapy, no evaluation of the Laetrile is possible.

Reviewer No. 3 - This is a patient with carcinoma of the breast who presumably has a relapse with ulceration of the mastectomy scar, but we have no measurements, no pictures, no data, no evidence for disease being treated with the drug. A totally inadequate record and no evidence that patient had previously received standard therapy.
Case No. 9, Mr. A.P., age 47, #550-331

Summary:

The record shows that on September 1, 1961, the patient underwent a laparotomy which resulted in a finding of generalized carcinomatosis with involvement and pelvic fixation of the sigmoid and ileum. There was additional tumor involvement of liver, stomach, mesentery, and aortic nodes. A specimen of the tumor was taken for biopsy and an anterior enterostomy performed. A pathologic diagnosis of "polymorphous reticulocarcinoma" is included in the record.

Blood studies before treatment with Laetrile showed 9.5 grams of hemoglobin and a red cell count of 3 million. One gram of Laetrile per day was given for 30 days and thereafter two times per week for an additional month. The total drug administered was approximately 35 grams.

Results:

It was stated that the patient had gained 20 pounds, was eating and sleeping well and that he "has a very good spirit now." There was no objective evidence indicating benefit from Laetrile.

Impressions:

Reviewer No. 1 - Record inadequate for objective evaluation of effect.

Reviewer No. 2 - This record is insufficient for evaluation, an operative report is needed as well as a statement concerning conventional therapy.

Reviewer No. 3 - Patient who has abdominal carcinoma and was given one vial of Laetrile daily for 30 vials, then Laetrile twice a week for a total of two months. "The patient is eating and sleeping normally and has gained twenty pounds. Very good effect on pain." This is all we know. We have no data on tumor mass or tumor size. Tumor is called a polymorphous reticulosarcoma. No evidence that the patient received conventional therapy or if this is reticulum cell or Hodgkin's Disease (sarcoma). Inadequate record.

Case No. 10, Mr. E.R., age 47, #2143

Summary:

Early in 1962 the patient began to vomit and to have "heavy" pains in the stomach. On April 14 a biopsy specimen of the stomach was taken and on April 25, 1962, one of liver. In both instances neoplastic tissue was demonstrated but a
specific pathologic diagnosis was not made. Laetrile was started and after 15 days, pain and vomiting ceased and the patient could eat and sleep normally. The dosage was one gram of Laetrile per day for 30 days, then one gram each three days for a total of approximately 65 grams.

Before beginning the Laetrile therapy a blood study showed 13.6 grams of hemoglobin, a hematocrit of 42% and a white count of 10,500. In August, after a recurrence of symptoms, the blood study revealed almost identical levels. Urinalyses before treatment with Laetrile and four and one-half months later were reported as normal.

\textbf{Results:}

There was no change in the blood picture. Subjective relief was reported but no objective proof of benefit was found in the record.

\textbf{Impressions:}

Reviewer No. 1 - Record inadequate to support claim of "extended life 4\frac{1}{2} months."

Reviewer No. 2 - No evidence is presented to justify the conclusion that \(4\frac{1}{2}\) months of life was saved in this particular patient.

Reviewer No. 3 - Has stomach cancer and hepatic metastases. Here the doctors say the patient received 1 vial of Laetrile daily for thirty days and then 1 every three days intravenously for 4\frac{1}{2} months and the statement is: "After 15 days of Laetrile the patient could eat normally, sleep good, no pain nor vomiting. Symptoms recurred August, 1962. I should say Laetrile gave this man at least 4\frac{1}{2} months of life. Good effect on pain." Once again this is a totally inadequate record. Doesn't tell us anything objective according to standard CCNSC criteria. Doesn't even tell us how the diagnosis of stomach cancer with hepatic metastases were made. Only data is that from McNaughton Research Foundation.

Case No. 11, Mr. I.R., age 48, #2452

\textbf{Summary:}

There is no date of admission nor copies of pathologic reports in the record. Nevertheless it was stated that the patient had an acute anemia due to recent hemorrhage which required four transfusions; that he had a gastric carcinoma; and that he received one gram of Laetrile per day for six weeks for a total of about 45 grams.
Results:

It was stated that the patient gained seven pounds, that his reported pain abated, and that he was eating and sleeping well.

Impressions:

Reviewer No. 1 - Record totally inadequate to provide objective evidence of improvement from Laetrile.

Reviewer No. 2 - This probably is the same patient that is abstracted as E.R. (No. 10). The records are not adequate to be sure these are different patients. A letter would clarify this matter.

Reviewer No. 3 - Had a gastric epithelioma. Only record is that of McNaughton Foundation. "Patient receiving 1 gram daily I V for 6 weeks and drug to be continued. Therapeutic results: the patient was almost dying. He gained from 140 to 147 pounds with no pain as he had on October 12, 1962. Had transfusions twice a week. He had abatement effect on pain." Received 4 transfusions without results of improvement. Patient is still on Laetrile, October 24, 1962. Given twice a week. He is in the hospital walking around, eating and sleeping well. Considered a terminal hopeless case. "This man should be dead; Laetrile did help him."

Once again, a subjective evaluation only in the McNaughton files.

Case No. 12, Mrs. O.S., age 63 (no number)

Summary:

In 1959 this patient was hospitalized because of right-sided abdominal pain and a weight loss of about 16 pounds. Barium enema revealed a mass at the hepatic flexure of colon. On December 11, 1959 a laparotomy was performed which revealed an annular, constricting lesion of the hepatic flexure attached to stomach, duodenum and pancreas and infiltrating the pericolic fat but without evidence of lymph node invasion. A right hemicolectomy was performed which revealed a well-differentiated adenocarcinoma of colon.

In February, 1962, X-rays revealed a large ulcer of the stomach and on March 2 a malignant, unresectable ulcer of the stomach which had perforated into the third portion of the duodenum was seen at surgery. Only palliative surgery was performed. The pathologic examination revealed adenocarcinoma of gastric wall, probably metastatic.
In July, 1962 "due to weight loss, anemia and apparent progress of disease," Laetrile was started in a dosage of one gram three times per week and at the time of last entry into the record on October 19, 1962, approximately 40 grams had been given.

Blood study before Laetrile was started revealed a hemoglobin of 12.2 grams, red cells numbering 2.97 million, white cells 8,900, and after an undetermined amount of Laetrile therapy had been given, a hemoglobin of 11.4 grams, red cells numbering 3.9 million and white cells 3,500 were noted. Urinalyses before Laetrile was started and later were normal.

Results:

Blood study after Laetrile had been started revealed an increase of one million red cells with a coincident decrease of approximately one gram of hemoglobin. A note in the record on September 14, 1962 indicates a continuing weight loss and an episode of bloody diarrhea on August 18, 1962. There is no objective evidence of benefit from Laetrile.

Impressions:

Reviewer No. 1 - No objective evidence of therapeutic benefit.

Reviewer No. 2 - This patient had a slow growing but widespread tumor. If one takes the record at face value, the statement of improvement must be recognized, although further evaluation is certainly in order.

Reviewer No. 3 - December 11, 1959, this patient had a right hemicolectomy and an end-to-end anastamosis for an ulcerating, well differentiated adenocarcinoma of the hepatic flexure with infiltration into pericolic fat but without evidence of lymph node invasion. On April 14, 1962 the patient was operated and found to have carcinoma of the stomach with involvement of the pancreas and a sinus tract from the prepyloric area into the third portion of the duodenum. Following this operation she developed a gastric fistula which cleared up within three weeks and the patient returned home April 14, 1962 after having had the operation on March 2, 1962.

On July 12, 1962 she was started on Laetrile receiving 1 gram three times a week plus Vitamin B-15. It is stated that the medication seems to have had some beneficial effect, slowing down the progress of her illness, and in a report of September 14 he says there seems to be some arrest of her disease but she is still losing weight. No measurements! Nothing objective to follow. Again an inadequate chart.
Case No. 13, Mrs. C.T., age 33 (no number)

Summary:

This patient gave a history of tumefaction of left breast for two years. On physical examination at time of hospitalization there was fixation to muscle and a palpable axillary lymph node. X-rays of the 12th thoracic and the 1st and 2nd lumbar vertebrae were suggestive of possible metastases. On May 15, 1952 a bilateral oophorectomy and a breast biopsy were performed. The pathologic report revealed carcinoma simplex of breast. At an unstated time Laetrile in a dosage of one gram three times a week for 30 days was started and then changed to two grams per week for a total time of ten weeks and a total dosage of approximately 24 grams. In addition, once a week 200 mg. of Laetrile was injected directly into the breast.

On July 27, 1962 a blood study revealed a hemoglobin of 11.6 grams, a hematocrit of 42%, and a white cell count of 3,000. On October 17th the hemoglobin was 13.4 grams, the hematocrit again 42%, red cells 4.3 million, and white cells 8,700. Urinalyses were essentially normal.

Results:

The record contains claims largely of subjective improvement such as a better appetite, lessening of fatigue, weight gain of 10 pounds and a blood picture showing a three fold increase in white cells, but otherwise with very little change.

Impressions:

Reviewer No. 1 - No objective evidence of therapeutic benefit from Laetrile therapy.

Reviewer No. 2 - A review of this record would indicate that the response of the patient could very likely be due to the oophorectomy which was carried out in addition to the Laetrile administration. Review of the films and histologic sections would be in order before a definite opinion could be given.

Reviewer No. 3 - This is a 33-year-old-woman who had a biopsy apparently of the left breast and bilateral oophorectomy on May 20, 1962, with a statement that she left the hospital improved. Final diagnosis was called a simplex carcinoma left breast with osteolytic metastases to the vertebrae and cranium. She was started on Laetrile 3 vials a week per month, and 2 vials a week for a month and the drug was accompanied by 2 cc of Vitamin B-15 IM, although the Laetrile was given intravenously. The patient had no pain; as far as we can
tell the diagnosis of osteolytic metastases in the vertebrae and cranium had not been definitely established because the radiology report hedges and we do not have the X-rays. We cannot tell when the drug was started but it appears to be May 15 to October 1, 1962 which means that it was started at about the time of her oophorectomy so that one would not be able to distinguish if she did indeed have metastases which of these two modalities of treatment influenced her tumor. This is an inadequate record from several standpoints.

Case No. 14, Mr. R.S. (from North End Medical Center, Montreal)

Summary:

On March 3, 1963, an inguinal mass was biopsied and found to be metastatic adenocarcinoma. On March 13, a cystoscopy was performed and examination of tissue from bladder neck and prostate revealed adenocarcinoma of the latter organ. The patient was placed on 5 mg. of stilbestrol per day and arrived at Montreal for treatment with Laetrile on May 27, 1963. He was placed on Laetrile and received a total of 100 grams but concurrently he also received 50 mg. of Estradurin intramuscularly every two weeks. Blood studies were as follows:

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Urinalyses on two occasions were negative. X-rays of lumbosacral spine on July 12, 1963 were negative for metastases.

Results:

There was a weight gain of ten pounds, a blood picture which was essentially unchanged except for an initial fall and then a marked rise in acid phosphatase. It was reported that the abdominal mass became soft and freely movable.

Impressions:

Reviewer No. 1 - The diagnosis of infiltrating adenocarcinoma of the prostate is reported as having been confirmed, but no actual pathology report is provided.

There is insufficient documentation provided to permit evaluation of the effect of therapy with Laetrile and Panganic acid. Dates of therapy are not provided and there is no information as to whether or not stilbestrol was continued as therapy. The reported gain in weight might be explained
by several factors unrelated to administration of Laetrile or Pangamic acid. Reports of hemoglobin levels show no improvement and the blood acid phosphatase increased in level, presumably during the period of therapy.

The report presents no evidence of the therapeutic effectiveness of Laetrile and Pangamic acid.

Reviewer No. 3 - This patient had metastatic adenocarcinoma of prostate, received stilbestrol and estradiol. If this therapy was given concurrently with any new agent, the new agent cannot be evaluated. In this particular case there is no evidence of beneficial effect as yet from any therapy as documented in the records supplied us.

Section II

Review of Literature

The search of the literature revealed some twenty-five references dealing with the presence of beta-glucosidase in mammalian tissue. These references were mostly concerned with studies on the gastrointestinal system in lower animals and only one, reference 18, mentions cancer and here it is stated that there is intense glucosidase activity in the reticuloendothelial cells in sarcoma of the colon and some similar effect in RE sarcoma, of mice. The same authors noted variable activity, often high, in different normal RE cells.

Of the entire series of available articles, four mentioned human tissue but only one, reference 7, appears to be concerned exclusively with human tissue and this with uterine mucosa. Virtually all research effort to date has been restricted to animal studies especially with intestinal mucosa in which beta-glucosidases have been found rather regularly.
References


3. Conchie, J., and Mann, T.: Glycosidases in Mammalian Sperm and Seminal plasma. NATURE 179:1190-1191, 1957 (Ram, bull, boar, stallion, rabbit, dog and man)


Section III

A comparative study of the composition and biochemical behavior of Laetrile manufactured in the United States and that manufactured in Canada was made by investigators from the Pharmaceutical Chemistry Division, Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Ontario and the Research Laboratories, McGill University Surgical Clinic, Montreal General Hospital, Montreal, Quebec.

In the laboratory of the California State Department of Public Health, two varieties of Laetrile supplied by the manufacturers were examined. One of these purported to contain added di-isopropyl ammonium iodide and allegedly in limited use and distribution in the United States did in fact contain 2.5 percent inorganic iodine. This product on recrystallization from boiling acetone developed no crystals whereas the second variety as well as amygdalin did and both showed rather sharp melting points of 210-215° C. It is concluded that the iodine containing variety corresponds to the United States brand available to the Canadian group.

LAETRILE: A STUDY OF ITS PHYSICOCHEMICAL AND BIOCHEMICAL PROPERTIES*

Leo Levi, Ph.D. and W.N. French, Ph.D., Ottawa, **Ont.
I.J. Bickis, Ph.D. and I.J. D. Henderson, M.D., Montreal ***

ABSTRACT

A study was made of the composition and biochemical behaviour of the drug, Laetrile, distributed for clinical trial in the United States and Canada. It was established that the Canadian and the American product are different pharmaceutical formulations displaying different physicochemical and biochemical properties. The investigation demonstrated, furthermore, that neither preparation can be considered as a palliative in cancer therapy on the basis of the biological rationale advanced by their manufacturers.

** Pharmaceutical Chemistry Division, Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Ontario.
*** Research Laboratories, McGill University Surgical Clinic, Montreal General Hospital, Montreal, Quebec.
Laetrile, a drug manufactured and distributed until recently for clinical trial in Canada and the United States to determine its value as a palliative in cancer therapy, has been the subject of considerable controversy. Its fundamental biological rationale, according to proponents of the preparation, derives from the Unitarian or Trophoblastic Thesis of Cancer (UTC), announced in 1902 by John Beard of Edinburgh, Scotland. According to this thesis, "the wandering germ cells of early life can later be activated to divide and produce trophoblast cells which, outside the canalization of pregnancy, are the malignant cells. Since the pregnancy trophoblast begins to disappear about the time the fetal pancreas develops, he (John Beard) also suggested the use of pancreatic extracts for the treatment of human malignancy." Later, H.H. Beard, expanding these concepts, postulated that cancer is a chymotrypsin and nutrition deficiency disease, and that "pancreatic chymotrypsin prevents about 80 percent of civilization from ever developing malignancy, while in the other 20 percent, benign or malignant tumors will always arise unless prevented by adequate screening tests and chemotherapy."

As a chemotherapeutic cancerocidal agent, Laetrile -- containing a glucoside obtained from bitter almond or peach kernels, generally known as amygdalin -- was believed to release, in the presence of B-glucuronidase (an enzyme occurring in malignant neoplasms), sufficient amounts of hydrogen cyanide to stop tumor respiration and thus destroy cancerous tissue with some degree of specificity.

The object of this communication is to report a study concerning the composition and cytotoxic action of two formulations of this drug. For the purposes of this paper, one of these, manufactured in the United States, is referred to as Laetrile (U.S.) while the other, manufactured in Canada, is designated Laetrile (Can.) Both formulations were distributed under the same name, "Laetrile", and recommended for the same use, namely, palliative therapy in cancer.

Part I. Physicochemical Data

A. Laetrile Manufactured in the United States Appearance, Optical Rotation and pH

The product was an amorphous solid. It failed to exhibit a sharp melting point, sintering gradually from 170 to 183° C. Dissolved in distilled water it displayed an optical rotation of -39° (c = 1% w/v), and a pH of 6.8 (c = 10% w/v).

Spectral Analysis

In the ultraviolet absorption spectrum of the product maxima observed at 267, 261 and 256 μm were generated by the major component present - amygdalin - and strong absorption beyond 250 μm was found to be due to the occurrence of iodide ions in the formulation.

The infrared absorption spectrum of the product identified the major component of the formulation - amygdalin - and revealed admixture with additional constituents.
Chemical Analysis

Iodometric titration of the product with 0.02 N potassium iodate showed that it contained approximately 2.5% of iodide, and direct non-aqueous titration with 0.05 N perchloric acid established the presence of a basic component in equivalent concentration. In order to determine the identity of the basic moiety the drug was steam-distilled from alkaline solution into dilute hydrochloric acid. Purification of the isolate by fractional crystallization from acetone - ether yielded practically pure di-isopropylammonium chloride. Similar treatment of amygdalin resulted in the formation of ammonium chloride (90% yield).

Thus the product of laetrile hydrolysis represented a binary mixture composed of di-isopropyl-ammonium chloride and ammonium chloride which was separated by fractional crystallization from acetone-ether.

Thin-layer chromatography confirmed the spectrophotometric data and established, moreover, the presence of 8 ± 2% of sucrose (adsorbent-silica gel G Merck; solvent-methylene dichloride:methanol:formamide-160:38:2; spray reagent-vanillin (5%) in concentrated sulfuric acid).

B. Laetrile Manufactured in Canada

Appearance, Optical Rotation and pH

The product was a colourless liquid with a pH of 3.9. Diluted with distilled water it displayed an optical rotation of -42.1° (C = 10% w/v).

Spectral Analysis

In the ultraviolet absorption spectrum of the product, maxima observed at 267, 261 and 256 μm were due to the presence of amygdalin in the formulation. Absorbance ratios were, however, not identical to those of a genuine reference standard assayed similarly. It was found that the discrepancies were attributable to the presence of phenol, a compound exhibiting intense absorption throughout the 255-275 μm region.

The glucoside was isolated from the preparation following the removal of the phenol by ether extraction, evaporation of the aqueous phase and repeated crystallization of the residue from aqueous acetone.

Chemical Analysis

Examination of the product in accordance with the procedures described proved the absence of both iodides and of any volatile basic components.

Thin-layer chromatography and x-ray diffraction analyses confirmed these observations and established, furthermore, the absence of sucrose.

The experimental data assembled are summarized in Table I. They illustrate clearly that the two preparations are different pharmaceutical formulations.
TABLE I. Composition of Laetrile (U.S.) and Laetrile (Can.)

<table>
<thead>
<tr>
<th>Physical criteria and composition</th>
<th>Laetrile (U.S.)</th>
<th>Laetrile (Can.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Label identification</td>
<td>A B-Cyanogenetic glucoside</td>
<td>A B-Cyanogenetic glucoside</td>
</tr>
<tr>
<td>Appearance</td>
<td>Amorphous solid</td>
<td>Colourless solution</td>
</tr>
<tr>
<td>Optical rotation</td>
<td>-39.0°</td>
<td>-42.0°</td>
</tr>
<tr>
<td>pH (10% in H2O)</td>
<td>6.8</td>
<td>3.9</td>
</tr>
<tr>
<td>Amygdalin</td>
<td>87 ± 2%</td>
<td>98 ± 2%</td>
</tr>
<tr>
<td>Di-isopropylammonium iodide</td>
<td>5%</td>
<td>Absent</td>
</tr>
<tr>
<td>Phenol</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Sucrose</td>
<td>8 ± 2%</td>
<td>Absent</td>
</tr>
<tr>
<td>l-Mandelonitrile-B-glucuronoside</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Mandelonitrile-glucuronoside</td>
<td>di-isopropylammonium salt*</td>
<td>Absent</td>
</tr>
</tbody>
</table>

*Literature distributed by manufacturer.

Part II. Biochemical Data

The compositional differences determined for Laetrile manufactured in the United States and Canada, respectively, were reflected in marked biochemical differences observed when evaluating both drugs as potential anti-cancer agents.

Experimental Method

The method, based principally upon incubation of surviving tumour tissue (slices or cell suspensions) in Warburg manometric vessels in the presence of radioactive tracers (amino acids, purines), has been previously described. During the incubation period (two hours), the tumour respiration (+ glucose) and glycolysis were measured. After incubation the tissue material was separated into protein, ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) fractions, and the incorporation of tracers -- indicating the rates of respective syntheses -- was assayed. The effects of drugs on these metabolic parameters were then assessed in comparison with control values, obtained with the same tumour material in the absence of drugs.

Results

The results obtained with the two preparations (Laetrile (U.S.) and Laetrile (Can.)) and with sodium cyanide (NaCN) are summarized in Tables II and III, respectively.

Table II shows the observed effects on tumour energy and metabolism, i.e. on respiration in the presence and absence of glucose, and on aerobic and anaerobic glycolysis. As can be seen, neither of the Laetriles at 1mM concentration had any significant effect on these parameters, whether in primary human tumours or in Ehrlich ascites carcinoma cells. NaCN, however, at much lower concentration (0.1mM.) (Table II, Expt. 6 and 7), almost completely
inhibited respiration of a human adenocarcinoma of the colon and of Novikov ascites hepatoma. NaCN also stimulated the aerobic glycolysis of both tumours to almost anaerobic levels.

TABLE II. - Effects of Laetriles and NaCN on Energy Metabolism of Primary Human Tumours and Animal Ascites Tumours in Vitro

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>Neoplasm and drugs added</th>
<th>( Q_02 ) (-G)</th>
<th>( Q_02 ) (+G)</th>
<th>( Q_2 )</th>
<th>( H_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Adenocarcinoma of breast (human)</td>
<td>0.6</td>
<td>0.6</td>
<td>1.3</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (U.S.) 4 mM</td>
<td>0.6</td>
<td>0.5</td>
<td>1.2</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (Can.) 4 mM</td>
<td>0.4</td>
<td>0.3</td>
<td>1.4</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>Astrocytoma (human)</td>
<td>2.6</td>
<td>2.6</td>
<td>1.0</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (U.S.) 4 mM</td>
<td>2.8</td>
<td>2.3</td>
<td>1.1</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (Can.) 4 mM</td>
<td>2.8</td>
<td>2.3</td>
<td>1.1</td>
<td>4.4</td>
</tr>
<tr>
<td>3</td>
<td>Metastases of bronchogenic carcinoma (human)</td>
<td>2.9</td>
<td>2.8</td>
<td>1.8</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (U.S.) 4 mM</td>
<td>2.5</td>
<td>2.6</td>
<td>1.8</td>
<td>3.4</td>
</tr>
<tr>
<td>4</td>
<td>Ehrlich ascites carcinoma</td>
<td>9.8</td>
<td>7.2</td>
<td>16.7</td>
<td>44.0</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (Can.) 4 mM</td>
<td>9.8</td>
<td>6.5</td>
<td>20.0</td>
<td>45.3</td>
</tr>
<tr>
<td></td>
<td>+benzaldehyde 0.1 mM</td>
<td>9.7</td>
<td>6.3</td>
<td>17.5</td>
<td>46.3</td>
</tr>
<tr>
<td>5</td>
<td>Ehrlich ascites carcinoma.</td>
<td>---</td>
<td>---</td>
<td>17.2</td>
<td>44.5</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (U.S.) 4 mM</td>
<td>---</td>
<td>---</td>
<td>18.5</td>
<td>42.2</td>
</tr>
<tr>
<td></td>
<td>+Laetrile (Can.) 4 mM</td>
<td>---</td>
<td>---</td>
<td>22.3</td>
<td>40.7</td>
</tr>
<tr>
<td></td>
<td>+phenol 0.01%</td>
<td>---</td>
<td>---</td>
<td>22.3</td>
<td>42.6</td>
</tr>
<tr>
<td>6</td>
<td>Adenocarcinoma of colon (human)</td>
<td>2.2</td>
<td>2.6</td>
<td>5.5</td>
<td>8.6</td>
</tr>
<tr>
<td></td>
<td>+NaCN 0.1 mM</td>
<td>0.2</td>
<td>---</td>
<td>7.3</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>+5-flourouracil 4 mM</td>
<td>---</td>
<td>---</td>
<td>4.8</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>+methotrexate 0.1 mM</td>
<td>---</td>
<td>---</td>
<td>5.3</td>
<td>---</td>
</tr>
<tr>
<td>7</td>
<td>Novikoff ascites hepatoma</td>
<td>10.5</td>
<td>6.7</td>
<td>29.8</td>
<td>59.3</td>
</tr>
<tr>
<td></td>
<td>+NaCN 0.1 mM</td>
<td>1.3</td>
<td>0.5</td>
<td>43.5</td>
<td>55.0</td>
</tr>
</tbody>
</table>

-23-
TABLE III. - Effects of Laetriles and NaCN on Protein and Nucleic Acid Synthesis in Primary Human Tumours and Animal Ascites Tumours in vitro

L-leucine-1-C\(^{14}\) 2mM.; 2x10\(^5\) c./min./vessel; Adenine-8-C\(^{14}\) 0.1mM.; 6x10\(^5\) c./min./vessel

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>Neoplasm and drugs added</th>
<th>In oxygen (-glucose)</th>
<th>In oxygen (+glucose)</th>
<th>In nitrogen (+glucose)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prot.</td>
<td>RNA</td>
<td>DNA</td>
<td>Prot.</td>
</tr>
<tr>
<td>1.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma of breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Laetrile (U.S.) 4mM.</td>
<td>14</td>
<td>17</td>
<td>1.1</td>
<td>14</td>
</tr>
<tr>
<td>+Laetrile (Can.) 4mM.</td>
<td>11</td>
<td>16</td>
<td>1.1</td>
<td>16</td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Astrocytoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Laetrile (U.S.) 4mM.</td>
<td>4</td>
<td>17</td>
<td>1.4</td>
<td>5</td>
</tr>
<tr>
<td>+Laetrile (Can.) 4mM.</td>
<td>5</td>
<td>15</td>
<td>1.7</td>
<td>5</td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastases of bronchogenic carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Laetrile (U.S.) 4mM.</td>
<td>23</td>
<td>34</td>
<td>2.9</td>
<td>85</td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ehrlich ascites carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Laetrile (Can.) 4mM.</td>
<td>208</td>
<td>412</td>
<td>39</td>
<td>352</td>
</tr>
<tr>
<td>+benzaldehyde 0.4mM.</td>
<td>171</td>
<td>369</td>
<td>27</td>
<td>338</td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ehrlich ascites carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+Laetrile (U.S.) 4mM.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>277</td>
</tr>
<tr>
<td>+Laetrile (Can.) 4mM.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>249</td>
</tr>
<tr>
<td>+phenol 0.01%</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>217</td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma of colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+NaCN 0.1mM.</td>
<td>47</td>
<td>113</td>
<td>14</td>
<td>87</td>
</tr>
<tr>
<td>+5-flurouracil 4mM.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>68</td>
</tr>
<tr>
<td>+methotrexate 0.1mM.</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>60</td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novikoff ascites hepatoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+NaCN 0.1mM.</td>
<td>374</td>
<td>405</td>
<td>34</td>
<td>481</td>
</tr>
</tbody>
</table>
Table III shows the drug effects on protein, RNA and DNA synthesis as measured by L-leucine-\(^1^4\)C and adenine-\(^2^\)H incorporation into respective fractions. Again, except for inhibition of DNA synthesis by Laetrile (Can.), no significant inhibition could be observed either in human or animal tumors. On the other hand, NaCN, aerobically in the absence of glucose, inhibited almost completely all three syntheses, both in human and in animal tumors. Such inhibition, however, was almost absent, aerobically and anaerobically, when NaCN was added to vessels containing glucose. Apparently the NaCN effect on respiration was compensated by the increase in aerobic glycolysis as recorded in Table II.

The specific effects of Laetrile (Can.) on DNA syntheses could not be correlated with known effects of HCN. For explanation the effects of benzaldehyde (possibly released from amygdalin on hydrolysis) and phenol (present in 0.5% concentration in Laetrile (Can.)), were investigated. As can be seen from experiments 4 and 5 in Tables II and III, benzaldehyde was without any effect, while phenol, in equivalent concentration, brought about exactly the same inhibition of DNA synthesis as did Laetrile (Can.) itself.

DISCUSSION AND CONCLUSIONS:

The experimental data obtained indicate that Laetrile had no significant effect on cancer cells from primary human tumors or from animal ascites during two-hour incubation in physiological media. The 1 mM concentration used in the experiments may have caused in some tumors, in the absence of glucose, a small non-specific (possibly osmotic) effect which is, however, in no way comparable to that obtained with only 0.1 mM NaCN. The somewhat stronger effects observed with Laetrile (Can.), especially on DNA synthesis, can be fully explained by the toxic effects of phenol added to this preparation. The results obtained with NaCN agree well with observations already reported, which have shown that cyanide is not cancerocidal as long as glucose is available. Therefore, even if Laetrile were hydrolysed along the lines claimed by its manufacturers, the biological evidence indicates that it would be ineffective as an anticancer agent, by virtue of cyanide release.

This study has demonstrated how compositional variations of a pharmaceutical formulation - considered to be minor ones by the manufacturer - brought about a dosage form displaying entirely different sets of biochemical characteristics. This phenomenon is known and recognized by some segments of the industry, but its importance remains to be more fully appreciated by the industry at large. From the data obtained neither product can be considered as a palliative in cancer therapy on the basis of the biological rationale advanced by the manufacturers.

The authors are indebted to Dr. L. I. Pugsley, Dr. E. Napke and Dr. J. B. Murphy of the Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Ont., for valuable discussions during the course of this study.

REFERENCES

SUMMARY AND CONCLUSIONS

The report of the committee which examined the clinical records, the comments of Dr. Paul L. Kirk, Professor of Chemistry and Criminalistics at the University of California at Berkeley regarding the papers found in the search of the literature and the paper by the Canadian investigators were reviewed by the entire Cancer Advisory Council and the following conclusions were reached.

These 14 records provided by the McNaughton Foundation were examined and fail to indicate that the patients treated with Laetrile secured either palliation or regression of their cancerous affliction as a consequence of the therapy. In several instances there is absolutely no evidence presented as to the response of the patient to the therapy and in other instances objective evidence which documents claims of benefit is not provided. It is concluded from careful review of these records that they are inadequate as reports of therapeutic use of Laetrile, and that they do not indicate that therapeutic benefit resulted from treatment with Laetrile, and do not indicate that this agent is of value in the treatment, cure, or palliation of cancer. In only one instance is there a statement by the examining physician indicating that a definite beneficial effect from Laetrile might have occurred.

The implications of literature research on glucosidase in mammalian tissue as it relates to the use of Laetrile (or amygdalin) in the treatment of cancer, are totally negative and totally inadequate for basing a theory of cancer treatment and there is currently no indication from any of the articles of any real likelihood of such information being found. There is little, if any indication, as regards glucosidase, that cancer tissues either in man or in animals have any significant difference from normal.
tissue and it must be accepted that if the glucosidase can split crydalgin in cancerous tissue, it also would do it in normal tissue and it would appear presumptuous to assume any significant differential concentration that would give any degree of specificity to a glucosidase in the treatment of cancer.

The paper of Levi, French, Dickis and Henderson appears to dispose of the clinical mechanism by which Laetrile is purported to influence cancer tissue. Because the paper reports controlled experiments with known components, the data could be rigorously interpreted in contrast to the situation generally prevailing in clinical trials. The techniques used, both for analysis of product and tests with tissue, are all standard accepted procedures of the biochemist and appear to have been applied properly throughout. Release of HCN by tumor β-glucuronidase, as postulated by its proponents is not the actual route of hydrolysis of Laetrile.

The additional material examined in no way alters the Council's conclusion in the original report.

Date: April 13, 1966

Joseph F. Ross, M.D., Chairman
Cancer Advisory Council