

Does Laetrile Work? Another Look at the Mayo Clinic Study (Moertel et al., 1982).

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Abstract

Moertel et. al. (1992) studied the impact of laetrile on 172 cancer patients and concluded that it had no effect. The study used a mixture of natural and synthetic laetrile that laetrile experts consider to be minimally or not effective, followed an inflexible schedule of administration of laetrile injections, and involved patients "for which no standard treatment was known to be curative or to extend life expectancy." The study is informative, but the results do not support Moertel et. al.'s conclusion that further investigation or use of laetrile is not justified.

Despite the widespread belief that Laetrile is ineffective against cancer, there have been only two large-scale clinical studies. I commented on the first study,^{1,2} arguing that descriptions of this study in the professional literature give an overly pessimistic view of the efficacy of Laetrile. In the second clinical study, done at the Mayo clinic, Moertel et. al. studied 172 cancer patients "in good general condition" treated with Laetrile and an accompanying diet, and concluded that Laetrile had no effect. They concluded with the recommendation that "further investigation or clinical use of such therapy is not justified (p. 205)."³

The Mayo study has been widely cited and is considered by many to be definitive. When it appeared, Time Magazine ran an article with the title "Laetrile flunks" with the subtitle "Test shows cancer quackery."⁴ The typical response of the profession is an article in the CA-A Cancer Journal for Physicians, "Unproven methods of cancer management," which proclaimed that the Mayo study "showed unequivocally that Laetrile is ineffective for cancer therapy" (p. 190).⁵

Laetrile supporters, however, have been vocal critics of the Mayo study. Soon after the study appeared, several letters to the editor commenting on Moertel et. al. appeared in the New England Journal of Medicine, and Charles Moertel, the first author of the Mayo study, responded, dealing with some of the criticisms but ignoring others, as we will see below.

My commentary will deal with the following points, expanding on remarks made by critics of the Mayo study.

1. The kind of Laetrile used.
2. The way the Laetrile was administered.
3. The use of terminal patients.
4. The interpretation of the results.

WHAT KIND OF LAETRILE?

In his letter to the editor of the New England Journal of Medicine, Culbert notes that the Mayo study did not use pure amygdalin but a "degraded or decomposed form of it (the putative 'RS-epimer racemic mixture')." ⁶

The RS epimer racemic mixture is a mixture of natural amygdalin (R-amygdalin) and an isomer, an artificial form (referred to as the S-isomer, or isoamygdalin). Krebs strongly argues against the use of this kind of amygdalin, and maintains that this mixture is less than half as effective as the pure form (see the Appendix below for suggestive evidence that the Mayo mixture might have been even weaker). Krebs, in fact, points out that the mixture "caused unpredictable, often severe, reactions in our patients" and that "all of our successful therapeutic studies were conducted using only pure natural amygdalin" (p. 279). He even speculates that the mixture might be "carcinogenic or promote metastasis" (p. 298).⁷

A number of other practitioners advise the use of "pure" amygdalin,⁸ but the meaning of the word "pure" is unclear: Moertel et. al. also refer to the mixture they used as "pure

amygdalin” (p. 202).

Moertel et. al.³ defended the use of the mixture because it is the same as that provided “by a major Mexican manufacturer” citing an analysis done by Jee, Pont, Cheung, and Lim⁹ of samples of Laetrile supplied by the National Cancer Institute. The samples Jee et. al. analyzed had been seized by US Customs as they were being transported illegally in the United States and were labeled as originating from Cyto Pharma de Mexico. According to its website, Cyto Pharma “was the first company to receive a license (under the direct supervision of Dr. Krebs which included his formula, process, technology and control methods) to produce Amigdalina (Amygdalin) ...”¹⁰

This is a strange, considering Krebs' strong disapproval of the mixture which Jee et. al. reported finding in containers with Cyto Pharma's marking.

The samples of injectable Laetrile Jee et. al. analyzed were indeed mixtures of natural and synthetic Laetrile but it is not clear that this was the kind of Laetrile used in studies of success reported in the professional literature. Clearly it would have been preferable if the Mayo researchers had contacted physicians who claimed success with Laetrile and had obtained “pure” Laetrile from them.

ADMINISTRATION OF LAETRILE: DOSE AND DURATION

Mayo researchers³ claimed that the dose of laetrile given was sufficient, actually in excess of that provided to patients by Laetrile supporters, a total of approximately 150 grams by injection, which was followed with oral Laetrile (.5 g three times per day).

The Mayo study used “a daily dose of 4.5 g per square meter of body-surface area” for 21 days.³ Using the Body Surface Area Calculator for medication doses (<http://www.halls.md/body-surface-area/bsa.htm>), this would mean that a 45 year old man 5' 9” weighing 175 pounds would get an injection of just under 9 grams per day, and a total dose of about 180 grams. A 45 year old 5' 4” woman weighing 140 pounds would receive a daily dose of about 7.5 grams, or a little under 160 grams in total.

This dose of injected Laetrile appears to be more than sufficient and is consistent with previous practice: Krebs and Bouziane¹¹ gave their 12 patients from 34 to 235 grams. Marrone¹² reported an average total dosage of 46.2 grams (range 9 to 133). Binzel¹³ generally administered a total of

about 177 grams. Rodriguez, Pulido and Prince¹⁴ administered between 54 to 72 grams. In all cases, oral Laetrile was also given, sometimes during the injection sequence, and always after.

VARIABLE DURATION OF INJECTIONS

There is, however, an important difference. In the Mayo study, Laetrile injections were given for three weeks, and then stopped, and oral Laetrile alone was used instead. The usual practice by Laetrile practitioners, however, is not to stop injections automatically after a given length of time: Rather, injections were continued until it appeared that the cancer was under control, and only then was oral Laetrile given for maintenance. The duration of treatment with injections in these studies varied according to the progress of the cancer. Moertel et. al., in contrast, mechanically switched from injection to oral Laetrile after three weeks.

Navarro¹⁵ writes that “Laetrile therapy may be discontinued after the Beard Anthrone test has become negative,” and makes it clear that Laetrile is administered by injection (p. 166). The average duration of treatment in Marrone¹² was 17.5 weeks, with some patients receiving injections for four to ten months (cases 6,7 and 8). Rodriguez et. al.¹⁴ note that in patients “with severe persistence in the symptomology or recurrence” injections continued one to three days per week “until palliation was achieved or the treatment was considered to have failed” (p. 4, chart 1).

This procedure was also reported in several case histories: Helen Curran reports that her doctor gave her intramuscular injections of laetrile every day until her cancer was in remission (p. 68).¹⁶ Similarly, in the case of Joanne Wilkinson (in Griffen, p. 120), injections (3 grams) were continued three times per week for six months.¹⁷

In addition, some practitioners continued Laetrile far longer than the Mayo clinics' 21 days as a general procedure: Krebs and Bouziane¹¹ kept all patients on a maintenance dose of 1 to 2 gram injections per week after “the base 30 grams” (p. 192). Richardson and Griffen¹⁸ administered daily injections of 6-9 grams for 20 days, then three times per week for a month, twice a week for another month, and once a week for a year or longer (see p. 116), supplemented with oral Laetrile.

Laetrile practitioners also start using injections again if the cancer returned.

Binzel's Case 6¹³ was put back on Laetrile injections

because “she did not feel as well as she did while on them. She went back on some injections for a few months, and she felt much better” (p. 116) and then returned to taking only oral Laetrile. Binzel’s Case 10 had been on tablets for two years, “without any problems” along with a nutritional program.” When the cancer returned years later, “She went back on her nutritional program again, except this time I added a series of intravenous Laetrile injections” (p. 118). Navarro¹⁹ had stopped all therapy in one patient for two months (case B) but resumed injections when the Beard Anthrone test showed cancer was still present. Also, as noted earlier Rodriguez et. al.¹⁴ used injections in cases of recurrence.

In contrast, Mayo researchers³ continued treatment until “definite evidence of progressive malignant disease or until severe clinical deterioration precluded further treatment and observation” (p. 202). In such cases, Laetrile practitioners would have presumably continued injections or would have returned to injections had they been stopped.

USE OF TERMINAL PATIENTS

The Mayo study³ only included patients who were considered to be terminal, “for which no standard treatment was known to be curative or to extend life expectancy” (p. 201). As Bross²⁰ notes, these were patients who were not expected to benefit from any orthodox therapy. Bross concludes that “all that has been learned from the Laetrile study is that there is a class of patients whom no treatment – orthodox therapy or Laetrile – can help. This really tells us very little” (p. 118).

In response to Bross, Moertel²¹ claims that although the patients were terminal they were in “very good clinical condition” (116 were considered 0 or 1 on the ECOG performance scale and 48 were classified as 2 or 3. None were rated 4 (completely disabled) or 5 (dead)) and Moertel does not discuss whether the use of terminally ill patients affected the validity of the study.

Physicians who have published case histories on the use of Laetrile have pointed out that Laetrile is of no or very limited use in terminal cases. Binzel (1994),¹³ in fact, notes that he did not include terminal cases in his analysis for this reason.

THE INTERPRETATION OF RESULTS

In the Mayo study,³ cancer had progressed in 46% of the patients in the first month, in 79% after two months, and in 90% after three months, which Mayo researchers interpret as

showing that the treatment was not successful.

Researchers have interpreted non-progression of tumors as both supportive and non-supportive of therapy.² In his letter to the *New England Journal of Medicine*, Culbert⁶ argued that this data could be interpreted as showing that the treatment did indeed have a positive effect, emphasizing the finding that in 46% of the patients, cancer had not progressed during the first month, which could have been because of the treatment, even though the Laetrile used was impure (see above). The cessation of the injections and automatic switch to tablets after three weeks could have played a role in the increase in cases showing progression.

“... the patients’ responses within the first three weeks of treatment (when most patients were on the 21-day injectable part of the program) indicate at least some fleeing antineoplastic action, even from the degraded product. Indeed, by any of the various semantic renderings of the results of the first three weeks of therapy, either a majority of patients or a sizable minority (46 per cent) had no signs of progressive disease during this part of the program ... would it not have been wise to continue giving injections and to make a real effort at a real metabolic program in these incurable patients” (p. 119)

Moertel²¹ responded to other criticisms but did not respond to this one, deeming it unworthy of comment.

CONCLUSIONS

The Moertel et. al. study³ teaches us a great deal: It shows that using a mixture of pure and synthetic Laetrile on a rigid schedule with terminal patients does not work. It does not address the impact of pure Laetrile with a more flexible schedule with other patients, or as a preventative. The study thus contains only one serious error: It concludes that its results show that “further investigation or clinical use of such therapy is not justified” (p. 205). This is clearly not the case.

APPENDIX: JAMES CASON AND LAETRILE

In his autobiography, James Cason²⁰ relates that he “personally inspected” an analysis of the amygdalin used in the Mayo study. The analysis was provided by Robert Bradford. Bradford had originally requested a sample of the actual amygdalin used in the Mayo study, and his request was refused by the Food and Drug Administration, according to Cason. Bradford “then demanded the specifications for the material to be used, under the Freedom of Information Act, so FDA sent technical data, including the infrared

spectrum” (Cason, p. 367). According to Cason:

“The amygdalin (Laetrile) used for these tests actually could not have contained more than 15% amygdalin, since its infrared spectrum (supplied by the FDA) showed no detectable absorption at about 4.4 μ , the position of absorption by the nitrile group. Ergo, there is no evidence that the 'amygdalin' used for the tests contained any amygdalin. An authentic sample of amygdalin shows absorption at this wavelength, as it must” (p. 367).

James Cason was a professor of Chemistry at the University of California at Berkeley from 1945 to 1983. He died in 2001 at age 91. To my knowledge, his observations about the amygdalin used in the Mayo study were not published in a professional journal.

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