CC/NUMBER 31
JULY 30, 1984

This Week's Citation Classic™

Bluming A Z, Vogel C L, Ziegler J L, Mody N & Kamya G. Immunological effects of BCG in malignant melanoma: two modes of administration compared. *Ann. Intern. Med.* 76:405-11, 1972.
[Solid Tumor Ctr., Uganda Cancer Inst., and Dept. Surg., Makerere Univ. Med. Sch., Kampala, Uganda]

Two modes of administering BCG were compared for effects on immunologic reactivity and survival of malignant melanoma patients following surgical excision of clinically apparent tumor and regional lymph nodes. A nonspecific potentiating effect on cellular reactivity to both primary and recall antigens was observed in the group treated by dermal scarification. No such effect was noted in the group treated by intradermal vaccination. Significantly longer remissions were observed in the former group. [The *SCI*® indicates that this paper has been cited in over 180 publications since 1972.]

Avrum Z. Bluming
Hematology-Oncology Medical Group
of the San Fernando Valley
16311 Ventura Boulevard
Encino, CA 91436

June 28, 1984

"He was a dignified, tall, well-muscled man. Traces of gray were visible in his tightly curled, thick, black hair. Several weeks earlier, a melanoma had been widely excised from the sole of his right foot, and the light pink color around the healing lymphadenectomy incision in his right groin stood out sharply against his black skin. He was sitting in an aluminum roofed clinic in his native Uganda while ritual scarring was applied to his right upper arm in an attempt to ward off the return of the devil illness called cancer. But the healer performing the ritual was a graduate of Columbia University's College of Physicians & Surgeons sent to Uganda by the National Cancer Institute to study tumors like his, and Pasteur Institute BCG was being applied to the 5 x 5 cm grid I had raked onto his upper arm.

"In 1969, Mathé[1] reported significantly increased remission duration in ALL patients treated with Pasteur Institute BCG, applied by dermal scratching following remission induction. In 1970, Hamilton Fairley[2] reported no such benefit when Glaxo BCG was used and applied by intradermal inoculation. In order to establish a standard BCG immunotherapy regimen, Chuck Vogel, John Ziegler, and I set up a study to document the proposed nonspecific immunopotentiating effect of BCG on humoral and cellular immunity in man. Using a battery of immunologic tests, we hoped to identify the most effective BCG preparation and route of administration to be used in subsequent clinical immunotherapy trials.

"Junctional nevi are frequently found on the soles of black Ugandans with a pattern of distribution remarkably consistent among the members of each tribe. Melanomas developed commonly on the soles of this largely barefoot population in a distribution reflecting the distribution of the junctional nevi. Earlier published studies had suggested that melanoma was an immunogenic tumor and that an immune reaction to the tumor correlated with a favorable prognosis. We therefore elected to study this available patient population. Informed consent, obtained from each patient, usually required prolonged discussions in Luganda, Lango, Toro, Bunyoro, or Swahili explaining why this study, remarkably similar in outward appearance to traditional medicine man ministrations, was imported from the US.

"We were able to show: 1) a nonspecific potentiating effect on cell-mediated immunity to both primary and recall antigens in the group treated with Pasteur Institute BCG; 2) a correlation between dose of administered BCG and immune potentiation; and 3) a significant prolongation of remission duration associated with the higher dose (Pasteur Institute) BCG administered by dermal scarification. This initial result was confirmed in a follow-up report published four years later.[3]

"Our attempts to 1) provide an immunologic parameter by which the potency of nonspecific immunotherapy could be assayed, and 2) define a standard preparation and application of BCG in this setting are probably responsible for the frequent references to this article.

"Although nonspecific immunotherapy may benefit a subset of melanoma patients in remission, subsequent large-scale studies have failed to confirm a reproducibly meaningful, beneficial effect."[4]

1. **Mathé G, Amiel J L, Schwarzenberg L, Schneider M, Cattan A, Schlumberger J R, Hayat M & de Vassal F.** Active immunotherapy for acute lymphoblastic leukaemia. *Lancet* 1:697-9, 1969. (Cited 610 times.)
2. **Hamilton Fairley G.** Immunotherapy of acute lymphoblastic leukemia. (Abstract.) *Abstracts of the XIII International Congress of Hematology, Munich, 2-8 August 1970.* Munich: Lehmann, 1970. p. 278.
3. **Bluming A Z.** Immunotherapy of cancer. (Homburger F, ed.) *The physiopathology of cancer, volume 2. Diagnosis, treatment, prevention.* Basel: Karger, 1976. p. 251-78.
4. **Veronesi U, Adamus J, Aubert C, Bajetta E, Beretta G, Bonadonna G, Bufalino R, Caschelli N, Cocconi G, Durand J, De Marsillac J, Ikonopisov R L, Kiss B, Lejeune F, MacKie R, Madej G, Mulder H, Mechl Z, Milton G W, Morabito A, Peter H, Priario J, Paul E, Rumke P, Sertoli R & Tomin R.** A randomized trial of adjuvant chemotherapy and immunotherapy in cutaneous melanoma. *N. Engl. J. Med.* 307:913-16, 1982.

